



REVIEW ARTICLE

SOLID DISPERSION-BASED APPROACHES FOR IMPROVING THE DISSOLUTION AND BIOAVAILABILITY OF GLICLAZIDE: A REVIEW

Rishikesh Kumar Dubey^{*1}, Rohit Verma², Vivek Tomar³, Jitendra Singh Choudhary³

Research Scholar¹, Associate Professor², Professor³, SR Group of Institutions (College of Pharmacy), Jhansi-284419, Uttar Pradesh, India.

Article History

Received: 12 March 2026

Revised: 02 May 2026

Accepted: 18 June 2026

Published: 25 June 2026

Correspondence should be addressed to

Rishikesh Kumar Dubey,
Research Scholar,
SR Group of Institutions
(College of Pharmacy), Jhansi-
284419, Uttar Pradesh, India.

Email- rishikeshgolu1999@gmail.com

ABSTRACT: Gliclazide belongs to a class of drugs known as sulfonylureas, which are used to treat type 2 diabetes mellitus. Due to its low water solubility and slow dissolution, however, it may also be poorly absorbed in the small intestine and may also be responsible for pharmacokinetic variability. This review assesses solid dispersion techniques used for the improvement of gliclazide dissolution and bioavailability by considering the selection of carrier, amorphization, the methods of manufacture, the characterization of the products and the *in vivo-in vitro* relationship. Structured literature search was done on PubMed, Scopus, Web of Science and Google Scholar up to October 2024. After screening and eligibility, 66 references comprising of experimental studies and technical sources were included. The evidence reviewed suggests that the dissolution of gliclazide can be improved to a greater or less extent by conventional and advanced solid dispersion systems. Various hydrophilic polymers (PVP K30, copovidone and Soluplus) and surfactant-based carriers (Poloxamer 188 and Gelucire 50/13) have been studied for increasing wettability and decreasing drug crystallinity. Animal studies, mostly in rodents, show increases in relative oral exposure and decreases in T_{max}, with some formulations and comparators showing greater and others less effects. Recrystallization, moisture instabilities, added tablet mass and possible change during compaction are all challenges. Solid dispersions have the potential to enhance the dissolution of gliclazide and the pharmacological activity in animals but have not been proven to be beneficial in humans. Additional studies to characterize formulation stability, manufacturing scale-up and human pharmacokinetic and clinical effects are required to validate for clinical relevance.

Keywords: Gliclazide, Solid Dispersions, Amorphous Systems, Dissolution Enhancement, BCS Class II, Hot-Melt Extrusion

I. INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a significant healthcare problem worldwide. In 2021, the IDF estimated that 537 million adults had diabetes, and this number is expected to reach 783 million by 2045 [1]. The characteristics of T2DM include insulin resistance, progressive beta-cell dysfunction and chronic hyperglycemia, which lead to vascular complications [2, 3]. Achievement of glycemic control, as measured by HbA1c, continues to be important in preventing complications [4].

Gliclazide is a second generation sulfonylurea, with a different clinical profile [5]. The GUIDE study and the ADVANCE trial have reported glycemic efficacy, and have analyzed safety and renal outcomes in appropriate populations [6,7]. Interpretation of clinical benefits should be based on the populations studied and the treatment regimens. The poor aqueous solubility and dissolution rate of conventional immediate-release gliclazide is pH dependent. It is generally considered to be BCS Class II, high permeability and dissolution limited absorption [8]. The

T_{max} reported depends on the formulation and research conditions [9].

Control of glucose after a meal is a therapeutic goal, however, the glucose response to gliclazide is dependent on the formulation and patient physiology and the relationship between dissolution and insulin secretion is rapid meal related glucose control [10]. Theoretically, increased dissolution will increase the likelihood of a better temporal alignment between the intestinal absorption of glucose and drug, however the potential for alleviating hypoglycemia risk or superior clinical performance must not be assumed based solely on this increased dissolution without dedicated human pharmacokinetic/ pharmacodynamic studies.

2. Literature Search and Review Methodology

The present structured narrative review includes references to literature available until October 2024. PRISMA 2020 is not meant as evidence of registration or formal systematic-review status, rather it is as a guidance for reporting [11].

2.1 Search Strategy and Database Retrieval

The databases PubMed/MEDLINE, Scopus, Web of Science Core Collection, and Google Scholar were searched for various combinations of the keywords “gliclazide” and “solid dispersion,” “amorphous solid dispersion,” “co-amorphous,” “eutectic,” “inclusion complex,” “nanosuspension,” “dissolution,” “solubility,” “bioavailability,” “hot-melt extrusion,” and “spray drying.” Foundational papers of formulation and relevant reviews were also screened.

2.2 Screening Funnel and Selection Criteria

A total of 284 records (PubMed 82, Scopus 94, Web of Science 61, Google Scholar 47) were identified. 188 records were screened for title/abstract after 96 were eliminated as duplicates. Of these, 104 were excluded due to irrelevant delivery routes, lack of data on isolated gliclazide formulation or lack of experimental characterization in solid state. 84 full texts were evaluated. 18 full texts were rejected for lack of quantitative dissolution data, lack of solid state confirmation (e.g., PXRD or DSC), or lack of an accessible English translation. The final set included 66 references, experimental studies and background/technical sources. Arithmetic checks of counts are done; the search log and eligibility decisions are kept to ensure the reproducibility. The accompanying literature includes information on pharmacology and solid-state properties, dissolution theory, carrier formulations, manufacturing/ characterization, and biorelevant testing, preclinical pharmacokinetics, stability, and quality by design.

