

Development and Characterization of a Solid Dispersion of an Anti-Diabetic Drug Using Pectin as a Natural Polymer

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Abstract

Aim: The current study sought to improve the solubility and oral bioavailability of gliclazide by creating solid dispersions and oral dispersible tablets (ODTs) with enhanced physicochemical characteristics and maintained antidiabetic action. **Methods:** Preformulation studies were conducted to evaluate the physicochemical properties of gliclazide, including physical appearance, melting point, solubility, and partition coefficient. Solid dispersions were prepared using hydrophilic carriers-pectin and PVP K30 and subsequently characterized by Fourier Transform Infrared Spectroscopy and X-Ray Diffraction analysis. The in vitro antidiabetic efficacy of the formulations was assessed through α -amylase and α -glucosidase inhibition assays. Additionally, in vitro dissolution profiles were evaluated. Stability studies were performed in accordance with ICH guidelines over six months. **Results:** Gliclazide was observed as a white crystalline powder with melting point of 173°C, confirming purity. It showed poor aqueous solubility (0.015–0.020 mg/mL) at physiological pH ranges and moderate lipophilicity (logP 1.82), which justified the solid dispersion formulation with pectin and PVP K30. The optimization of formulation F3 showed enhanced in vitro antidiabetic activity with 49.2% and 57.5% of α -amylase and α -glucosidase, respectively. Physical and chemicals integrity of the formulation was maintained through six months of ICH recommended conditions, confirmed by stability studies, supporting its commercial potential. **Conclusion:** Solid dispersion-based ODTs offer an effective approach to improving the solubility, formulation performance, and therapeutic potential of Gliclazide. Formulation F3 emerged as the optimized candidate with superior physicochemical properties, antidiabetic activity, and stability.

Keywords: Gliclazide, oral dispersible tablets, solid dispersion, solubility enhancement, antidiabetic activity, stability studies

INTRODUCTION

Diabetes mellitus has transformed into a worldwide health emergency, with its prevalence widespread dramatically over the past few decades driven by urbanization, aging populations, demographic and environmental shifts and emphasizes behaviors like diet and inactive lifestyles. According to the International Diabetes Federation (IDF, 2021), approximately 537 million adults aged 20–79 years were living with diabetes worldwide in 2021, representing one in ten adults a nearly 50% increase within two decades. The burden falls disproportionately on South-East Asia and Western Pacific regions, with China and India serving as epicenters of the epidemic; India alone had an estimated 77 million people with diabetes in 2019, projected to reach 134 million by 2045 (IDF, 2021). Type 2 diabetes mellitus (T2DM) accounts for 90–95% of cases, while Type 1 diabetes and

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gestational diabetes constitute the remainder (American Diabetes Association, 2022). The mortality burden is substantial, with diabetes causing approximately 6.7 million deaths worldwide in 2021, equivalent to one death every five seconds, accompanied by healthcare expenditures reaching USD 966 billion, a 316% rise over fifteen years, with over 75% of this burden falling on low- and middle-income nations (IDF, 2021; World Health Organization, 2022).

The pathophysiology of DM comprises chronic hyperglycemia resulting from impaired insulin secretion, insulin action, or both due to β -cell dysfunction, leading to interruption in carbohydrate, fat, and protein metabolism with resulting chronic metabolic dysfunction of multiple organ systems (American Diabetes Association, 2022). T1DM, a class of DM, consequence of autoimmune-mediated destruction of pancreatic β -cells influenced by genetic susceptibility and environmental triggers (Knip and Siljander, 2016), while T2DM is characterized by β -cells function impaired and insulin insensitivity in peripheral tissues, including adipose tissues, skeletal tissues, and hepatic tissues, which are closely associated with obesity and chronic metabolic inflammation (DeFronzo et al., 2015).

Prevailing therapeutic management, including constrained lifestyle, oral medication, and insulin therapy, possesses inherent shortcomings in long-term glycemic control. Several oral hypoglycemic medications illustrated lack of water solubility, leading to inconsistent and unpredictable therapeutic effects and variable absorption due to variable oral bioavailability (Savjani et al., 2012). The Biopharmaceutical Classification System (BCS) categorizes numerous hypoglycemic medications including pioglitazone, glibenclamide, repaglinide, and glimepiride as Class II compounds (low solubility, high permeability), where dissolution represents the rate-limiting step for absorption (Amidon et al., 1995; Babu et al., 2010). This poor aqueous solubility results in reduced dissolution rates, inadequate absorption, highly variable bioavailability, delayed onset of action, and compromised glycemic control (Lipinski, 2002; Kawabata et al., 2011). Furthermore, higher required doses increase the risk of dose-dependent adverse effects and reduce patient compliance (Di et al., 2012).

