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Original Research Paper

FORMULATION AND OPTIMIZATION OF IMMEDIATE RELEASE VILDAGLIPTIN TABLETS BY FULL FACTORIAL DESIGN AND ITS IN-VITRO DRUG RELEASE STUDY.

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Abstract:

The conventional dosage forms some time fails to maintain postprandial blood sugar level. Therefore, modified drug delivery is used for overcoming these issues. The present research work is aimed at the formulation and development of an immediate-release tablet for treating Diabetes mellitus by QbD approach. 3^2 full factorial design was used for developing IR tablet. In, full factorial design two independent and two dependent variables were selected. The concentration of the superdisintegrant, sodium starch glycolate, and the binder, microcrystalline cellulose, was optimized to achieve desirable formulation characteristics. The selected quantities of these excipients were incorporated to enhance tablet disintegration, improve mechanical strength, and maintain the required drug release profile of the immediate-release dosage form. These two independent variables while two dependent variables or responses were considered. i.e., disintegration time and % of drug release at 45 min. According to selected design, 9 batches developed formulations were subjected to comprehensive evaluation of pre-compression parameters, particularly powder flow characteristics, to confirm the suitability and processability of the formulation blend for tablet production. The fabricated tablets were further assessed for critical post-compression quality attributes, including thickness, hardness, friability, weight uniformity, disintegration time, and in-vitro dissolution behaviour. Furthermore, the effect of formulation variables on the selected response parameters was investigated through response surface methodology, and the corresponding response surface plots were generated to demonstrate the relationship between independent variables and formulation performance. Percent drug release at 45 min. increases with increasing superdisintegrant concentration and decreasing binder concentration while disintegration time decreases with decreasing binder concentration and increasing superdisintegrant concentration. The prepared tablet met the requirements of immediate release tablet. From the above study, it can be concluded that, developed immediate-release vildagliptin tablets maintain the blood glucose level in type-II DM patients and provides a high degree of patient compliance.

Keywords: Diabetes Mellitus, QbD, superdisintegrant, binder etc.

Introduction:

Oral administration represents one of the most widely utilized and preferred routes for drug delivery, enabling both local and systemic therapeutic effects. This route is extensively employed due to its ease of administration, patient acceptability, and overall effectiveness in achieving desired pharmacological outcomes.[1] Oral medication is one of the most popular method of drug administration and the reason behind its benefits i.e., patient comfort, oral drug administration, cost-effectiveness as well as simplicity of the large-scale manufacturing of oral dosage forms is extensively practiced in the pharmaceutical industry due to their convenience, stability, and patient acceptability. The oral route remains the predominant pathway for drug

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administration, accounting for a significant proportion of commercially available small-molecule therapeutic agents, with approximately 60% of approved medicinal products being delivered through this route.[2]

Various solid pharmaceutical dosage forms are administered through the oral route, including tablets, powders, capsules, and cachets. A compacted solid dosage form, known as a tablet, typically contains medications, either with or without an excipient.[3] Tablets are the most often recommended dosage form because they are easy to use, offer dosage homogeneity from tablet to tablet, are stable over long periods of time and under various storage circumstances, and can be made using high-speed compression, labelling, and packing equipment. Technology has advanced to improve acceptance and bioavailability, and the typical compressed tablet has been modified.[4] Two types of tablets are present in the market i.e., IR and SR. In Immediate Release tablets without any specific rate-controlling mechanisms, immediate-release tablets are formulated to rapidly disintegrate, dissolve, and release the incorporated drug substance after administration, thereby facilitating prompt drug availability and achieving the desired therapeutic effect. While in Sustained Release tablets long-lasting dose form a well-characterized, reproducible dosage form known as a sustained release dosage form, controls the drug release profile at a predetermined pace to obtain the appropriate concentration of the drug substance present in the systemic circulation (blood plasma) or at the intended site of action plays a crucial role in determining the therapeutic efficacy and pharmacological response of the formulation.[5]

Diabetes mellitus is a heterogeneous group of chronic metabolic disorders characterized by persistent elevation of blood glucose levels (hyperglycemia).[6,7] This condition occurs due to impaired insulin secretion from pancreatic β-cells, reduced insulin action, or a combination of both factors, resulting in inadequate regulation of glucose metabolism. The prolonged increase in blood glucose concentration may lead to characteristic clinical manifestations, including polydipsia (excessive thirst), polyphagia (increased appetite), and polyuria (frequent urination). Diabetes mellitus is primarily classified into three major categories:[7] Type I diabetes mellitus (insulin-dependent diabetes mellitus), Type II diabetes mellitus (non-insulin-dependent diabetes mellitus), and gestational diabetes mellitus, which develops during pregnancy.