3. Physicochemical Bottlenecks and Solid-State Characteristics of Gliclazide

3.1 Molecular Structure, Ionization Behavior, and Aqueous Solubility

Gliclazide ($C_{15}H_{21}N_3O_3S$; molecular weight, 323.41 g/mol) has a tolyl ring, a sulfonylurea bridge, and a bicyclic ring that is related to its pharmacological activity [12]. It contains a sulfonylurea group which is responsible for weaker acid ionization and intermolecular hydrogen bonding within the crystal. Reported pKa values are in the range 5.80-5.98. The majority of the molecule is ionized in acidic media (pH ~ 1.2), and the aqueous solubility is often less than 0.03 mg/mL. The solubility increases with the ionization of the drug and the increasing pH, but is limited for a poorly soluble oral dose (Fig. 1) [13,14].

At pH 6.8–7.4, reported equilibrium solubility is about 0.05–0.08 mg/mL [15]. They are study dependent estimates but are indicative of the small amount of solubility in water for this drug [16].

3.2 Crystallography, Polymorphism, and Thermodynamic Parameters

Polymorphism is known to affect the dissolution rate and stability of gliclazide. In general, commercial material is referred to as the stable form I, which is monoclinic in lattice type and involves sulfonylurea and carbonyl/sulfonyl hydrogen-bond networks [17,18].

The enthalpy of fusion is reported to be around 130-138 J/g, or ~42.0-44.6 kJ/mol when multiplied by the molecular weight (323.41 g/mol). Specific enthalpy (J/g) should not be confused with molar enthalpy (kJ/mol). Before publishing these numerical ranges should be verified with the original thermal studies [19-21].

Another, less stable Form II has also been found, which melts at a lower temperature and enthalpy than Form I [22]. It could be more quickly dissolved under certain circumstances, but metastable forms can change to the stable form when in aqueous suspension. The amount and speed of conversion will vary with experimental conditions and cannot be extrapolated [23].

3.3 Biopharmaceutics Classification System (BCS) Bottlenecks

Gliclazide is typically categorised as BCS Class II, which have limited aqueous solubility and permeability in the gut [24]. It is reported to have a log P of about 2.1–2.6. Therefore, the rate and extent of dissolution may affect absorption, but absorption is also dependent on factors other than the rate and extent of dissolution such as dosage form, gastrointestinal conditions, and patient factors [25].

Non-compression immediate release products have been linked to a lag time to peak and inter- and intra-individual variability. Food can change the speed and structure of stomach emptying and the contents of the stomach. The intent of solid dispersions is to enhance wetting, apparent solubility and dissolution rate, however their clinical significance will need to be defined by suitable *in vivo* studies [26].

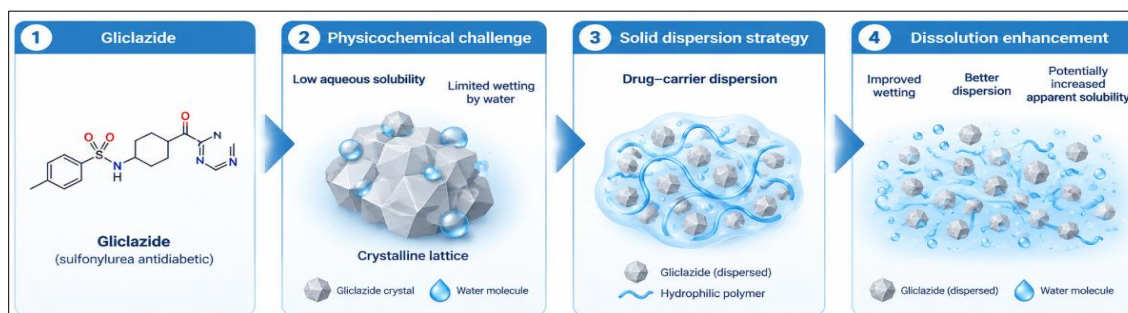


Figure 1: Physicochemical Limitations of Gliclazide and Dissolution Enhancement by Solid Dispersions

4. Theoretical Principles and Release Kinetics of Solid Dispersions

4.1 Classification and Evolution of Solid Dispersion Systems

Dispersions, which are solid dispersions, are used to increase the dissolution by dispersing a drug at molecular or amorphous or microcrystalline level in a carrier. It was developed early in the study of eutectic systems, and has been extended to polymeric matrices and to modern manufacturing processes [27].

- First generation are systems that are based on crystalline carriers, like PEG 4000/6000, or urea. They can enhance the wetting and can also create a eutectic or a microcrystalline system, however, the enhancement can be restricted by the crystallinity of the carrier itself [28].
- In second generation systems, amorphous polymers like PVP, copovidone, Soluplus or HPMC are added to avoid crystallization and to maintain supersaturation [29].
- Third generation systems involve the inclusion of surfactants or lipidic carriers (*e.g.* poloxamers, Gelucires) to enhance wetting and solubilisation; a ternary polymer–surfactant system may contain both of these properties combined [30].
- Other sophisticated techniques are co-amorphous systems and loading of drugs in mesoporous silica. Drug-specific interactions, pore properties, loading and evidence of solid-state stabilization are all important to their performance; claims are directly primary evidence for gliclazide-specific claims [31].