Multiple tactics have been exploited to address solubility limitations in the recent past. Several conventional techniques, including micronization, salt formation, and surfactant addition, offer only minor enhancements and are frequently insufficient for highly fat-dissolving substances (Savjani et al., 2012). Advanced nanotechnology formulations, such as cyclodextrin complexes and lipid-based systems, offer convenience and are associated with rise in production cost, complex manufacturing processes, and regulatory challenges (Liu et al., 2013; Loftsson and Brewster, 2010; Pouton, 2006). Studies show that solid dispersions of glibenclamide, pioglitazone, and repaglinide have demonstrated a significant increase in dissolution rate and bioavailability (Patel et al., 2014).

Given the rising global burden of diabetes, the prevalence of solubility-limited anti-diabetic medications, and the limitations of existing formulation approaches, there exists a critical need for safe, effective, and economical strategies to enhance the oral bioavailability of these therapeutic agents. Pectin-based solid dispersions represent a promising approach that combines the solubility-enhancing capabilities of solid dispersion technology with the biocompatibility, safety, and sustainability of natural polymers. The present study, therefore, aims to develop, formulate, and characterize pectin-based solid dispersions of a selected poorly soluble anti-diabetic drug, with the objectives of enhancing solubility and dissolution rate, improving oral bioavailability and therapeutic efficacy, exploring natural polymer carriers as safer alternatives to synthetic excipients, and evaluating formulation stability and reproducibility to ensure practical applicability in chronic diabetes management.

MATERIALS AND METHODOLOGY

Chemicals Used

The drug as well as different excipients and reagents utilized in this study are standard grades, Gliclazide (Sigma-Aldrich), Pectin (Loba Chemie), PVP K30 (HiMedia), Microcrystalline Cellulose (MCC, Avicel PH101) (HiMedia), Sodium Starch Glycolate (SSG) (HiMedia), Magnesium Stearate (HiMedia), Colloidal Silicon Dioxide (HiMedia), and distilled water.

Drug Profile

Gliclazide, an anti-diabetic drug from the sulfonylurea class, is chemically designated as 1-(3-azabicyclo [3.3.0] oct-3-yl)-3-(4-methylphenylsulfonyl) urea, with a molecular formula of $C_{15}H_{21}N_3O_3S$ and molecular weight of 323.41 g/mol. It stimulates insulin secretion from pancreatic β -cells while reducing hepatic glucose output, achieving approximately 70–80% oral bioavailability with extensive plasma protein binding of 94–96%. The drug undergoes hepatic metabolism primarily via CYP2C9 and has an elimination half-life of 10–12 hours, with excretion predominantly through urine. Gliclazide is available in tablet dosages of 30 mg, 60 mg, 80 mg, and 120 mg, and exhibits a melting point of 179–181°C. It is practically insoluble in water but soluble in organic solvents such as methanol. Common adverse effects include hypoglycemia, nausea, headache, dizziness, and weight gain.

Physicochemical Parameters of Drug Gliclazide

Pre-Formulation Appearance of the Drug

Sense Organ investigated Gliclazide's physical appearance. It was described physically using organoleptic traits such as color, taste, and odor. All physical properties are compared to specified specifications.

Determination of the Melting Point Method

The melting point of gliclazide was determined using a digital capillary melting point apparatus (Mel-Temp). The dried sample was deposited in closed capillary tubes and placed into the apparatus channels, with the heating rate carefully controlled to ensure gradual temperature elevation. The melting process was observed through a lens positioned approximately 15 cm from the sample, recording both the onset and completion temperatures to establish the melting range. After complete melting, capillaries were removed and properly discarded, with compressed air used to accelerate cooling. The procedure was performed in triplicate, and the observed melting point was compared with literature values to assess drug purity. The experimental melting point range of 179–181°C corresponded with the standard reference value reported in the literature (Sweetman, 2009).

Determination of Solubility

The shake-flask method was introduced to assess for determining drug equilibrium solubility. The drug mixed in solvent placed in closed container and shaking at constant temperature (25°C or 37°C) for 24–48 hours until saturation. Filtered and removed undissolved particles. The concentration in the filtrate represents equilibrium solubility. Experiments are performed in triplicate, with results expressed as mean $\pm$ standard deviation (Baka et al., 2008).

Determination of Partition Coefficient (P)

The partition coefficient (P) quantifies drug lipophilicity, defined as the ratio of the concentration of an un-ionized substance distributed between two immiscible phases at equilibrium, typically n-octanol (representing lipids) and water (representing an aqueous environment). It is expressed as $P = C_{octanol}/C_{water}$, where $C_{octanol}$ and C_{water} are the drug's equilibrium concentrations in the octanol and aqueous phases, respectively. The value is commonly reported as the logarithmic form, $\log P$. A high $\log P$ indicates greater lipophilicity (preference for the lipid phase), whereas a low $\log P$ indicates greater hydrophilicity (preference for the aqueous phase) (Leo et al., 1971; Sangster, 1997).

Characterization of Drug Gliclazide

Fourier Transform Infrared (FTIR) Spectroscopy

FTIR spectroscopy of pure gliclazide drug powder was performed using the potassium bromide (KBr) pellet technique. Spectral data were acquired in transmittance mode at a resolution of 4 cm^{-1} over the range of 4000–400 cm^{-1} using a ParkinElmer. The characteristic peaks corresponding to gliclazide functional groups were analyzed and compared with reference spectra and literature values to confirm drug identity and purity.