Glucose homeostasis in the human body is regulated by a complex interplay of multiple hormones, among which insulin and glucagon are considered the principal regulators. Following an increase in blood glucose concentration, pancreatic β-cells respond by releasing insulin, which promotes the maintenance of normal glycemic levels. Insulin lowers blood glucose by suppressing hepatic glucose production through inhibition of glycogenolysis and gluconeogenesis, while simultaneously enhancing glucose uptake and utilization by peripheral tissues, including the liver, skeletal muscle, and adipose tissue. In addition to insulin and glucagon, other regulatory peptides such as glucagon-like peptide-1 (GLP-1), amylin, and glucose-dependent insulinotropic polypeptide (GIP) contribute significantly to the modulation of glucose metabolism and maintenance of physiological glucose balance.[8]

For treating Diabetes Mellitus oral hypoglycemic agents are used such as Sulfonylureas, Biguanides, Meglitinides, Thiazolidinediones, Dipeptidyl peptidase-4 (DPP4) inhibitor, Various classes of oral antidiabetic agents, including alpha-glucosidase inhibitors and sodium-glucose co-transporter-2 (SGLT2) inhibitors, are currently used in the management of type 2 diabetes mellitus. The increasing global prevalence of type 2 diabetes has become a major health concern due to the associated risk of severe microvascular and macrovascular complications. Therefore, effective therapeutic strategies focus on achieving optimal glycemic control and maintaining glucose homeostasis to minimize disease-related complications. Dipeptidyl peptidase-4 (DPP-4) inhibitors represent a newer class of antidiabetic medications that were introduced into clinical practice in 2006 and have subsequently become an important option for the management of type 2 diabetes mellitus. Due to their benign side-effects, good efficacy, and low hypoglycaemic risk have become widely accepted for treating type 2 DM. It is important to regulate insulin secretion for maintaining euglycemia. Deteriorating insulin secretion and development of peripheral insulin resistance in type 2 DM, leads to hyperglycaemia. DPP-4 inhibitors are also known as gliptins. They inhibit the enzyme dipeptidyl peptidase 4 enzyme which is accountable for delaying the inactivation of Incretin hormones, primarily gastric inhibitory polypeptide (GIP) and glucagon-like peptide-1 (GLP-1), are important physiological regulators involved in glucose metabolism. These gut-derived peptides enhance glucose-dependent insulin secretion and contribute to the maintenance of normal blood glucose levels. These hormones are essential for physiologically maintaining glucose homeostasis. Insulin synthesis from β-cells is stimulated by GIP and GLP-1. Glucagon secretion from α-cells of the pancreas is diminished by GLP-1. Collectively all these effects lead to improved glycaemic control in type 2 patients.[9,10]

Previous studies have shown that immediate-release vildagliptin tablets can be successfully developed using the direct compression method. The optimization of super disintegrants such as

Pharmaburst and croscarmellose sodium significantly improves tablet disintegration and drug release, achieving about 95–100% drug release within 30–45 minutes. Appropriate excipients further enhance tablet quality and manufacturability, resulting in formulations that meet pharmacopeial standards and provide rapid and effective drug delivery.

Need:

Development of an immediate-release vildagliptin tablet is necessary to achieve rapid disintegration, faster drug dissolution, and prompt therapeutic action. Optimizing super disintegrants and excipient combinations can enhance tablet performance while maintaining acceptable physicochemical properties and manufacturability.

Materials and Methods:

Materials:

Therapeutic agent was received as a gift sample and excipients like Microcrystalline cellulose (binder), Sodium starch glycolate (super disintegrant), Mannitol (diluent), and Magnesium stearate (lubricant) were procured from the pharmaceutics lab.

Methods:

Preparation of Immediate Release Vildagliptin tablets:[11] Vildagliptin immediate-release tablets were developed using the direct compression technique. The required amounts of vildagliptin, microcrystalline cellulose, sodium starch glycolate, mannitol, and magnesium stearate were accurately weighed. Microcrystalline cellulose, mannitol, and sodium starch glycolate were initially blended uniformly in a mortar using a pestle to ensure proper mixing of the formulation components. The resulting powder blend was subsequently passed through sieve no. 40 to achieve uniform particle size distribution and improve blend homogeneity prior to compression. Add vildagliptin to the mixture and mix thoroughly using a pestle. Ensure that the vildagliptin is distributed evenly throughout the mixture. Add the magnesium stearate to the mixture and mix thoroughly using a pestle. Magnesium stearate is a lubricant that facilitates the compression process. Place the mixture in a tablet compression machine and compress it into tablets using a 9 mm punch. The compression pressure was appropriately adjusted to obtain tablets with desirable mechanical strength, adequate hardness, and acceptable overall quality attributes while maintaining the required performance characteristics of the formulation.