4.2 Mathematical Dissolution Kinetics: Modified Noyes-Whitney Principles

$$dM / dt = (D \cdot A / h) \cdot (C_s - C_t)$$

$$dC / dt = (1 / V) \cdot (dM / dt) = (D \cdot A / (V \cdot h)) \cdot (C_s - C_t)$$

- High energy amorphous drug production may result in increased apparent saturation concentration, but it is only transient and system dependent [32].
- Effective surface area can be enhanced by dispersion of the drugs and better deaggregation [33].
- The diffusion boundary layer can be affected by rapid polymer hydration which can enhance wetting and local mixing [34].
- Limited agglomeration can be achieved by the use of hydrophilic carriers and surfactants, which reduce the interfacial tension [35].

4.3 Thermodynamic Driving Force: The 'Spring and Parachute' Paradigm

Amorphous dispersions can be supersaturated as the amorphous state is more free energy than the stable crystal state [36]. The solution obtained will be metastable and precipitate or crystallize.

This process can be explained using the 'spring and parachute' model: the 'spring' is the high initial concentration of the drug in solution, and the 'parachute' is a suitable polymer which slows nucleation, crystal growth, and/or precipitation [37]. This supersaturation time needs to be determined for each formulation and should not be taken for granted (Fig. 2).

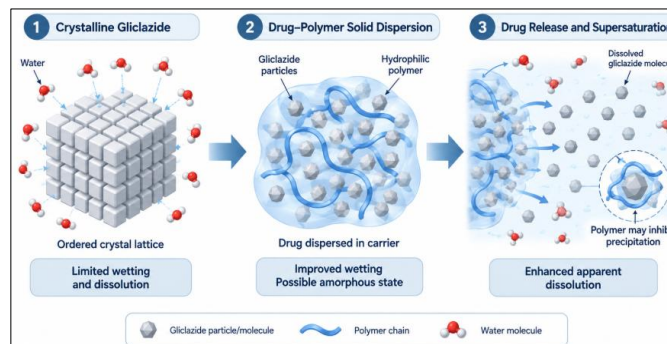


Figure 2: Mechanisms of Dissolution Enhancement by Solid Dispersions of Gliclazide

5. Polymer and Carrier Matrix Selection: Mechanisms and Performance

The initial dissolution and supersaturation along with the potential for recrystallization in storage are influenced by the carrier selected [38]. There is no universal polymer that works best for all drug loadings and processes.

5.1 First-Generation Crystalline Carriers: Polyethylene Glycol and Urea

Early gliclazide dispersions were composed of PEG 4000/6000 and urea. Chowdary and Rao showed that PEG and urea based systems exhibited enhanced dissolution than pure drug [39]. The surface activity of PEG can enhance wetting and decrease agglomeration, however the semi-crystalline nature and low melting range can allow for phase separation and/or recrystallization. The results are dependent on the carrier ratio and the preparation method [40].

5.2 Second-Generation Polymeric Matrices: PVP, Copovidone, and Soluplus

To enhance dissolution and crystal inhibition, polymeric amorphous matrices like PVP K30, copovidone and Soluplus are employed [41]. The interaction with PVP is not directly referenced from the Biswal et al. paper, which refers to gliclazide–PEG 6000. The Biswal et al. paper refers to gliclazide–PEG 6000, not PVP, and should not be cited as direct evidence of PVP interactions. Dissolution percentages and stability information should be checked against each of the primary papers [42] for exactness.

5.3 Third-Generation Surfactant and Lipid Carriers: Poloxamers and Gelucires

In third generation systems surface active carriers like poloxamers are used to enhance wetting and solubilization.

The author of this work, Cirri et al., examined gliclazide–poloxamer dispersions [43] and the release results should only be quoted with the method and medium used in the original work.

Gelucires are a mixture of glycerides and PEG esters, and can affect wetting and dispersion behaviour. The reported dissolution results of gliclazide also differ depending on the grade, ratio, and the way the preparation is prepared [44].

Polymer–surfactant dispersions can be a mixture of polymer-mediated inhibition of crystallization and enhanced wetting. Mishra and Singh examined the influence of PVP K30 and sodium lauryl sulfate on gliclazide [45].

5.4 Advanced Architectures: Co-Amorphous Systems and Mesoporous Silicas

A co-amorphous system involves mixing a low-molecular-weight co-former with the drug to stabilise the drug:co-former amorphous mixture, and the mesoporous silica can be used to trap drug molecules in the pores, and to reduce crystal growth. Ambrogi *et al.* investigated the loading of gliclazide in ordered mesoporous silicas as SBA-15 and MCM-41 and reported improved dissolution [46]. The level of amorphization and the proposed stabilization mechanism should be based on the data of the solid-state samples and not the size of the pore.

6. Manufacturing Technologies for Gliclazide Solid Dispersions

6.1 Hot-Melt Extrusion (HME) and Polymer Thermoplasticity

Hot-melt extrusion (HME) is a continuous process, where the drug and carrier are mixed and fed into a heated barrel and

screw system [46–48]. It can be used for scale-up, but suitability will depend on polymer thermoplasticity, drug stability, residence time and process design.

The HME is typically solvent-free, minimizing the use of organic solvents, but various parameters such as thermal degradation, process safety and product quality controls must be assessed.

6.2 Spray Drying and Solvent Evaporation

Spray drying is a method that generates dispersions by atomizing a drug-carrying dispersion solution and quickly removing the solvent, which may result in the drug being trapped in an amorphous dispersion matrix. The residual solvent content, particle properties and physical stability are affected by the solvent used, feed composition, inlet/outlet temperatures, and drying conditions [48].

