

Development and In-Vitro Evaluation of Sitagliptin Fast Dissolving Tablets for Enhanced Oral Bioavailability

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ABSTRACT

Diabetes mellitus is a chronic metabolic disorder characterized by persistent hyperglycemia resulting from impaired insulin secretion, insulin action, or both. The present study aimed to formulate and evaluate fast dissolving tablets (FDTs) of Sitagliptin in order to improve drug dissolution, patient compliance, and oral bioavailability. Fast dissolving tablets were prepared by the direct compression method using different concentrations of superdisintegrants such as croscarmellose sodium (CCS) and sodium starch glycolate (SSG). Six formulations (S1–S6) were developed and evaluated for pre-compression and post-compression parameters. Preformulation studies indicated that Sitagliptin possessed suitable physicochemical properties with bulk density 0.46 g/ml, tapped density 0.54 g/ml, Carr's index 14.81, Hausner's ratio 1.17, and angle of repose 28.6°, confirming good flow characteristics. FTIR compatibility studies revealed no significant interaction between the drug and excipients. The prepared tablets were evaluated for weight variation, hardness, friability, thickness, disintegration time, wetting time, water absorption ratio, drug content, and in vitro dissolution. Among the developed formulations, S3 showed the best performance, exhibiting rapid disintegration (21 sec), high water absorption ratio (90%), and drug content of 100.2%. The dissolution study demonstrated that formulation S3 released 65.3% of drug within 5 minutes, indicating rapid drug release. In vitro permeability studies using the Caco-2 cell model showed improved apparent permeability for the optimized formulation ($P_{app} 4.21 \times 10^{-6}$ cm/s) compared with the marketed tablet (2.85×10^{-6} cm/s). Stability studies conducted for three months showed no significant change in physical appearance, drug content, disintegration time, or dissolution profile. The results indicate that the developed Sitagliptin fast dissolving tablets provide rapid drug release and enhanced permeability, suggesting improved oral bioavailability and better patient compliance compared to conventional tablet formulations.

Keywords: Sitagliptin, Fast Dissolving Tablets (FDTs), Direct Compression, Superdisintegrants, Caco-2 Cell Model

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INTRODUCTION

1.1. Diabetes mellitus

Diabetes mellitus is a complex chronic metabolic disease characterized by elevated blood glucose levels that result from abnormalities in insulin secretion, action or both. [1,2] As one of the leading global killers, the disease represents a major problem for global health due to its rising prevalence, chronicity requiring life-long pharmacotherapy and strong association with processes that generate off-target morbidity. [3,4] Diabetes accounts for a considerable clinical burden and it has been associated with high socioeconomic impact such as higher healthcare expenditure, lower quality of life, loss of productivity along with premature deaths. [5]

There is a worrisome rise in the frequency of diabetes over recent decades, induced by rapid changes in diet and lifestyle practices, population ageing, sedentary life habits, nutrition transition, increasing prevalence of obesity etc. As reported by the International Diabetes Federation (IDF) Diabetes Atlas in 2021 (tenth edition) [6], there were worldwide approximately 537 million adults (aged between 20 and 79 years old) living with diabetes in 2021. This figure is expected to increase to 643 m by 2030 and 783 m by 2045, making it one of the fastest growing global health challenges of the twenty-first century. [7]

The World Health Organization (WHO) has acknowledged that diabetes significantly contributes to global mortality rates. In 2019, diabetes was estimated to be the ninth leading cause of death globally, directly

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accounting for around 1.6 million fatalities, with an even higher number of deaths linked indirectly to diabetes-related cardiovascular and renal issues.[8] The impact of diabetes is not confined to high-income countries; in fact, over 75% of individuals with diabetes live in low- and middle-income nations, where healthcare resources are frequently scarce and access to effective diabetes management remains insufficient.[9] Type 2 diabetes mellitus (T2DM) represents roughly 90–95% of all diabetes cases worldwide. The increasing incidence of T2DM is strongly associated with changes in lifestyle, such as decreased physical activity, higher intake of calorie-rich diets, and growing obesity levels.[10] The epidemiological shift seen in numerous developing nations has led to a combined challenge of infectious diseases and chronic metabolic conditions, placing additional pressure on healthcare systems.[11]