Optimization using 3^2 factorial design:

A 3^2 full factorial design was applied in the present study to systematically investigate the influence of formulation variables on the characteristics of the developed tablets. The design comprised two independent factors, each evaluated at three different levels, resulting in a series of experimental formulations. The selected independent variables were the concentration of sodium starch glycolate as the superdisintegrant (Factor A) and the concentration of microcrystalline cellulose as the binder (Factor B). The response variables considered for optimization were percentage drug release at 45 minutes (DR_{45}min) and tablet disintegration time (DT).

Table no.1**:** 3^2 full factorial design batches

Formulation Code	Independent variable-A	Independent variable-B
B1	-1	0
B2	0	0
B3	-1	+1
B4	+1	+1
B5	0	+1
B6	0	-1
B7	+1	0
B8	+1	-1
B9	-1	-1

Table no. 2 : Trial batches for development of IR Vildagliptin tablet by 3^2 factorial design

Ingredients	Formulation Code/ Ingredient (mg)								
	B1	B2	B3	B4	B5	B6	B7	B8	B9
Vildagliptin	50	50	50	50	50	50	50	50	50
SSG	05	7.5	05	10	7.5	7.5	10	10	05
MCC	75	75	100	100	100	50	75	50	50
Mg. stearate	02	02	02	02	02	02	02	02	02
Mannitol	118	115	93	88	90	140	113	138	143
Total	250	250	250	250	250	250	250	250	250

Preformulation Studies:[12,13,14]

According to the design of experiment (DoE) approach, the prepared powder blends were subjected to evaluation prior to the development of immediate-release tablets. The flow properties of the powder mixtures were assessed by determining various pre-compression parameters, including bulk density, tapped density, Carr's compressibility index, Hausner's ratio, and angle of repose.

Bulk Density and Tapped Density:

The powder blend obtained from each formulation was carefully transferred into a 50 mL graduated measuring cylinder, and the initial volume occupied by the powder (Vb) was recorded. The cylinder was

then placed in a tapped density apparatus and subjected to tapping until the required number of taps was completed. After 100 taps, the final volume of the powder bed (Vt) was measured. The analysis was performed in triplicate for each formulation (n = 3), and the mean values were calculated. Bulk density (BD) and tapped density (TD) were subsequently determined using the respective standard equations.

Bulk density = Weight of powder blend/Bulk Volume of Powder blend

Tapped Density = Weight of powder blend/Tapped volume of powder blend

Carr's Index or Compressibility Index: Carr's index of dried powder mixture was calculated by the following formula.
Carr's Index = 100 × Tapped Density - Bulk Density / Tapped Density

Hausner's Ratio:
The Hausner's ratio of the dried powder blends was calculated to evaluate the flowability and packing characteristics of the formulations. It was determined using the relationship between tapped density and bulk density as represented by the following equation:

Hausner's Ratio = Tapped Density / Bulk Density

Angle of Repose:
The angle of repose was measured to assess the flow behavior of the powder blends. A known quantity of powder from each formulation was allowed to flow freely through a funnel fixed at a specific height onto a flat surface, forming a conical heap. The funnel position was adjusted to maintain a height slightly above the apex of the powder pile. The height (h) and radius (r) of the resulting powder cone were measured, and the angle of repose was calculated using the following equation:

$$\tan \theta = h/r$$

Where,
h = height of the powder heap
r = radius of the powder cone

The obtained values were used to evaluate the flow characteristics of the prepared powder blends.

Post-compression studies:[12]

Thickness and Diameter:
The thickness and diameter of the compressed tablets were determined using a Vernier caliper. Three tablets were randomly selected from each formulation batch, and the measurements were recorded. The mean values obtained were used for further analysis.

Weight Variation:
The uniformity of tablet weight was assessed by randomly selecting twenty tablets from each batch and individually weighing them. The average tablet weight was calculated and compared with the weight of each individual tablet. For tablets with a nominal weight of 250 mg, the acceptable pharmacopoeial limit for weight variation was maintained within ±7.5% of the average weight (±18.75 mg).