6.3 Supercritical Fluid (SCF) Processing and Electrospinning

Precipitation using pressurized CO₂ as antisolvent is called supercritical-fluid methods and these methods have been employed for the precipitation of drug–carrier particles. While depressurization can be used to remove CO₂, it is sometimes necessary to use other organic co-solvents, and levels of residual solvent must be measured [49].

Electrospinning is a technique to produce small drug–polymer fibers from their solution via a high-voltage field. The high surface area can lead to fast dissolution, but problems associated with throughput, solvent handling, and conversion of low density fibres to conventional dosage forms are scale-up challenges (Table 1) [50].

Table 1: Comparative Evaluation of Pharmaceutical Manufacturing Technologies for Solid Dispersions

Manufacturing Technology	Working Principle	Key Processing Conditions	Industrial Advantages	Technical Limitations & Critical Risks	Scalability & Regulatory Status
Hot-Melt Extrusion (HME) [51]	Continuous thermal melting, distributive/dispersive screw mixing, and mechanical extrusion through a shaping die.	Barrel temp: 130–150 °C; Residence time: 1–3 min; High shear twin-screw profile.	Generally solvent-free; continuous processing; potential for good content uniformity and high throughput when appropriately controlled.	Risk of thermal degradation for heat-sensitive drugs; high torque with unplasticized polymers (e.g., native HPMC).	High industrial scalability (PAT-enabled); established regulatory status for commercial ASD products.
Spray Drying [52]	Atomization of drug-carrier solution into heated gas stream; millisecond solvent evaporation and kinetic vitrification.	Inlet temp: 70–120 °C; Outlet temp: 45–65 °C; Nitrogen inertization; Atomization: 1–3 bar.	Applicable to thermally labile compounds; produces spherical, free-flowing microparticles; tunable size.	Requires organic solvents; explosion hazard; requires secondary drying and ICH Q3C residual solvent testing.	High industrial scalability; widespread commercial utilization; requires solvent recovery plant.
Solvent Evaporation (Lab-Scale) [53]	Co-dissolution in organic solvent followed by rotary vacuum evaporation, ambient casting, or tray drying.	Vacuum: 0.1–0.5 bar; Temp: 40–50 °C; Extended drying: 12–48 h.	Low equipment cost; highly accessible for initial academic screening and small-scale prototyping.	Batch-to-batch variability; irregular cake formation requiring milling; variable residual solvent; poor scalability.	Low scalability; restricted to preclinical formulation screening and early-phase laboratory research.
Supercritical Fluid (SCF / SAS) [54]	Atomization of drug solution into supercritical CO ₂ antisolvent; rapid extraction drives instantaneous precipitation.	Pressure: 80–150 bar; Temp: 35–45 °C; scCO ₂ flow rate: 10–50 g/min.	Mild thermal conditions; tunable particle morphology; low viscosity; recyclable fluid medium.	High capital equipment cost; high-pressure vessel qualification; organic co-solvents still require testing.	Moderate scalability; niche commercial implementation for specialty high-value therapeutics.
Electrospinning [55]	High-voltage electrostatic field draws polymer-drug jet into ultrafine whipping nanofilament; rapid desolvation.	Voltage: 10–25 kV; Flow rate: 0.5–3.0 mL/h; Tip-to-collector distance: 10–20 cm.	Ultra-high surface-area-to-volume ratio; flexible nanofibrous mats; rapid dissolution kinetics.	Low mass throughput per spinneret; safety hazards with high-voltage solvent vapors; difficult tablet processing.	Low to emerging scalability; multi-needle / needleless pilot platforms under active development.

7. Solid-State Analytical Characterization Techniques

7.1 Powder X-Ray Diffraction (PXRD)

The PXRD characterises long range crystalline order. The crystalline reflections may be reduced or even become invisible after the amorphization process, and they are replaced by a diffuse halo [56]. There is a limit of sensitivity to low levels of residual crystals and very small domains using PXRD. The presence of an amorphous halo does not rule out the molecular level homogeneity [57].

7.2 Thermal Analysis: DSC, mDSC, and Gordon-Taylor Miscibility

DSC quantifies the temperature changes or transitions in the material. The absence of the gliclazide melting endotherm may be indicative of reduced crystallinity, but it is dependent on the level of drug loading, the scan conditions and the possibility that the crystals may dissolve into the polymer during heating [58].

Miscibility can be achieved in a single composition-dependent glass transition; it cannot be precluded by nanoscale phase separation. The Gordon–Taylor relationship is often used to model the glass transition of a binary mixture [59].

$$T_{g,mix} = (w_1 \cdot T_{g1} + K \cdot w_2 \cdot T_{g2}) / (w_1 + K \cdot w_2)$$

The Gordon – Taylor equation with component weight fractions w_1 and w_2 , glass transition temperature of each

component, T_{g1} and T_{g2} , and empirical parameter K , which is dependent on the component properties [60].

7.3 Spectroscopic Probing: FTIR and Raman Spectroscopy

FTIR and Raman spectroscopy can give information about the vibrations and possible drug–carrier interactions. The broadening and/or shift can be due to hydrogen bonding or other effects in the environment [61]. In the study by Biswal *et al.* [62] the drug–PEG interaction was not clearly defined. This citation should not be cited as direct evidence for the hydrogen bonding between PVP and copolyvidone. The appropriate primary formulation study [63] is required for specific assignments.