Classification Of Diabetes Mellitus

- Type 1 diabetes mellitus
- Type 2 diabetes mellitus
- Gestational diabetes mellitus
- Other specific types of diabetes[16]



Fig 1: Classification Of Diabetes Mellitus

1.2. Fast Dissolving Tablets (FDTs)

Fast dissolving tablets (FDTs), also called mouth-dissolving tablets or orally disintegrating tablets (ODTs), are solid oral dosage forms that dissolve quickly in saliva, typically in a matter of seconds to a minute, without the need for water. FDTs quickly moisten and disintegrate when placed on the tongue, creating an easily ingested drug-containing dispersion. After that, the medication is primarily absorbed through the digestive system, though in certain circumstances, partial pre-gastric absorption may occur.[12]

The US FDA's Centre for Drug Evaluation and Research (CDER) describes Oral Disintegrating Tablets (ODT) as “A solid dosage form containing active therapeutic components that dissolve

rapidly, generally within a few seconds, once placed on the tongue.”[13]

A rapidly dissolving tablet can be described as a firm dosage format that disintegrates into tiny particles, gradually dissolving in the mouth. The time required for these rapidly dissolving tablets to break down varies from a few moments to more than a minute, influenced by the formulation and size of the tablet.[14]

MATERIALS AND METHOD

The drug Sitagliptin was received as gift sample from Akums Pharma as gift sample and all other chemicals were purchased from N.V.D. Scientific Pvt. Ltd.

Lucknow.

2.1. Preformulation

Preformulation studies were carried out to investigate the physicochemical properties of Sitagliptin prior to formulation development. These studies help in understanding the characteristics of the drug substance and its interaction with selected excipients used in the formulation of fast dissolving tablets.[15]

2.1.1. Organoleptic Evaluation

Organoleptic evaluation of Sitagliptin was performed to assess its physical appearance including color, odor, and general characteristics. The drug sample was visually inspected and described using standard descriptive terminology. Sitagliptin was observed as a white to off-white crystalline powder with no characteristic odor.[16]

2.1.2. Solubility Testing

Solubility testing of Sitagliptin was carried out in various solvents to determine its solubility characteristics. An excess amount of drug was added to different solvents such as distilled water, methanol, and phosphate buffer solutions and shaken until equilibrium was reached. The solutions were then filtered and analyzed to determine the solubility of the drug. Solubility is an important parameter affecting dissolution rate and bioavailability of the drug in oral dosage forms.[17]

2.1.3. Melting Point

The melting point of Sitagliptin was determined using the capillary method to assess the purity and crystalline nature of the drug. A small quantity of the drug was filled in a capillary tube and placed in a melting point apparatus. The temperature at which the drug started melting and completely liquefied was recorded. A sharp melting point range indicates purity of the drug substance.[16,17]

2.1.4. Physicochemical Characterization

2.1.4.1. Density Measurement

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The density of Sitagliptin powder was evaluated to understand its compressibility and packing behavior. Density measurements provide information about the flow properties and suitability of the powder for tablet compression. Two important density parameters determined were bulk density and tapped density.[18]

a) Bulk Density

Bulk density of Sitagliptin powder was determined by accurately weighing a known quantity of powder and transferring it into a graduated cylinder without disturbing the powder bed. The volume occupied by the powder was recorded as bulk volume.[19]

$$\text{Bulk density} = \text{Weight of powder} / \text{Bulk volume}$$

b) Tapped Density

Tapped density was determined by placing the graduated cylinder containing the powder into a tapped density apparatus. The cylinder was tapped at a constant rate until a constant volume was obtained. The final volume recorded after tapping was considered as tapped volume.[20]

$$\text{Tapped density} = \text{Weight of powder} / \text{Tapped volume}$$

2.1.4.2. Flow Property

The flow properties of Sitagliptin powder were evaluated to determine its suitability for direct compression in tablet formulation. Flow characteristics influence uniform die filling during tablet compression and affect tablet weight uniformity.[21]

a) Carr's Index

Carr's Index, also known as percentage compressibility, was calculated using bulk density and tapped density values to assess powder flow properties.[22]

$$\text{Carr's Index (\%)} = [(\text{Tapped Density} - \text{Bulk Density}) / \text{Tapped Density}] \times 100$$

b) Angle of Repose

Angle of repose was determined by allowing the powder to flow through a funnel to form a conical heap. The height and radius of the heap were measured and the angle of repose was calculated.[23]