X-Ray Diffraction (XRD) Analysis

To investigate the crystalline nature of pure gliclazide, XRD analysis was carried out. The drug sample was carefully triturated into a fine powder and uniformly placed onto the sample holder. XRD patterns were recorded using an X-ray diffractometer equipped with a Cu-K α radiation source ($\lambda = 1.5406 \text{ \AA}$). The scanning was performed over a 2θ range of 5° to 40° at ambient temperature. The resulting X-ray diffractogram exhibited the presence of sharp and distinctive peaks, characteristic of crystalline substance of gliclazide.

In Vitro Evaluation Studies

α -Amylase and α -Glucosidase Inhibition Assays

The α -amylase and α -glucosidase inhibitory activity of gliclazide was evaluated using a method, as reported by Young et al. (2008). A stock solution for gliclazide was prepared in 5% DMSO. From this, 50 μg of the drug was mixed with 500 μL of 20 mM sodium phosphate buffer (Na-PB) (pH 6.8) containing 20 μL of α -glucosidase enzyme solution (0.5 mg/mL). The reaction mixture was pre-incubated at 37°C for 10 minutes. Following pre-incubation, 500 μL of 1 mM p-nitrophenyl- α -D-glucopyranoside (pNPG) substrate prepared in 0.02 M Na-PB was added, and the mixture was further incubated at 37°C for 15 minutes to allow enzymatic action. The reaction was terminated by adding 1.0 mL of 0.1 M Na_2CO_3 , and the yellow-colored p-nitrophenol formed was quantified by measuring absorbance at 405 nm using a UV-Vis spectrophotometer. All tests were performed in triplicate. Control reactions were performed in the same manner, excluding gliclazide. The percentage inhibition of α -amylase and α -glucosidase activity was calculated using the standard formula:

$$\text{Inhibition (\%)} = \left(\frac{\text{Absorption of control} - \text{Absorption of compound}}{\text{Absorption of control}} \right) \times 100.$$

In Vitro Dissolution Study

In vitro dissolution studies of gliclazide solid dispersion tablets were conducted using a USP Type II (paddle) apparatus to evaluate drug release behavior. The dissolution medium consisted of 900 mL phosphate buffer (pH 6.8) maintained at $37 \pm 0.5^\circ\text{C}$ with a paddle rotation speed of 50 rpm to simulate physiological conditions. One tablet was placed in each dissolution vessel, and 5 mL samples were withdrawn at predetermined time intervals of 5, 10, 15, 30, 45, and 60 minutes. Each withdrawn sample was immediately replaced with an equal volume of fresh dissolution medium maintained at the same temperature to preserve sink conditions. The collected samples were filtered through 0.45 μm membrane filters, appropriately diluted, and analyzed using a UV-visible spectrophotometer at the λ_{max} of gliclazide. The cumulative percentage of drug released was calculated from a calibration curve. All dissolution tests were performed in triplicate. Dissolution profiles of various formulations were compared to identify the optimal formulation and to assess the influence of polymer concentration on the release characteristics of gliclazide (Nathi et al., 2023).

Stability Studies as Per the ICH Guidelines

Stability studies of drug substances are essential to assess the environmental factors such as temperature, humidity, and light influence over period of time. These studies follow guidelines established by the International Council for Harmonisation (ICH), which outlines requirements for stability testing of new drug substances and products. Drugs are stored under controlled conditions simulating expected storage and distribution environments. At predetermined intervals, samples are withdrawn and evaluated for physical, chemical, and microbiological stability using validated analytical methods. Key parameters assessed include potency, degradation products, dissolution rate, and appearance. The resulting data determines the product's shelf life, storage conditions, and handling recommendations. Stability testing also supports regulatory submissions and ensures that the product maintains its quality and efficacy throughout its intended shelf life, playing a critical role in patient safety and regulatory compliance (ICH, 2003).

RESULTS AND DISCUSSIONS

Physicochemical Parameters of Drug Gliclazide

Physical Appearance

As part of the pre-formulation evaluation, the physical characteristics of gliclazide were assessed to confirm its identity and suitability for formulation development. Table 1 represents the physical and organoleptic appearance of the drug. The physical appearance of fine powder of crystalline Gliclazide drug is shown in Figure 1.

Table 1. Physical appearance.

Parameter	Observed value
Colour	White / Off-white.
Odour	Odourless / characteristic.
Taste	Slightly bitter.
Physical Form	Crystalline powder.



Figure 1. Physical appearance of finely powdered crystalline Gliclazide.