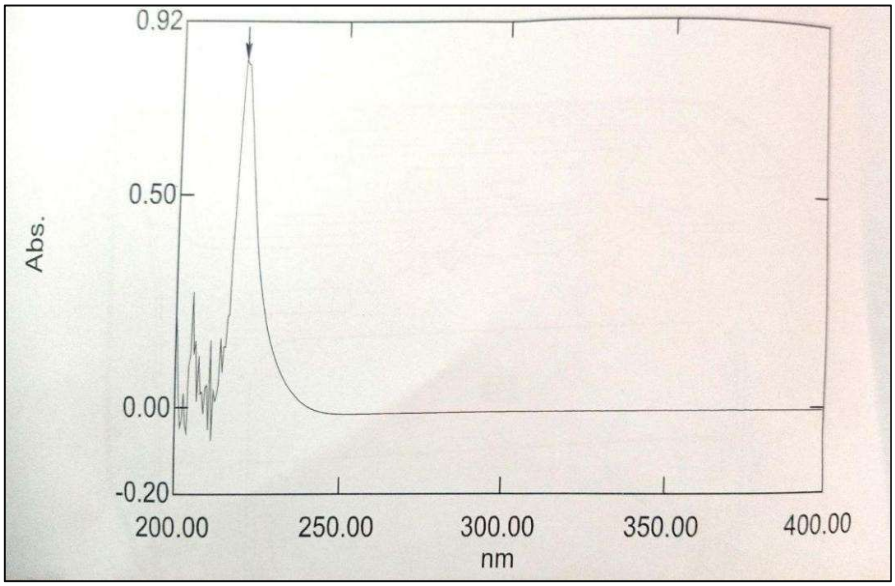
Friability Test:
Tablet friability was evaluated using a friabilator to determine the mechanical resistance of the tablets to abrasion and shock. Ten tablets were randomly selected, accurately weighed, and subjected to 100 revolutions at a rotational speed of 25 rpm for 4 minutes. Following the test, the tablets were dedusted and reweighed. Percentage friability was calculated using the following equation:

Friability (%) = [(Initial Weight − Final Weight) / Initial Weight] × 100

A friability value of less than 1% was considered acceptable, indicating adequate tablet strength.

Hardness Test:
The mechanical strength of the tablets was determined using a Monsanto hardness tester. Tablets were randomly selected from each formulation batch, and the force required to break each tablet was recorded. The average hardness value was subsequently calculated.

Disintegration Test:
Tablet disintegration was assessed using a standard disintegration test apparatus. Six tablets from each formulation were randomly selected and tested in



the specified disintegration medium maintained at 37 ± 0.5°C. The time required for complete disintegration of each tablet was recorded. Immediate-release tablets were expected to disintegrate within 15 minutes in accordance with pharmacopeial requirements.

In Vitro Dissolution Study:

The drug release profile of the formulations was evaluated using a USP Type II (paddle) dissolution apparatus. Dissolution testing was performed in 900 mL of 0.1 N hydrochloric acid maintained at 37 ± 0.5°C with a paddle rotation speed of 50 rpm. At predetermined time intervals (0, 5, 15, 30, 45, and 60 minutes), 5 mL aliquots were withdrawn and immediately replaced with an equal volume of fresh dissolution medium to maintain sink conditions. The collected samples were analyzed using a UV–Visible spectrophotometer at a wavelength of 219 nm, and the cumulative percentage drug release was calculated.

Result and Discussion:

Drug Identification and Characterization:

The sample drug was found to be slightly yellowish white in colour, crystalline in nature with faint characteristic odour. The melting point of the drug Vildagliptin was found to be 152-154°C by using the capillary tube method.

UV Spectrophotometric Analysis: (Determination of λmax):

UV- Spectra of the drug Vildagliptin was obtained from UV- Spectrophotometer and the λmax (absorption maximum) was found to be 219 nm.

Figure no.1: λmax of Vildagliptin

Calibration Curve:

The standard calibration curve of vildagliptin was established in 0.1 N hydrochloric acid (HCl), and the corresponding absorbance values for different concentrations were recorded. A series of standard solutions within the concentration range of 5–30 µg/mL was prepared and analyzed. The obtained results demonstrated good linearity, indicating compliance with Beer's law within the selected concentration range. The regression coefficient (R^2) for vildagliptin in 0.1 N HCl was calculated to be 0.9979, confirming the linear relationship between concentration and absorbance.