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

Where:

h = height of pile

r = radius of pile

c) Hausner's Ratio

Hausner's ratio was calculated to further evaluate the flowability of the powder blend.

$$\text{Hausner's Ratio} = \text{Tapped Density} / \text{Bulk Density}$$

A value less than 1.25 indicates good flow properties of the powder, whereas a value greater than 1.50 indicates poor flow.[24]

2.1.5. UV Spectroscopic

UV-Visible spectrophotometry was used for quantitative estimation of Sitagliptin in formulation studies including drug content and dissolution analysis. The technique is simple, accurate, and widely used for pharmaceutical analysis.[25]

a) Determination of λ_{max} :

A standard solution of Sitagliptin was prepared and scanned in the wavelength range of 200–400 nm using a UV-Visible spectrophotometer with suitable solvent as blank. The wavelength corresponding to maximum absorbance (λ_{max}) was determined. Sitagliptin showed maximum absorbance at approximately **267 nm**, which was selected for further analysis.[26]

b) Preparation of Calibration Curve:

A series of standard solutions of Sitagliptin with different concentrations (20–100 $\mu\text{g/mL}$) were prepared from the stock solution. The absorbance of each solution was measured at **267 nm** using a UV-Visible spectrophotometer. A calibration curve was constructed by plotting concentration against absorbance. The linear regression equation and correlation coefficient were calculated to determine the linearity of the method. The calibration curve was used for estimation of drug content and dissolution samples.[27]

2.1.6. Drug-Excipient Compatibility Study (FTIR Analysis)

Fourier Transform Infrared (FTIR) spectroscopy was performed to evaluate the compatibility between Sitagliptin and selected excipients used in the formulation of fast dissolving tablets. The FTIR spectra of pure Sitagliptin and its physical mixtures with excipients such as microcrystalline cellulose PH 102, mannitol, croscarmellose sodium, sodium starch glycolate, magnesium stearate, and aspartame were recorded using the **KBr pellet method** in the range of **4000–400 cm^{-1}** . The spectra were analyzed to identify characteristic peaks of Sitagliptin and to detect any possible interaction between the drug and excipients.[28]

2.2. Formulation Development of Sitagliptin Fast Release Tablets

Table. 1. Formulation of Sitagliptin

Ingredient (mg)	S1	S2	S3	S4	S5	S6
Drug	50	50	50	50	50	50
CCS	6	8	10	–	–	–
SSG	–	–	–	6	8	10
MCC PH 102	60	58	56	60	58	56
Mannitol	80	78	76	80	78	76
Aspartame	2	2	2	2	2	2

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Magnesium Stearate	2	2	2	2	2	2
Total Weight (mg)	200	200	200	200	200	200

2.3. Procedure for Preparation of Fast Release Tablets[29,30]

All ingredients required for each Sitagliptin formulation batch (S1–S6) were accurately weighed using an analytical balance according to the formulation design table, ensuring precision and avoiding cross-contamination between batches. The active pharmaceutical ingredient, Sitagliptin, along with superdisintegrants (croscarmellose sodium and/or sodium starch glycolate), diluents (microcrystalline cellulose PH 102 and mannitol), and sweetener (aspartame), were individually passed through a #60 mesh sieve to break lumps and obtain a uniform particle size distribution. The sieved drug and excipients, except magnesium stearate, were transferred to a clean and dry mortar and blended thoroughly for 10–15 minutes using the geometric dilution technique to ensure uniform distribution of the drug within the powder mixture, which is essential for achieving content uniformity in the final tablets. Magnesium stearate, previously passed through a #60 mesh sieve, was then added as a lubricant and gently blended with the mixture for about 2–3 minutes to avoid over-lubrication that could adversely affect tablet hardness, disintegration, and dissolution characteristics. The final lubricated blend was evaluated for pre-compression parameters including bulk density, tapped density, angle of repose, Carr's index, and Hausner's ratio to assess the flow properties and suitability of the blend for direct compression. Finally, the prepared blend was compressed into tablets using a rotary tablet compression machine fitted with flat-faced punches of appropriate diameter, and the compression force was optimized to obtain tablets with adequate mechanical strength while ensuring rapid disintegration, with in-process checks for tablet weight and thickness performed at regular intervals.