Melting Point

The drug Gliclazide exhibited a sharp melting point at 173°C, which agrees with reported literature values by Rajamma et al. (2015) on the polymorphism of gliclazide, which identified three distinct polymorphic forms with different melting endotherms. Using differential scanning calorimetry (DSC), Form I exhibited an endothermic peak at 162.93°C, Form II melted between 171.2–172.35°C, and Form III between 168.93–169.86°C

Solubility

The solubility of gliclazide was evaluated in various solvents and buffer systems to understand its dissolution behavior, which directly influences oral bioavailability. From Table 2, the drug exhibited poor aqueous solubility, with a value of 0.015 ± 0.002 mg/mL in distilled water. In 0.1 N HCl (pH 1.2), solubility increased slightly to 0.020 ± 0.003 mg/mL, indicating marginal improvement under simulated gastric conditions. In phosphate buffer systems representing intestinal pH, solubility remained consistently low, measuring 0.018 ± 0.002 mg/mL at pH 6.8 and 0.017 ± 0.002 mg/mL at pH 7.4. These findings confirm that gliclazide is practically insoluble across physiologically relevant pH ranges, highlighting the need for solubility enhancement strategies. Approaches, such as solid dispersion with polymers like pectin and PVP K30, may, therefore, be beneficial in improving the dissolution rate and oral absorption of gliclazide. These findings align closely with previously reported values on Seedher and Kanojia (2009), reported that the aqueous solubility of various antidiabetic drugs, including gliclazide, was less than 0.04 mg/mL, with minimal pH-dependent variation.

Table 2. Solubility of gliclazide in various solvents and their solubility.

Solvent / medium	Observed solubility (mg/mL) $\pm$ SD
Distilled Water	0.015 $\pm$ 0.002
0.1 N HCl (pH 1.2)	0.020 $\pm$ 0.003
Phosphate Buffer (pH 6.8)	0.018 $\pm$ 0.002
Phosphate Buffer (pH 7.4)	0.017 $\pm$ 0.002

Partition Coefficient

The lipophilicity of gliclazide was assessed by determining its partition coefficient (log P), which serves as an indicator of the drug's membrane permeability and overall absorption potential. The observed log P value of 1.82 ± 0.05 indicates moderate lipophilicity, reflecting a balanced affinity for both lipid and aqueous environments. While this characteristic supports adequate membrane permeability, it also contributes to the drug's limited solubility in purely aqueous media.

This finding aligns with previously reported values in the literature. Remko (2009) computed partition coefficients for various hypoglycemic agents using theoretical methods and reported values ranging from 1.8 to 5.9, classifying these compounds as lipophilic drugs with gliclazide falling at the lower end of this spectrum. Another study investigating solid-state properties reported log P value of 2.04 for gliclazide, consistent with moderate lipophilic character (Wassvik et al., 2006). In contrast, a more recent investigation using the shake-flask method at physiological pH reported a log D value of 0.34 at pH 7.4 in n-octanol/water systems, highlighting the pH-dependent nature of gliclazide's partitioning behavior due to its weakly acidic nature (pKa 5.8) (Maggi et al., 2015).