Table no.3: Standard calibration curve of Vildagliptin in 0.1N HCl

Sr. No.	Concentration (µg/ml)	Absorbance
1	05	0.02
2	10	0.037
3	15	0.059
4	20	0.074
5	25	0.097
6	30	0.111

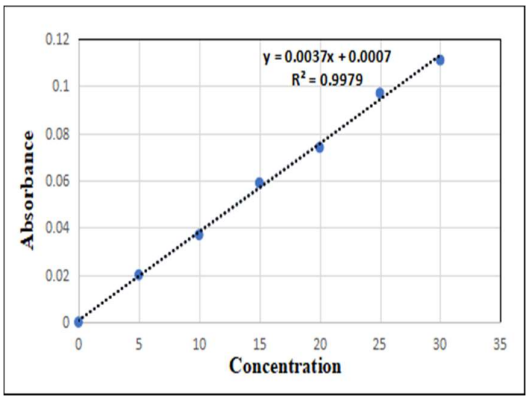


Figure no.2: The calibration curve of Vildagliptin in 0.1N HCl

Pre-compression parameter evaluation:

As described earlier, the powder blends containing the active pharmaceutical ingredient (API) and excipients were prepared and evaluated for various pre-compression characteristics prior to tablet formulation. The bulk density of the prepared blends was found to be within the range of 0.3014–0.3863 g/cm³, whereas the tapped density values ranged from 0.4661–0.5834 g/cm³. Based on these parameters, Hausner's ratio and Carr's compressibility index were calculated to assess the flow and packing properties of the powder mixtures.

The Hausner's ratio values for all formulations were observed between 1.13 and 1.18, indicating good to excellent flow characteristics of the powder blends. The Carr's index values ranged from 10.42% to 13.28%, suggesting acceptable compressibility and favorable flow behavior. Additionally, the angle of repose values were found to be within the range of 30.18°–37.19°, further confirming the good flowability of the prepared powder blends. The detailed results of the evaluated pre-compression parameters are presented in the following table.

Table no.4: Evaluation of Precompression parameters

Formulation Code	Bulk Density (gm/cm³)	Tapped Density (gm/cm³)	Angle of repose (°C)	Carr's Index (%)	Hausner's ratio
B1	0.3385 ±0.011	0.3806 ±0.009	30.18 ±1..07	11.06 ±0.02	1.1243±0.06
B2	0.3014 ±0.014	0.3444 ±0.012	34.32 ±1.12	12.50 ±0.04	1.1429±0.03
B3	0.3318 ±0.009	0.3859 ±0.007	33.60 ±1.09	14.03 ±0.02	1.1632±0.04
B4	0.3522 ±0.012	0.4166 ±0.011	37.12 ±1.18	15.46 ±0.03	1.1829±0.06
B5	0.3536 ±0.011	0.4194 ±0.012	37.19 ±1.06	15.70 ±0.03	1.186 3±0.02
B6	0.3742 ±0.006	0.4218 ±0.007	32.86 ±1.26	11.30 ±0.02	1.1274±0.06
B7	0.3332 ±0.007	0.3736 ±0.009	33.24 ±1.08	10.82 ±0.04	1.1214±0.09
B8	0.3814 ±0.013	0.4322 ±0.014	34.36 ±1.06	11.76 ±0.03	1.1334±0.02
B9	0.3863 ±0.007	0.4515 ±0.005	35.98 ±1.04	14.44 ±0.02	1.1689±0.04

Post-compression parameter evaluation:

The prepared vildagliptin tablets were evaluated for various post-compression quality attributes, including appearance, weight variation, thickness, hardness, friability, disintegration time, and in-vitro drug release profile. The obtained results demonstrated that all evaluated parameters were within the acceptable pharmacopeial limits, indicating satisfactory tablet quality and performance.