Weighing of Ingredients (Sitagliptin, MCC
PH102, Mannitol,
Croscarmellose Sodium / Sodium Starch
Glycolate, Aspartame, Mg Stearate)
↓
Sieving of All Ingredients (#60 Mesh Sieve)
↓
Mixing of Sitagliptin with Diluent and

Superdisintegrants
(Geometric dilution for 10–15 minutes)
↓
Addition of Sweetener (Aspartame) and Further
Blending
↓
Addition of Lubricant (Magnesium Stearate)
(Gentle mixing for 2–3 minutes)
↓
Pre-compression Evaluation of Powder Blend
↓
Compression of Blend using Rotary Tablet
Compression Machine

2.4. Evaluation.

2.4.1. Physical Appearance

The physical appearance of Sitagliptin fast dissolving tablets was evaluated visually to assess general tablet characteristics. Tablets were examined for size, shape, color, odor, surface texture, and the presence of any physical defects such as cracks, chipping, capping, or lamination. Uniform appearance and smooth surface are important indicators of proper compression and formulation stability.[31]

2.4.2. Weight Variation

The weight variation test was carried out to ensure uniformity of tablet weight and dosage. Twenty tablets were randomly selected from each batch and weighed individually using a digital analytical balance. The average weight of the tablets was calculated, and the percentage deviation of each tablet from the average weight was determined. According to the United States Pharmacopeia (USP), not more than two tablets should deviate from the permissible percentage limits, and none should deviate by more than twice the specified limit.[32]

Percentage deviation = [(Tablet weight - Average weight) / tablet weight] * 100

Table 2: USP Specification for uniformity of weight.

S.No	Weight (mg)	Maximum percentage difference allowed
1.	130 or Less	10
2.	130 - 324	7.5
3.	More than 324	5

2.4.3. Friability

Friability testing was performed to evaluate the mechanical strength of the Sitagliptin tablets and their ability to withstand abrasion and shock during handling, transportation, and packaging. The test was conducted using a Roche friabilator.

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A sample of pre-weighed tablets was placed in the friabilator and rotated at 25 rpm for 4 minutes (100 revolutions). After completion of the test, the tablets were dedusted and reweighed. The percentage weight loss was calculated and should not exceed 1%, indicating acceptable mechanical strength.[33]

$$\text{Percentage friability} = [(w_2 - w_1) / w_1] * 100$$

Where, W₁ = Weight of tablets before test; W₂ = Weight of tablets after test

2.4.4. Thickness

Tablet thickness was measured using a vernier caliper to ensure uniformity of tablet dimensions. Thickness depends on the amount of fill in the die and the compression force applied during tablet compression. Consistent thickness is important for uniform packaging, tablet appearance, and mechanical stability of the dosage form.[34]

2.4.5. Hardness (Crushing Strength)

Hardness testing was performed to determine the mechanical strength of the Sitagliptin tablets. The hardness of tablets was measured using a Monsanto or Pfizer hardness tester. Adequate hardness ensures that tablets can withstand mechanical stress during packaging, handling, and transportation. For fast dissolving tablets, hardness must be optimized to maintain sufficient strength while allowing rapid disintegration in the oral cavity.[35]

2.4.6. Disintegration Test

The disintegration test was performed using a USP disintegration test apparatus. The apparatus consists of six glass tubes, each fitted with a 10-mesh screen at the bottom. One tablet was placed in each tube and the basket rack assembly was immersed in a one-liter beaker containing distilled water maintained at 37 ± 2°C. The basket was allowed to move up and down at a frequency of 28–32 cycles per minute. The time required for the tablets to completely disintegrate without leaving any residue on the screen was recorded as the disintegration time.[36]

2.4.7. Wetting time:

Wetting time was determined to evaluate the ability of the tablet to absorb water and initiate disintegration. A circular tissue paper was placed in a petri dish containing 10 mL of distilled water with a small amount of eosin dye to visualize the wetting process. A tablet was carefully placed on the surface of the tissue paper, and the time required for water to reach the upper surface of the tablet was recorded as the wetting time.[37]

2.4.8. Water absorption ratio:

The water absorption ratio indicates the amount of water absorbed by the tablet, which influences the

disintegration process. A piece of tissue paper folded twice was placed in a petri dish containing 6 mL of water. A pre-weighed tablet was placed on the tissue paper and allowed to absorb water. After complete wetting, the tablet was removed and reweighed;[38]

$$R = 100 (W_a - W_b) / W_b$$

Where,

W_b; The weight of the tablet before keeping in the petridish.