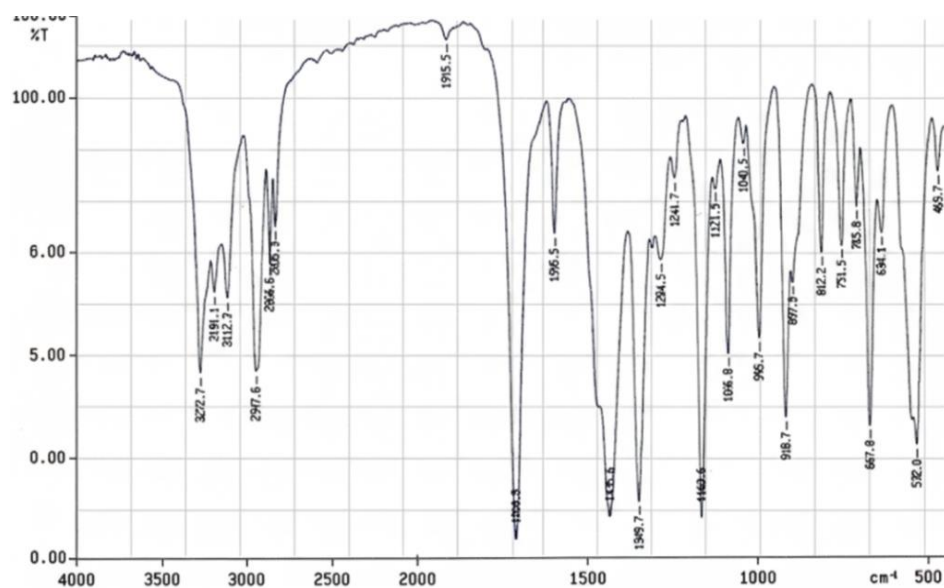
FTIR Analysis of Gliclazide

The FTIR spectrum of pure gliclazide confirmed the presence and integrity of characteristic functional groups essential for its pharmacological activity. Broad, medium-intensity N–H stretching vibrations observed in the region of 3300–3400 cm^{-1} corresponded to primary and secondary amines capable of hydrogen bonding, which may influence solubility and tablet disintegration behavior. As shown in Figure 2(a), a sharp, intense C=O stretching band in 1700–1720 cm^{-1} confirmed the urea carbonyl functionality, a critical component of the sulfonylurea pharmacophore responsible for the antidiabetic effect. Aromatic C–H stretches appearing at 3000–3100 cm^{-1} confirmed the stability of the aromatic ring system, while C–N stretching vibrations in the 1200–1350 cm^{-1} region indicated intact amine linkages. The presence of strong, well-defined S=O stretching bands at 1150–1350 cm^{-1} confirmed the integrity of the sulfonyl group, which is essential for gliclazide's bioactivity. N–H bending vibrations observed at 1600–1650 cm^{-1} further supported the retention of amine functionalities. These spectral features are consistent with previously reported FTIR characterizations of gliclazide. Rajamma et al. (2015) reported characteristic absorption bands for gliclazide at 3269 cm^{-1} (N–H stretching), 1712 cm^{-1} (C=O stretching), and 1348 cm^{-1} (S=O stretching), confirming the identity of the drug in its pure form.

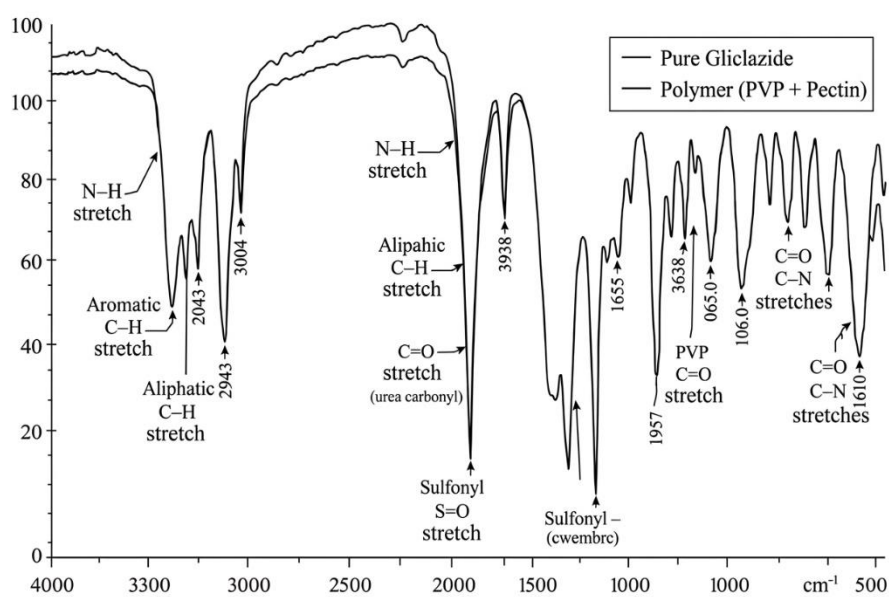
The FTIR spectra of gliclazide in combination with pectin and PVP K30 displayed all characteristic peaks of the pure drug, confirming that no chemical degradation or alteration of functional groups occurred during the solid dispersion preparation process. The absence of new peaks or significant shifts in existing peaks indicated chemical compatibility between gliclazide and the selected polymers. However, slight broadening of some absorption bands was observed, particularly in the N–H and O–H stretching regions (3200–3500 cm^{-1}) and the carbonyl region (1700–1750 cm^{-1}) (Figure 2(b)). This peak broadening suggests physical interactions, such as hydrogen bonding between the drug and polymer matrices, rather than chemical bond formation or degradation. These observations align with findings from previous compatibility studies. Febriyenti et al. (2019) reported that solid dispersions of gliclazide with PVP K30 and PEG 6000 retained all major peaks of gliclazide with only minor broadening, indicating physical interaction without chemical incompatibility.

XRD Patterns of Pure Gliclazide

The X-ray diffraction pattern of pure gliclazide exhibited multiple sharp, well-defined diffraction peaks at characteristic 2θ values of approximately 10.5° , 15.2° , 17.8° , 18.6° , 22.3° , and 25.7° (Figure 3). The presence of these intense and narrow peaks confirms the highly crystalline nature of the drug, indicating an ordered molecular arrangement within the crystal lattice. This crystalline structure is typical of pure gliclazide and is directly associated with its poor aqueous solubility, as tightly packed crystal lattices require greater energy for dissolution. These findings are consistent with previously reported XRD patterns for gliclazide in the literature. Rajamma et al. (2015) characterized gliclazide polymorphs and reported characteristic diffraction peaks for the stable form (Form II) at 2θ values of 10.6° , 15.4° , 17.9° , 18.8° , 22.4° , and 25.9° , which closely correspond to the observations in the present study. The sharp, well-resolved peaks were indicative of a highly crystalline structure with minimal amorphous content.



(a)



(b)

Figure 2. (a) FTIR of pure dug gliclazide, (b) FTIR of pure drug + polymer.