Table no.5: Evaluation of Post compression parameters

Formulation Code	Weight Variation (mg)	Thickness (mm)	Hardness (Kg/cm²)	Friability (%)	Disintegration time (Sec.)
B1	248± 2.512	4.76± 0.062	4.21± 0.027	0.24 ±0.07	29.28±0.04
B2	247± 1.912	4.76± 0.066	4.16± 0.046	0.71 ±0.04	28.31±0.07
B3	246± 2.016	4.74± 0.044	4.32± 0.014	0.25 ±0.08	42.12±0.01
B4	245± 2.118	4.69± 0.094	4.22± 0.021	0.57 ±0.06	38.02±0.03
B5	249± 1.880	4.80± 0.072	4.38± 0.047	0.40 ±0.09	39.98±0.06
B6	248± 2.226	4.72± 0.029	4.28± 0.018	0.62 ±0.05	22.56±0.04
B7	250± 2.124	4.73± 0.042	4.16± 0.072	0.74 ±0.09	27.09±0.07
B8	252± 1.988	4.76± 0.076	4.08± 0.032	0.64 ±0.02	21.16±0.05
B9	249± 1.120	4.78± 0.045	4.26± 0.029	0.72 ±0.07	23.60±0.02

Dissolution Profile:

Table no.6: Dissolution Profiles

T	% Drug release of formulations

time (min.)	B1	B2	B3	B4	B5	B6	B7	B8	B9
00	00	00	00	00	00	00	00	00	00
05	20.16±0.04	27.26±0.07	16.32±0.09	30.34±0.06	22.08±0.02	33.74±0.02	35.44±0.06	39.26±0.06	21.48±0.02
15	53.22±0.07	60.64±0.04	32.78±0.05	51.66±0.12	47.46±0.11	61.63±0.07	73.21±0.04	72.84±0.07	48.23±0.08
30	69.24±0.06	75.22±0.06	53.68±0.11	76.47±0.07	65.86±0.07	80.18±0.05	86.76±0.03	85.76±0.04	62.87±0.05
45	81.86±0.11	87.82±0.07	76.76±0.04	85.58±0.03	79.42±0.02	89.28±0.09	92.82±0.09	95.58±0.09	76.94±0.07
60	95.32±0.09	97.98±0.09	90.96±0.03	93.94±0.02	91.38±0.06	97.74±0.08	99.02±0.03	99.86±0.10	82.98±0.11

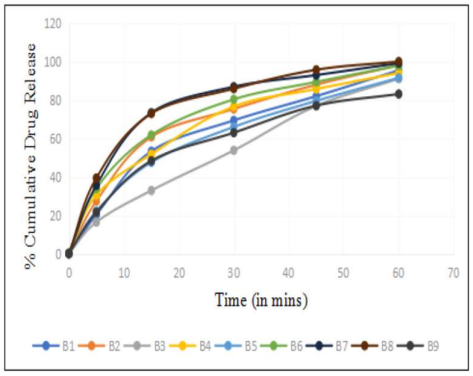


Figure no.3: Cumulative % drug release

Factorial Design:

A 3-level, 2-factor full factorial design approach was utilized to study the effect of formulation variables on the selected response parameters, including percentage drug release at 45 minutes (DR_{45}min) and disintegration time (DT). The experimental design and statistical analysis were performed using Design Expert software (Version 11.0.3). The obtained response data were analyzed and fitted to quadratic polynomial models, and the generated equations were used to evaluate the influence of independent variables on the selected responses.

Table no.7: Experimental Runs and Observed Responses

Run	Factor 1 A-Amount of superdisintegrant (mg) (X_1)	Factor 2 B-Amount of Binder (mg) (X_2)	Response 1 DR_{45min}(%) (Y_1)	Response 2 Disintegration Time (sec) (Y_2)
1	5	75	81.86	29.28
2	7.5	75	88.10	28.31
3	5	100	76.76	42.12
4	10	100	84.35	38.02
5	7.5	100	79.42	39.98
6	7.5	50	89.28	22.56
7	10	75	92.82	27.09
8	10	50	95.50	21.16
9	5	50	77.98	23.60

Equation for Y_1 factor (% drug release at 45 min.):

$$Y_1=88.07+6.01X_1-3.71X_2-2.48X_1X_2-0.7217X_1^2-3.71X_2^2 \quad (1)$$

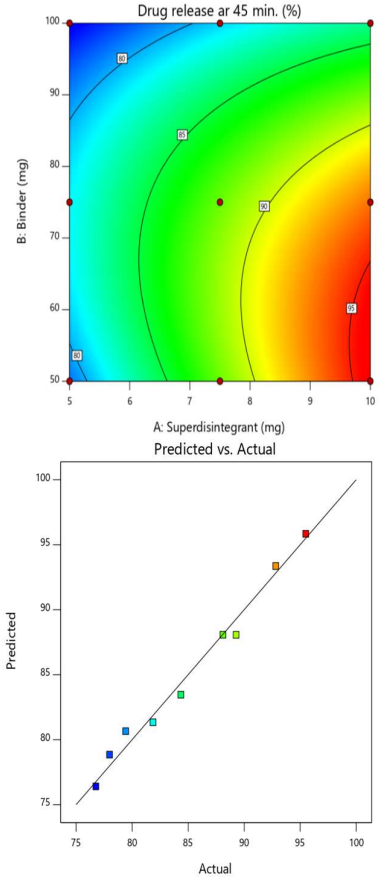
The obtained coefficient of determination (R^2 = 0.9601) indicated a strong correlation between the experimental data and the selected quadratic model, demonstrating an appropriate model fit. The polynomial equation generated from the design can be interpreted based on the magnitude and sign (positive or negative) of the regression coefficients, which indicate the effect of individual formulation variables on the response.