W_a; The wetted tablet from the petridish is taken and reweighed.

2.4.9. Dissolution

The in vitro dissolution study of Sitagliptin tablets was performed using a USP Type II (paddle) dissolution apparatus. Six tablets were placed individually in dissolution vessels containing 900 mL of distilled water maintained at 37 ± 0.5°C. The paddle was rotated at an appropriate speed, and samples were withdrawn at predetermined time intervals. Each withdrawn sample was replaced with an equal volume of fresh dissolution medium to maintain sink conditions. The samples were filtered and analyzed spectrophotometrically at 267 nm using a UV-Visible spectrophotometer. The percentage drug release was calculated using the following formula.[39]

$$\% \text{ DRUG RELEASE} = \frac{\text{Absorbance} \times 900 \times \text{Dilution}}{\text{Slope} \times 1000 \times \text{Label Claim}} \times 100$$

2.4.10. Estimation Of Drug Content:

Drug content analysis was performed to determine the amount of Sitagliptin present in the tablets. Ten tablets were weighed and finely powdered. A quantity of powder equivalent to 100 mg of Sitagliptin was dissolved in 100 mL of 0.1 N HCl, filtered, and suitably diluted. The absorbance of the resulting solution was measured at 267 nm using a UV-Visible spectrophotometer. The drug concentration was calculated using the previously prepared calibration curve.[40]

2.4.11. Uniformity Of Dispersion

Uniformity of dispersion was evaluated by placing a tablet in a small volume of water and allowing it to disperse completely. The dispersion was visually observed for the presence of lumps or aggregates. A smooth and uniform dispersion indicates proper tablet formulation and ensures better patient acceptability.[41]

2.4.12. Drug Content Uniformity

Content uniformity was evaluated to ensure that each tablet contains the intended amount of Sitagliptin. Tablets were analyzed individually and the amount of drug present in each tablet was determined

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spectrophotometrically. The results were compared with pharmacopeial specifications to confirm uniform distribution of the drug in the formulation.[42]

2.4.13. In-Vitro Bioavailability Study (Permeability Study)

The Caco-2 cell model was used to evaluate the intestinal permeability of Sitagliptin from the developed fast dissolving tablets. Caco-2 cells are derived from human colorectal adenocarcinoma and differentiate into epithelial-like cells when cultured under suitable laboratory conditions. These cells form tight junctions and microvilli, closely resembling the intestinal epithelial barrier. In the permeability study, Sitagliptin samples were applied to the apical side of the Caco-2 monolayer and the amount of drug transported to the basolateral side was measured over time. This model helps in predicting intestinal absorption and provides insight into the potential improvement in bioavailability of the formulated fast dissolving tablets.[43]

$$P_{app} = \frac{dQ/dt}{A \times C_0}$$

Where:

P_{app} = Apparent permeability coefficient (cm/s)

dQ/dt = Rate of drug transport across the membrane

A = Surface area of the cell monolayer (cm²)

C₀ = Initial drug concentration in the donor compartment

2.4.14. Stability Studies:

Stability studies assess the ability of the formulation to maintain quality, safety, and efficacy over time.[44]

3. Result And Discussion

3.1. Pre formulation Studies

3.1.1. Organoleptic Evaluation

Table 3: Organoleptic Properties

Drug	Appearance	Color	Odor	Taste
Sitagliptin	Crystalline powder	White	Odorless	Slightly bitter

3.1.2. Physicochemical Characterization

Table 4: Physicochemical Characterization

Parameters	Results
Bulk Density	0.46 ± 0.02 g/ml
Tapped Density	0.54 ± 0.02 g/ml
Carr's Index	14.81
Hausner's Ratio	1.17
Angle of Repose	28.6 ± 1.2

3.1.3. Particle Size Distribution

Table 5: Particle Size Distribution of Final Blends

Sieve No.	% Retained
#20	2.4
#40	8.6
#60	18.2
#80	24.5
#100	21.3
#140	14.7
#200	8.1
Pan	2.2