7.4 Advanced High-Resolution Techniques: Solid-State NMR and Nanoscale Thermal Analysis

Solid-state NMR can be used to complement PXRD and DSC and to provide local chemical-environment information. Chemical-shift changes and line broadening may be supportive of altered molecular environments but may be subject to conclusions based on acquisition and analysis [64]. Using proton rotating-frame relaxation measurements, information can be obtained about mixing at nanoscale domain lengths, with some method-specific assumptions. Local thermal methods such as AFM-nanoTA can potentially give more spatial information; these methods are specialized and should be used depending on the question and available evidence (Fig. 3, Table 2)) [65].

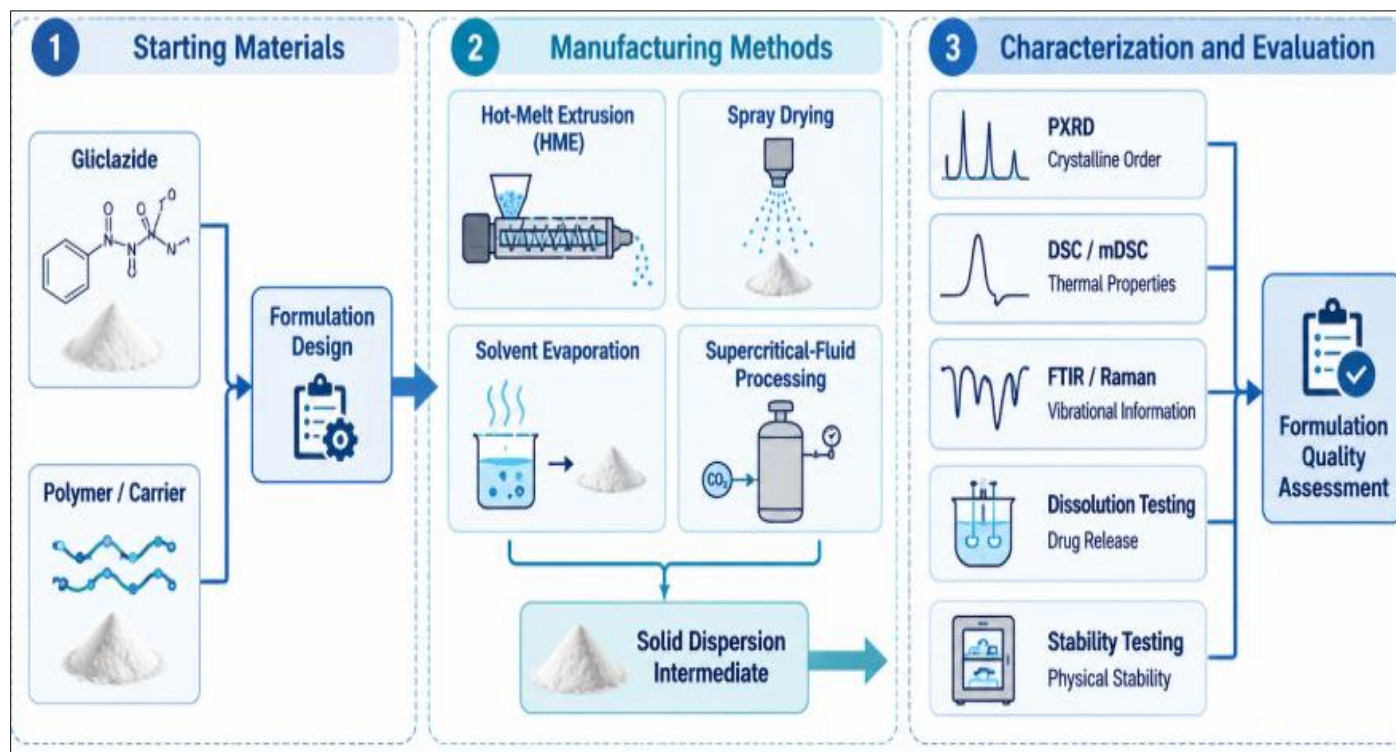


Figure 3: Manufacturing and Characterization of Gliclazide Solid Dispersions

Table 2: Multi-Technique Analytical Matrix for Solid-State Characterization of Gliclazide Solid Dispersions

Analytical Technique	Primary Property Probed	Diagnostic Gliclazide Signal / Endpoint	Spatial Domain Resolution	Detection Limit (LOD)	Operational Limitations & Potential Artifacts
Powder X-Ray Diffraction (PXRD) [66]	Long-range crystalline lattice periodicity and phase identification.	Disappearance of Form I sharp Bragg peaks (10.6°, 14.9°, 18.2°, 22.1° 2θ); emergence of diffuse amorphous halo.	>5–10 nm (crystal coherency length)	~1–5% w/w crystalline drug in polymer	Cannot detect sub-5 nm nanocrystals; preferred orientation artifacts; X-ray beam heating may alter metastable states.
Differential Scanning Calorimetry (DSC / mDSC) [67]	Thermodynamic phase transitions (T _g , T _c , T _m , ΔH _{fus}).	Disappearance of sharp Form I melting endotherm (168–172 °C, ΔH _{fus} = 130–138 J/g); detection of single composition-dependent T _g .	10–30 nm	~1–2% w/w crystalline drug	Single T _g does not guarantee sub-10 nm molecular homogeneity; high heating rates can induce in situ drug-polymer dissolution.
Fourier-Transform Infrared (FTIR) [68]	Vibrational stretching/bending; specific intermolecular H-bonding.	Bathochromic shift of sulfonylurea -NH- stretch from 3270 cm ⁻¹ to 3225–3230 cm ⁻¹ ; broadening of carbonyl peak (1708 cm ⁻¹).	Sub-nanometer (bond-level)	~3–5% w/w crystalline phase	Overlapping polymer absorption bands can obscure minor drug signals; moisture absorption interferes with -OH/-NH- regions.
Raman Spectroscopy & Chemical Imaging [69]	Polarizability vibrations; chemical mapping of surface domains.	Shifts in sulfonyl (-SO ₂ -) symmetric stretch (1160–1180 cm ⁻¹) and tolyl ring breathing modes (1600 cm ⁻¹).	0.5–1.0 μm (confocal laser spot)	~1–3% w/w crystalline phase	Fluorescence interference from aromatic excipients or thermal degradation products; localized laser-induced thermal degradation.
Solid-State NMR (13C CP/MAS & T1ρH) [70]	Isotropic chemical shifts; local electronic environment; proton relaxation miscibility.	¹³ C resonance broadening; identical single proton rotating-frame relaxation time (T1ρH) for drug and polymer resonances.	2–5 nm (sub-nanometer molecular miscibility)	<1% w/w crystalline phase	High instrument capital cost; prolonged acquisition times (hours to days); requires expert spectral deconvolution.