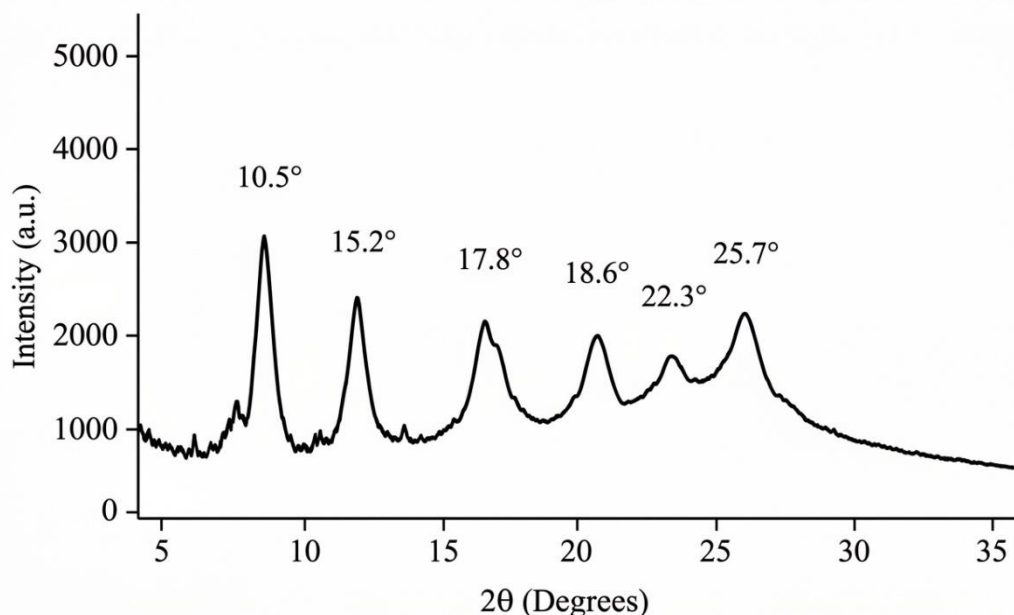


Figure 3. X-ray diffraction (XRD) patterns of pure gliclazide.

***In Vitro* Inhibition Activity (α -Amylase and α -Glucosidase Inhibition Assays)**

The *in vitro* antidiabetic potential of pure Gliclazide and its oral dispersible tablet (ODT) formulations were evaluated at a concentration of 50 $\mu\text{g/mL}$ by assessing their inhibitory effects on α -amylase and α -glucosidase. The pure drug served as the reference standard, demonstrating $45.2 \pm 1.5\%$ inhibition of α -amylase and $52.8 \pm 1.8\%$ inhibition of α -glucosidase. All ODT formulations exhibited slightly enhanced inhibitory activity compared to the pure drug, suggesting that the solid dispersion of pectin and excipients may improve enzyme interaction. Among the formulations, F3 showed the highest inhibition, with $49.2 \pm 1.1\%$ against α -amylase and $57.5 \pm 1.6\%$ against α -glucosidase. The other formulations (F1, F2, F4, F5) also displayed moderate enhancement, with inhibition ranging from 47.5–48.5% for α -amylase and 55.3–56.8% for α -glucosidase (Figure 4). Overall, the results confirm that solid dispersion-based ODT formulations of Gliclazide maintain effective antidiabetic activity while offering the advantages of improved solubility and patient compliance. These findings align with study conducted by Patil and Kumar (2023) suggested that the solid dispersion formulation strategy simultaneously and proportionally enhances the inhibitory potential of Gliclazide against both carbohydrate-hydrolyzing enzymes, supporting its potential for improved postprandial glycemic control.

***In vitro* Dissolution Study**

The *in vitro* dissolution profiles of five gliclazide solid dispersion tablet formulations (F1–F5) were evaluated using USP apparatus II (paddle method) in phosphate buffer pH 6.8 maintained at $37 \pm 0.5^\circ\text{C}$. All formulations demonstrated progressive drug release over the 60-minute study period, confirming the effectiveness of the solid dispersion approach in enhancing the dissolution characteristics of poorly soluble gliclazide. As shown in Figure 5, formulation F3 exhibited the fastest and highest cumulative drug release among all formulations, with release values of $25.8 \pm 1.5\%$ at 5 minutes, $62.5 \pm 2.0\%$ at 15 minutes, and $96.4 \pm 2.8\%$ at 60 minutes. This superior dissolution profile indicates optimal solubilization and rapid drug availability in aqueous medium, attributable to the effective conversion of crystalline gliclazide to an amorphous or molecularly dispersed state within the polymer matrix. Formulation F5 demonstrated the second-highest release, achieving $93.5 \pm 2.7\%$ drug release at 60 minutes. Formulations F1 and F4 showed comparatively slower release rates, with cumulative releases of $88.5 \pm 2.5\%$ and $85.3 \pm 2.4\%$ at 60 minutes, respectively. Formulation F2 exhibited intermediate behavior, with $91.8 \pm 2.6\%$ drug released at the end of the study period. These dissolution patterns align with findings reported in previous investigations of gliclazide solid dispersions. Febriyenti et al. (2019)

reported that gliclazide solid dispersions prepared with PVP K30 and PEG 6000 demonstrated significantly enhanced dissolution rates compared to pure drug, with optimized formulations achieving over 90% drug release within 60 minutes. The rapid dissolution was attributed to improved wettability and reduced crystallinity of gliclazide within the polymer matrix.