3.1.4. UV Spectroscopic Analysis

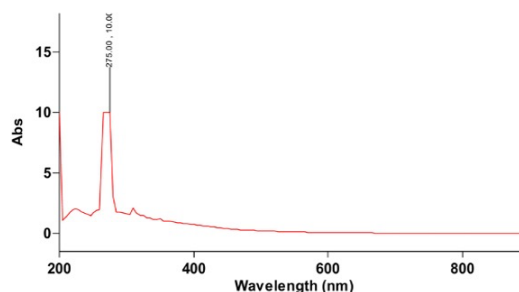


Fig 2: UV Spectra of Sitagliptin

6.1.4.1. Calibration Curve Results

Table 6: Calibration Curve Data for Sitagliptin (λ_{max} = 267 nm)

S. No.	Concentration (µg/mL)	Absorbance (Mean ± SD)
1	0	0.000 ± 0.000
2	2	0.095 ± 0.002
3	4	0.189 ± 0.003
4	6	0.273 ± 0.004
5	8	0.361 ± 0.004
6	10	0.452 ± 0.005

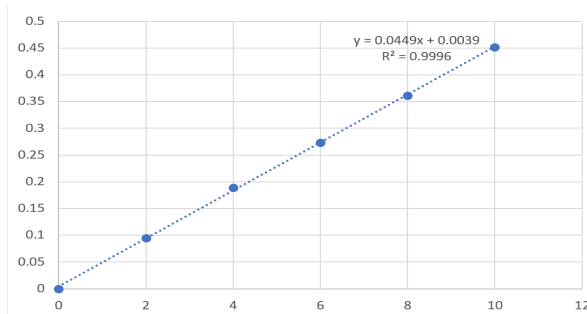


Fig 3: Calibration Curve of Sitagliptin

3.1.5. Drug-Excipient Compatibility (FTIR)

Table 7: FTIR Compatibility Summary

Sample	Characteristic Peaks Observed	Peak Shifts/New Peaks	Compatibility
Pure Sitagliptin	Present	None	Compatible
Drug + Excipient	Retained	None	Compatible

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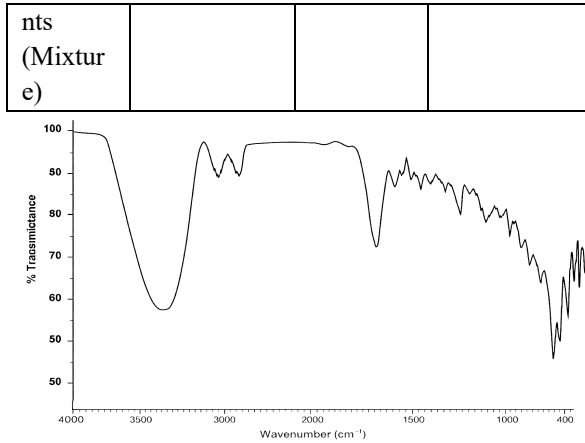


Fig 4: FTIR Spectra of Sitagliptin



Fig 5: FTIR Spectra of Sitagliptin and Polymer

3.1.6. Solubility Testing

Table 8: Solubility of Sitagliptin

Medium	Solubility
Distilled Water	Freely soluble
0.1 N HCl	Soluble
Phosphate Buffer pH 6.8	Freely soluble
Methanol	Freely soluble
Ethanol	Soluble
Acetone	Slightly soluble
Chloroform	Sparingly soluble
Acetonitrile	Freely soluble
Dimethyl Sulfoxide (DMSO)	Freely soluble

3.1.7. Melting point:

Table 9: Melting Point

Drug	Trial 1 (°C)	Trial 2 (°C)	Trial 3 (°C)	Average Melting Point (°C)	Reported Range (°C)
Sitagliptin	216	217	218	217	215–220

3.2. Evaluation of Formulation

3.2.1. Physical Appearance of Tablets

Table 10: Physical Appearance (S1–S6)

Batch	Shape	Color	Surface Texture	Defects (Cracks/Chipping)
S1	Round	White	Smooth	None observed
S2	Round	White	Smooth	None observed
S3	Round	White	Smooth	None observed
S4	Round	White	Smooth	None observed
S5	Round	White	Smooth	None observed
S6	Round	White	Smooth	None observed