8. In Vitro Dissolution and Biorelevant Profiling

8.1 Biorelevant Media and In Vitro Dissolution Methodologies

Compendial dissolution tests are suitable for comparison and quality control purposes, can be performed with acidic or phosphate-buffer dissolution media, and can be using paddle apparatus or basket apparatus, but cannot entirely predict *in vivo* gastrointestinal performance.

- The gastric environment of the FaSSGF is an acidic fasted gastric environment; the composition and pH of the FaSSGF should be based on the selected published recipe [71].
- FaSSIF: fasted intestinal conditions (bile salt and phospholipid components) [72].
- FeSSIF mimics fed intestinal conditions, which have a distinct pH and increased amounts of solubilising components [73].

8.2 Mathematical Release Modeling: Korsmeyer-Peppas Power Law Kinetics

Release-model fitting may be useful to explain the contribution from diffusion, polymer relaxation or erosion in release, but the choice of the appropriate model should be correlated with the geometry of the dosage form and the range of data analysed [74].

$$M_t / M_{\infty} = k \cdot t^n \quad (\text{valid for } M_t / M_{\infty} < 0.60)$$

The Korsmeyer–Peppas model is of the form $M_t/M_{\infty} = k \cdot t^n$, where M_t/M_{∞} is the fractional release at time t , k is a rate constant, and n is the release exponent. The interpretation which is commonly used applies to the early part of release (usually $M_t/M_{\infty} < 0.60$) and the dosage-form geometry [75].

9. In Vivo Pharmacokinetics and Preclinical Evaluation

9.1 Preclinical Pharmacokinetic Outcomes in Animal Models

Various preclinical pharmacokinetic studies were performed in rodents with formulations of gliclazide, but the study designs, carriers, doses, comparators and analytical methods varied. Estimates from results should not be pooled but should be treated as evidence from the formulation. An improvement of dissolution and relative oral exposure of a gliclazide solid dispersion was reported in a rodent model by Patel *et al.* [76]. C_{max}, AUC and relative-bioavailability should be compared to the original paper prior to repeat use as definitive values.

In an animal model, a self-emulsifying formulation of gliclazide was reported to be more exposed [77]. This is an "evidence about this" type of formulation evidence to be distinguished from "evidence that this yields this".

9.2 Translational Disconnect: Rodent vs. Human Gastrointestinal Physiology

Although rodent studies are proof-of-concept, they do not predict human exposure because gastrointestinal volume, bile salts, pH, transit and metabolism are different between species [59,60].

9.3 Pharmacodynamic Correlation and Clinical Qualification of Hypoglycemia Risk

Dissolution of gliclazide has been suggested to be improved to better time the drug exposure with the postprandial glucose absorption [78]. This is yet another speculation and not a proven clinical advantage. All assertions of decreased hypoglycemia or improved postprandial control should be backed up by human pharmacokinetic/pharmacodynamic

studies, such as measures of drug exposure, glucose profiles, and safety outcomes. Animal experiments can help in continued research but cannot prove clinical superiority, optimum dosing or a decreased risk of hypoglycemia in patients [79].

10. Physical Stability, Recrystallization Thermodynamics, and Storage

10.1 Thermodynamic Driving Forces and Excess Gibbs Free Energy

Amorphous dispersions are not as thermodynamically stable as crystalline drug, and can recrystallize during storage. Molecular mobility, temperature, moisture, and interactions between the drug and the polymer are important factors for stability [80].

10.2 Kinetic Anti-Plasticization and Molecular Mobility Constraints

High T_g polymers can minimize molecular mobility when the storage temperature is kept low enough. This is a good design factor, but it is not a guarantee for the shelf-life stability [81].

10.3 Moisture Plasticization, the Fox Equation, and Packaging Strategies

The absorbed water may plasticize the matrix and reduce the T_g, which is a significant problem for hygroscopic amorphous systems.

The Fox equation can be used as an approximate model for the depression of T_g for a drug–polymer–water mixture. It's assumptions may not necessarily represent non-ideal interactions or phase separation [82].

$$1 / T_{g,mix} = (w_1 / T_{g1}) + (w_2 / T_{g2})$$

T_g, mix, T_{g1}, T_{g2} are the glass transition temperatures in Kelvin of mixture and components, respectively, while w₁/w₂ are weight fractions.