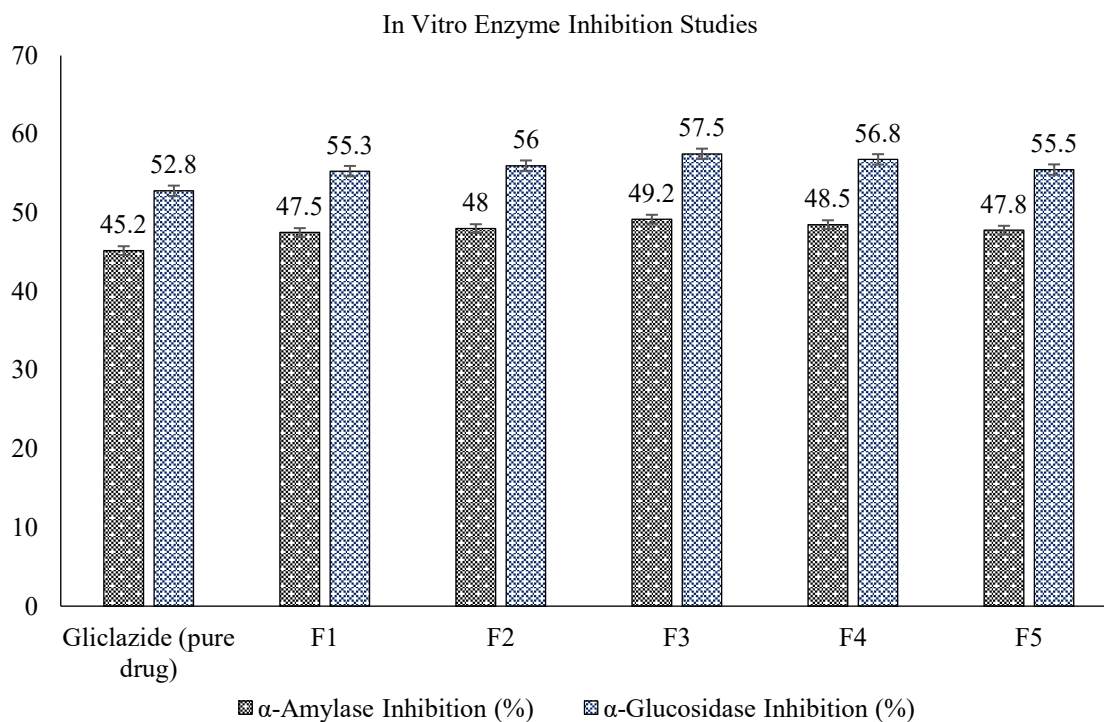


Figure 4. *In Vitro* enzyme inhibition studies.