3.2.2. Weight Variation, Friability, Hardness Thickness & Disintegration Time of Sitagliptin Tablets

Table 11: Weight Variation, Friability, Hardness Thickness & Disintegration Time (S1–S6)

Batch	Weight Variation (%)	Friability (%)	Hardness (kg/cm ²)	Thickness (mm)	Disintegration Time (sec)
S1	1.8	0.62	2.8	3.6	32
S2	1.6	0.59	2.9	3.5	29
S3	1.7	0.55	3.0	3.5	21
S4	1.9	0.64	2.7	3.6	35
S5	1.8	0.61	2.8	3.6	31
S6	1.9	0.58	2.9	3.5	24

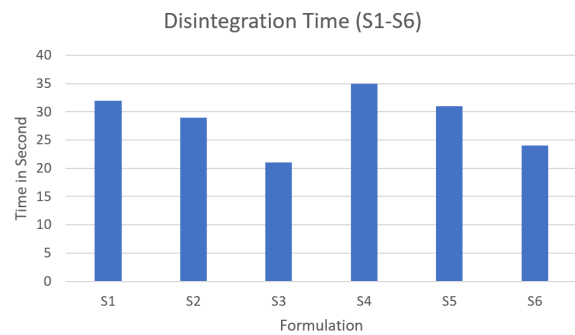


Fig 6: Disintegration Time

3.2.3. Water Absorption Ratio, Wetting Time and Drug Content % of Sitagliptin Tablets

Table 12: Water Absorption Ratio, Wetting Time and Drug Content % (S1–S6)

Batch	Water Absorption Ratio (%)	Wetting Time (sec)	Drug Content (%)
S1	1.8	0.62	2.8
S2	1.6	0.59	2.9
S3	1.7	0.55	3.0
S4	1.9	0.64	2.7
S5	1.8	0.61	2.8
S6	1.9	0.58	2.9

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S1	78	28	98.4
S2	82	25	99.1
S3	90	18	100.2
S4	75	30	97.9
S5	80	27	98.7
S6	88	20	99.8

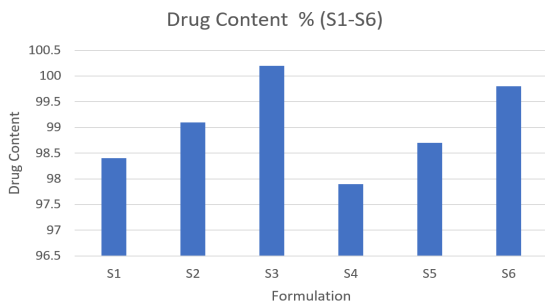


Fig 7: % Drug Content (S1-S6)

3.2.4. In Vitro Drug Release study of Sitagliptin Tablets

Table 13: In Vitro Drug Release of Sitagliptin Tablets (S1-S6)

Batch	0 min	1 min	2 min	3 min	4 min	5 min
S1	0	12.4	23.8	36.7	47.9	55.2
S2	0	13.6	25.7	38.9	49.8	58.6
S3	0	18.6	31.4	45.7	56.8	65.3
S4	0	11.2	21.5	33.4	44.3	52.0
S5	0	13.1	24.6	37.2	48.6	56.4
S6	0	16.0	28.9	42.1	53.4	62.1

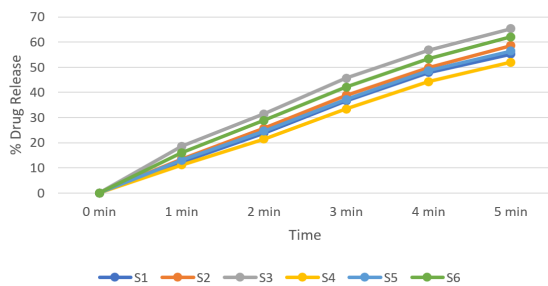


Fig 8: In Vitro Drug Release of Sitagliptin Tablets (S1-S6)

3.2.5. Uniformity Of Dispersion of Sitagliptin Tablets

Table 14: Uniformity Of Dispersion of Sitagliptin Tablets

Batch	Observation	Residue on Sieve (#22)
S1	Uniform dispersion observed	No residue
S2	Uniform dispersion observed	No residue
S3	Rapid and uniform dispersion	No residue