The percentage drug release at 45 minutes (DR_{45}min) was observed to increase with an increase in the concentration of sodium starch glycolate (X_1), whereas an increase in the concentration of microcrystalline cellulose (X_2) resulted in a reduction in drug release. The response surface plot (Figure) further illustrated the relationship between the independent variables and their influence on the drug release profile. The analysis revealed that both X_1 and X_2 significantly affected the DR_{45}min response.

The predicted R^2 value of 0.8177 showed good agreement with the adjusted R^2 value of 0.9601, as the difference between both values was within the acceptable limit (<0.2), indicating satisfactory predictive capability of the model. The adequacy precision value represents the signal-to-noise ratio, and a value greater than 4 is considered desirable. The obtained adequacy precision value of 17.821 confirmed an adequate signal, suggesting that the model was suitable for exploring the design space. Additionally, the model F-value of 39.52 indicated that the developed model was statistically significant.

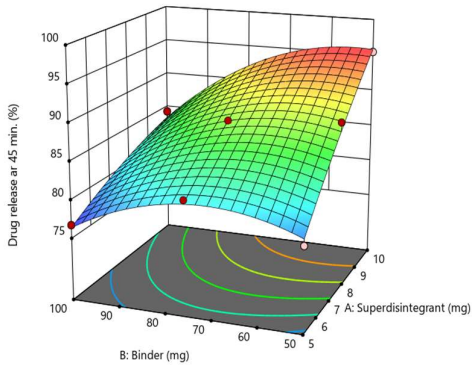
Table No.8: ANOVA's for Response 1 (% drug release at 45 min.)

Source	Model	X_1	X_2	X_1^2	X_1^2	X_2^2	Residual	Core total
Sum of Square	352.45	216.84	82.36	24.65	1.04	27.55	5.35	357.80
Degree of freedom	5	1	1	1	1	1	3	8
Mean Square	70.49	216.84	82.36	24.65	1.04	27.55	1.78	-
F-value	39.52	121.56	46.17	13.82	0.5839	15.45	-	-
P-value	0.0061	0.0016	0.0065	0.0339	0.5004	0.0293	-	-



(a) Counter Plot

(b) Predicted vs Actual plot



(c) 3-D Surface plot

Figure no.4: Plots illustrating effect of Superdisintegrant and binder on percent drug release at 45 min.

Equation for Y_2 factor (Disintegration time):

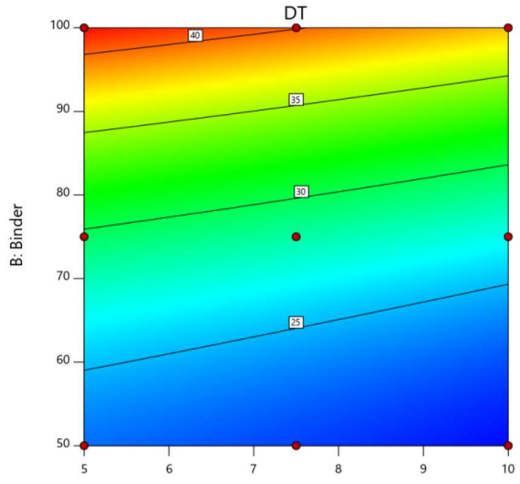
$$Y_2 = 28.27 - 1.45X_1 + 8.80X_2 - 0.4150X_1X_2 - 0.0717X_1^2 + 3.01X_2^2 \quad (2)$$

High r^2 (0.9978) showed that the quadratic model fit the data well. The polynomial equations can also be used to infer inferences based on the magnitude of the coefficient and the mathematical sign, positive or negative, that it bears. The DT decreases with decrease in concentration of superdisintegrant is indicated by the positive coefficient of variable A, or sodium starch glycolate in the case of response,