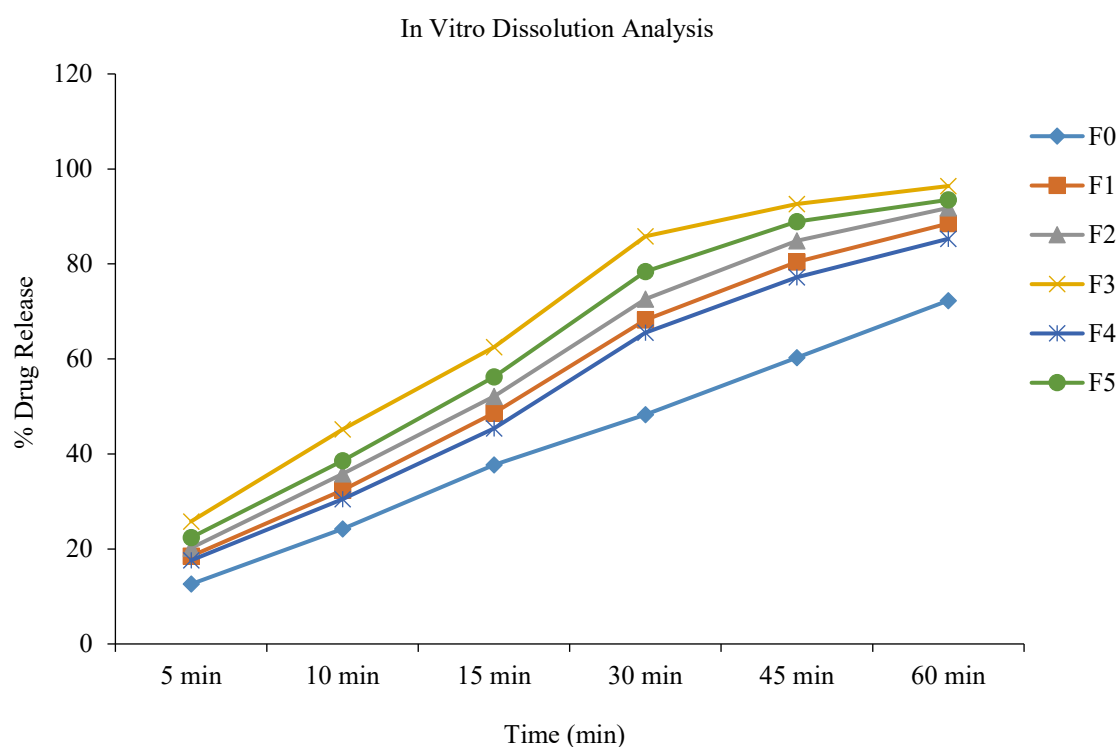


Figure 5. *In-Vitro* dissolution study of gliclazide and its formulation.

Stability Studies as Per the ICH Guidelines

The stability of the optimized gliclazide oral dispersible tablet (ODT) formulation was evaluated under International Council for Harmonisation (ICH) recommended storage conditions over a period of six months represented in Table 3. Tablets were stored at controlled room temperature ($25^{\circ}\text{C} \pm 2^{\circ}\text{C}$ / $60\% \text{ RH} \pm 5\% \text{ RH}$) and under accelerated conditions ($40^{\circ}\text{C} \pm 2^{\circ}\text{C}$ / $75\% \text{ RH} \pm 5\% \text{ RH}$) to assess physical and chemical stability throughout the study period.

The optimized formulation demonstrated excellent physical and chemical stability when stored at $25^{\circ}\text{C}/60\% \text{ RH}$ over the six months. Tablets maintained their original white appearance with a smooth surface throughout the study duration. Hardness values remained consistently within the range of $4.9\text{--}5.0 \text{ kg/cm}^2$, indicating no significant softening or hardening of the tablet matrix. Friability values ranged from 0.20% to 0.25% , remaining well below the pharmacopoeial limit of 1% and confirming adequate mechanical strength. Drug content analysis revealed consistently high values between 99.0% and 99.5% of the labeled claim, indicating no significant drug degradation. Dissolution studies demonstrated robust release characteristics, with over 91% of drug released within 30 minutes throughout the storage period. These findings confirm that the formulation maintains its quality attributes under ambient storage conditions.

Under accelerated storage conditions, minor physical changes were observed over the six months. Slight tablet softening was noted between one and three months of storage, accompanied by minor color changes at the six-month time point. Hardness values showed a modest decrease to 4.6 kg/cm^2 at the end of the study period, while friability increased marginally to 0.32% , though remaining within acceptable limits. Drug content remained above 98% of the labeled claim throughout the study, indicating good chemical stability of gliclazide within the formulation matrix. Dissolution testing revealed 89.5% drug release at 30 minutes after six months of accelerated storage, representing a slight reduction compared to initial values but still indicating acceptable release characteristics.

Table 3. Stability study of optimized gliclazide ODT formulation.

Storage condition	Time interval	Appearance	Hardness (kg/cm^2)	Friability (%)	Drug content (%)	Dissolution (% drug released at 30 min)
$25^{\circ}\text{C}/60\% \text{ RH}$	0 months	White, smooth	5.0 ± 0.12	0.20	99.5 ± 0.5	92.0 ± 1.5
$25^{\circ}\text{C}/60\% \text{ RH}$	3 months	No change	5.0 ± 0.10	0.22	99.3 ± 0.4	91.5 ± 1.6
$25^{\circ}\text{C}/60\% \text{ RH}$	6 months	No change	4.9 ± 0.13	0.25	99.0 ± 0.5	91.0 ± 1.7
$40^{\circ}\text{C}/75\% \text{ RH}$	0 months	White, smooth	5.0 ± 0.12	0.20	99.5 ± 0.5	92.0 ± 1.5
$40^{\circ}\text{C}/75\% \text{ RH}$	1 month	Slight softening	4.8 ± 0.14	0.28	98.8 ± 0.6	90.5 ± 1.8
$40^{\circ}\text{C}/75\% \text{ RH}$	3 months	Slight softening	4.7 ± 0.15	0.30	98.5 ± 0.7	90.0 ± 1.9
$40^{\circ}\text{C}/75\% \text{ RH}$	6 months	Minor color change	4.6 ± 0.16	0.32	98.0 ± 0.8	89.5 ± 2.0

CONCLUSION

In conclusion, the systematic evaluation of gliclazide solid dispersions successfully established that the solid dispersion approach, particularly formulation F3 with optimized polymer composition, significantly enhances the dissolution rate of poorly soluble gliclazide. These findings align with previous studies demonstrating the efficacy of solid dispersion technology for BCS Class II drugs. The optimized formulation F3 represents a promising candidate for improving oral bioavailability and therapeutic efficacy of gliclazide in the management of diabetes mellitus. Further studies involving *in vivo* pharmacokinetic evaluation and long-term stability assessment are recommended to establish the clinical potential of this formulation.

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