S4	Uniform dispersion observed	No residue
S5	Uniform dispersion observed	No residue
S6	Uniform dispersion observed	No residue

Fig 6.2.8: Uniformity Of Dispersion of Sitagliptin Tablets

3.3. In Vitro Bioavailability Study

Table 15: In Vitro Permeability of Sitagliptin Formulations (Caco-2 Cell Model)

Formulation	Drug	Apparent Permeability Coefficient (P _{app} × 10 ⁻⁶ cm/s)	Transport Rate (%)
Marketed Tablet	Sitagliptin	2.85 ± 0.12	68.4 ± 1.5
Optimized FDT (S3)	Sitagliptin	4.21 ± 0.16	82.6 ± 1.8

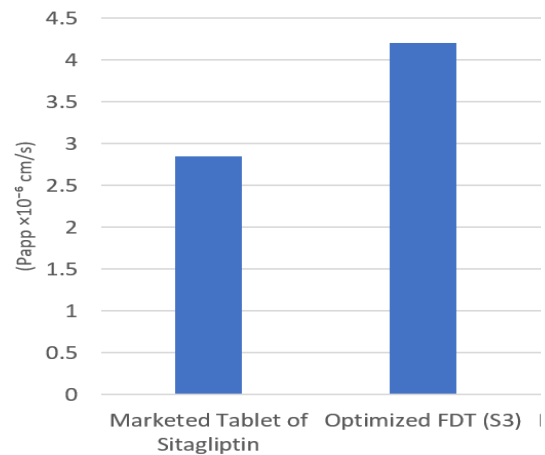


Fig 9: In Vitro Permeability of Sitagliptin Formulations

Table 16: Cumulative Drug Permeation Across Caco-2 Cell Monolayer

Time (min)	Sitagliptin Marketed (%)	Sitagliptin FDT S3 (%)
15	22.3	34.6
30	39.5	55.2
45	54.1	70.8
60	68.4	82.6

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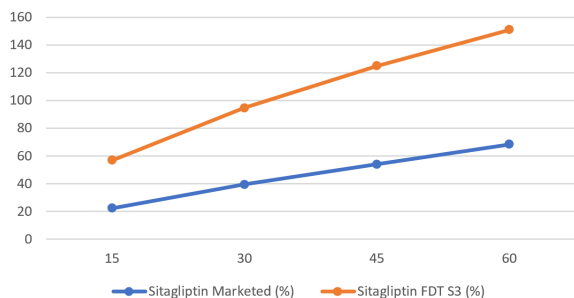


Fig 10: Cumulative Drug Permeation Across Caco-2 Cell Monolayer

3.4. Stability Study

Table 17: Stability Study of Optimized Sitagliptin Formulation (S3)

Time	Physical Appearance	Drug Content (%)	Disintegration Time (sec)	% Drug Release (5 min)
Initial	White, smooth tablet	100.2	21	65.3
1 Month	No change	100.2	21	65.1
2 Months	No change	99.7	21	64.8
3 Months	No change	99.4	24	64.3

CONCLUSION

The present study successfully developed and evaluated fast dissolving tablets of Sitagliptin using the direct compression technique with different superdisintegrants. Preformulation studies confirmed that the drug possessed suitable physicochemical characteristics and compatibility with selected excipients, ensuring stability of the formulation. All prepared formulations (S1–S6) complied with pharmacopeial requirements for weight variation, hardness, friability, and drug content, indicating acceptable tablet quality. The presence and concentration of superdisintegrants significantly influenced the wetting time, disintegration time, and drug release profile of the tablets.

Among all formulations, S3 containing croscarmellose sodium demonstrated superior performance with the lowest disintegration time, highest water absorption ratio, and maximum drug release within a short time period. In vitro permeability evaluation using the Caco-2 cell model further confirmed enhanced permeability of the optimized formulation compared with the

marketed tablet, indicating improved potential oral bioavailability. Stability studies performed for three months showed that the optimized formulation remained physically stable with minimal changes in drug content, disintegration time, and dissolution profile.

Therefore, the developed Sitagliptin fast dissolving tablet formulation (S3) can be considered a promising patient-friendly dosage form for the management of type 2 diabetes mellitus, offering rapid drug release, improved absorption, and enhanced patient compliance compared to conventional tablets.

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