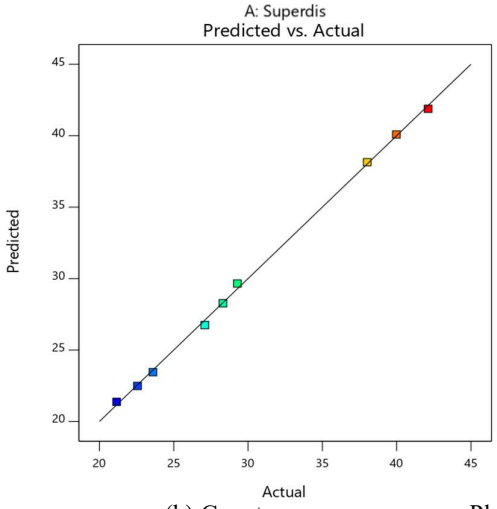
or disintegration time. The relationship between the variables was further illustrated by using the response face plot shown in Figure. A high position of factor X_1 gave a least disintegration time. The predicted R^2 value of 0.9898 is reasonable agreement with adjusted R^2 value of 0.9978. This may indicate a good fitting of the model. Adequate precision measures the signal to noise rate. A rate lesser than 4 is desirable. rate of 67.46 indicates an acceptable signal. This model can be used to navigate the design space. The Model F value of 715.77 implies that the model is significant. Details are mentioned in below table.

Table No.9: ANOVA's for Response 2 (Disintegration time)

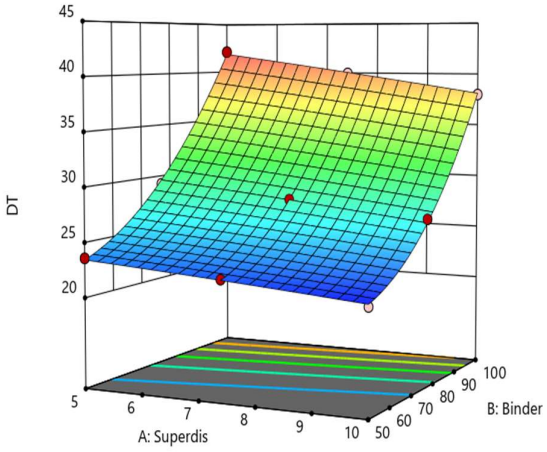
Source	Model	X_1	X_2	X_1^2	X_1^2	X_2^2	Residual	Core total
Sum of Square	496.20	12.70	464.64	0.6869	0.0103	18.16	0.4159	496.62
Degree of freedom	5	1	1	1	1	1	3	8
Mean Square	99.24	12.70	464.64	0.6889	0.0103	18.16	0.1386	-
F-value	715.77	91.61	3351.22	4.97	0.0741	130.98	-	-
P-value	< 0.0001	0.0024	< 0.0001	0.1121	0.8031	0.0014	-	-



(b) Counter Plot



(b) Predicted vs Actual plot



(c) 3-D Surface plot

Figure no.5: Plots illustrating effect of Superdisintegrant and binder on disintegration time

To identify the optimal levels of the selected independent variables for obtaining the desired formulation characteristics, an optimization study was carried out using Design Expert software. The optimization procedure was performed through both graphical and numerical approaches to determine

the most suitable formulation composition. The predicted responses generated by the software were compared with the experimentally obtained values for the optimized formulation. The results demonstrated that the observed drug release profile of the optimized vildagliptin immediate-release tablet was in close agreement with the predicted values, confirming the reliability and suitability of the optimization model.

Conclusion:

Effective management of diabetes mellitus requires the use of oral hypoglycemic agents to achieve and maintain optimal glycemic control. Vildagliptin formulated as an immediate-release tablet may provide rapid drug availability and contribute to the reduction of postprandial blood glucose levels. In the present study, vildagliptin immediate-release tablets were developed using a systematic statistical optimization approach.

A 3^2 full factorial design was employed to establish the influence of formulation variables on the selected responses. The design effectively evaluated the relationship between independent variables, including the amount of superdisintegrant (X_1) and binder (X_2), and the dependent variables, namely percentage drug release at 45 minutes (DR_{45}min) and disintegration time. The optimized formulation was selected based on the comparison between predicted and experimental response values, which showed close agreement, confirming the validity of the developed model.

Based on the findings of the study, the developed immediate-release vildagliptin tablet formulation demonstrated desirable drug release characteristics and may serve as an effective approach for improving glycemic management in patients with type II diabetes mellitus.

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