11. Industrial Manufacturability, Scalability, and Future Perspectives

11.1 Downstream Tableting Challenges: Compaction-Induced Recrystallization

For dosage-form manufacture downstream, it is necessary to control flow, compressibility, uniformity of content and physical stability. High polymer loads can lead to an increase in the mass of the tablet and influence disintegration, hardness and tolerability. The choice of excipients and the amount of drug loading need to be carefully balanced for dissolution and manufacturability [83].

11.2 Quality by Design (QbD) Framework and In-Line Process Analytical Technology (PAT)

Quality by Design (QbD) is a method of relating critical quality attributes (CQAs) to critical material attributes and

process parameters. Residual solvent, assay/content uniformity, dissolution, crystallinity, moisture and stability are some of the CQAs that may be considered for gliclazide dispersions [46–50,66].

Parameters of relevance for HME are screw design, barrel temperature, feed rate, screw speed, residence time and torque. Spray drying involves controlling feed concentration, solvent constituents, atomization, drying temperature and residue of solvent. Methods should be validated for the product with respect to monitoring and process analytical technology may be used to help.

11.3 Prospective Research Horizons

Future studies should focus on studies of gliclazide only and also be reproducible in the presence of biorelevant dissolution and appropriate pharmacokinetic evaluation. Reports should include details of the form of the drug, the carrier grade and ratio, preparation conditions, residual solvent, moisture and complete dissolution profiles. In supersaturation studies, the molecularly dissolved amount of the drug should be separate from the apparent total amount of drug and should be determined at a series of times.

- Co-amorphous systems: Run experiments for test candidate co-formers specific to gliclazide to confirm phase behavior, stability and dissolution.
- Make sure to establish long-term stability, loading, pore occupancy and solid state, not just inferring amorphization based on pore size alone.
- Extruded and printed dosage forms can be used to create dose flexibility and enhance dosage form performance without compromising dosage form stability or release control; assess if additive manufacturing can enhance dose flexibility and performance [85].

CONCLUSION

Enhancement of the aqueous solubility is a sensible formulation goal to achieve for Gliclazide. The wetting property and solid state, apparent solubility and precipitation inhibition can be enhanced by solid dispersion, depending on carrier and process. The use of polymeric and surfactant systems is well studied, and there are other systems with various balances of scale-up potential, solvent/thermal burden and stability, such as HME, spray drying, and mesoporous architectures. Any technology without formulation-specific evidence should not be preferred. There are some animal studies selected, which have demonstrated better exposure for certain formulations, but there are some differences in the design and comparator. Better dissolution does not necessarily lead to proportional bioavailability, glycemic control or decreased hypoglycemia in humans. The primary source data and long-term stability testing, compaction effect control, biorelevant dissolution and QbD-based scale-up are all essential for translation. Acceptable limits of dissolution, residual solvents, physical stability, content uniformity and

mechanical performance should be specified as product development parameters. Application of stability-indicating methods should be made after storage and compaction. Drug exposure, glucose profiles and hypoglycemia-related outcomes should be evaluated in human PK/PD studies to determine if increased exposure is associated with clinical benefit.

ACKNOWLEDGEMENT: Author are thankful to his guide for his valuable suggestion throughout this work.

CONFLICT OF INTEREST: Nil

REFERENCES:

1. Rob A, Hoque A, Asaduzzaman MM, Khatoon MA, Khalil R, Thomas D, Ilyas M, Mahmood H, Chowdhury TA. The global challenges of type 2 diabetes. *Bangladesh Journal of Medicine*. 2025 May 5;36(2):92-8.
2. LeRoith D. β -cell dysfunction and insulin resistance in type 2 diabetes: role of metabolic and genetic abnormalities. *The American journal of medicine*. 2002 Oct 28;113(6):3-11.
3. Meerarani P, Badimon JJ, Zias E, Fuster V, Moreno PR. Metabolic syndrome and diabetic atherothrombosis: implications in vascular complications. *Current molecular medicine*. 2006 Aug 1;6(5):501-14.
4. Jeffcoate SL. Diabetes control and complications: the role of glycated haemoglobin, 25 years on. *Diabetic Medicine*. 2004 Jul;21(7):657-65.
5. Tomlinson B, Li YH, Chan P. Evaluating gliclazide for the treatment of type 2 diabetes mellitus. *Expert Opinion on Pharmacotherapy*. 2022 Nov 22;23(17):1869-77.
6. Tian J, Ohkuma T, Cooper M, Harrap S, Mancia G, Poulter N, Wang JG, Zoungas S, Woodward M, Chalmers J. Effects of intensive glycemic control on clinical outcomes among patients with type 2 diabetes with different levels of cardiovascular risk and hemoglobin A1c in the ADVANCE trial. *Diabetes Care*. 2020 Jun 1;43(6):1293-9.
7. Vaduganathan M, Claggett BL, Jhund PS, Cunningham JW, Ferreira JP, Zannad F, Packer M, Fonarow GC, McMurray JJ, Solomon SD. Estimating lifetime benefits of comprehensive disease-modifying pharmacological therapies in patients with heart failure with reduced ejection fraction: a comparative analysis of three randomised controlled trials. *The Lancet*. 2020 Jul 11;396(10244):121-8.
8. Grbic S, Parojcic J, Ibric S, Djuric Z. In vitro-in vivo correlation for gliclazide immediate-release tablets based on mechanistic absorption simulation. *Aaps PharmSciTech*. 2011 Mar;12(1):165-71.
9. Calamante F, Christensen S, Desmond PM, Østergaard L, Davis SM, Connelly A. The physiological significance of the time-to-maximum (Tmax) parameter in perfusion MRI. *Stroke*. 2010 Jun 1;41(6):1169-74.
10. Del Prato S. In search of normoglycaemia in diabetes: controlling postprandial glucose. *International journal of obesity*. 2002 Sep;26(3):S9-17.
11. Klobucká S, Chamutyová K, Klobucký R, Šiarnik P, Podracká Ľ, Kollár B. Evidence and Practice in the Rehabilitation of Patients with Cerebral Palsy: A Structured Narrative Review Informed by a Systematic Literature Search. *Bratislava Medical Journal*. 2026 May;127(5):1790-812.
12. Ullah S, El-Gamal MI, El-Gamal R, Pelletier J, Seigny J, Shehata MK, Anbar HS, Iqbal J. Synthesis, biological evaluation, and docking studies of novel pyrrolo [2, 3-b] pyridine derivatives as both ectonucleotide pyrophosphatase/phosphodiesterase inhibitors and antiproliferative agents. *European journal of medicinal chemistry*. 2021 May 5;217:113339.
13. Güven A. Acidity study on 3-substituted pyridines. *International Journal of Molecular Sciences*. 2005 Nov 1;6(11):257-75.
14. Chaudhary A, Nagaich U, Gulati N, Sharma VK, Khosa RL, Partapur MU. Enhancement of solubilization and bioavailability of poorly soluble drugs by physical and chemical modifications: A recent review. *J Adv Pharm Educ Res*. 2012;2(1):32-67.
15. Yuvaraja K, Khanam J. Enhancement of carvedilol solubility by solid dispersion technique using cyclodextrins, water soluble polymers and hydroxyl acid. *Journal of pharmaceutical and biomedical analysis*. 2014 Aug 5;96:10-20.
16. Singh BN. A quantitative approach to probe the dependence and correlation of food-effect with aqueous solubility, dose/solubility ratio, and partition coefficient (Log P) for orally active drugs administered as immediate-release formulations. *Drug development research*. 2005 Jun;65(2):55-75.
17. Samie A, Desiraju GR, Banik M. Salts and cocrystals of the antidiabetic drugs gliclazide, tolbutamide, and glipizide: solubility enhancements through drug-coformer interactions. *Crystal Growth & Design*. 2017 May 3;17(5):2406-17.
18. Zweifel H. Stabilization of polymeric materials. *springer science & business media*; 2012 Dec 6.
19. Liu T, Zhang M, Kang Y, Tian X, Ding J, Li D. Material extrusion 3D printing of polyether ether ketone in vacuum environment: Heat dissipation mechanism and performance. *Additive Manufacturing*. 2023 Jan 25;62:103390.
20. Greenbowe T, Meltzer D. Student learning of thermochemical concepts in the context of solution calorimetry. *International Journal of Science Education*. 2003 Jul 1;25(7):779-800.
21. Chon CH, Kihm KD, Lee SP, Choi SU. Empirical correlation finding the role of temperature and particle size for nanofluid (Al₂O₃) thermal conductivity enhancement. *Applied physics letters*. 2005 Oct 10;87(15).
22. Gu CH, Grant DJ. Estimating the relative stability of polymorphs and hydrates from heats of solution and solubility data. *Journal of pharmaceutical sciences*. 2001 Sep 1;90(9):1277-87.
23. Censi R, Di Martino P. Polymorph impact on the bioavailability and stability of poorly soluble drugs. *Molecules*. 2015 Oct 15;20(10):18759-76.
24. Đanić M, Pavlović N, Zaklan D, Stanimirov B, Lazarević S, Al-Salami H, Mikov M. Computational studies for pre-evaluation of pharmacological profile of gut microbiota-produced gliclazide metabolites. *Frontiers in Pharmacology*. 2024 Dec 3;15:1492284.
25. Martinez MN, Amidon GL. A mechanistic approach to understanding the factors affecting drug absorption: a review of fundamentals. *The Journal of Clinical Pharmacology*. 2002 Jun;42(6):620-43.
26. Bornhorst GM, Paul Singh R. Gastric digestion in vivo and in vitro: how the structural aspects of food influence the digestion process. *Annual review of food science and technology*. 2014 Feb 28;5(1):111-32.

27. Zhang X, Xing H, Zhao Y, Ma Z. Pharmaceutical dispersion techniques for dissolution and bioavailability enhancement of poorly water-soluble drugs. *Pharmaceutics*. 2018 Jun 23;10(3):74.
28. Van Duong T, Van den Mooter G. The role of the carrier in the formulation of pharmaceutical solid dispersions. Part I: crystalline and semi-crystalline carriers. *Expert opinion on drug delivery*. 2016 Nov 1;13(11):1583-94.
29. Li J, Wang Y, Yu D. Effects of additives on the physical stability and dissolution of polymeric amorphous solid dispersions: a review. *AAPS PharmSciTech*. 2023 Aug 21;24(7):175.
30. Vasconcelos T, Sarmiento B, Costa P. Solid dispersions as strategy to improve oral bioavailability of poor water soluble drugs. *Drug discovery today*. 2007 Dec 1;12(23-24):1068-75.
31. Bremmell KE, Prestidge CA. Enhancing oral bioavailability of poorly soluble drugs with mesoporous silica based systems: Opportunities and challenges. *Drug development and industrial pharmacy*. 2019 Mar 4;45(3):349-58.
32. Albarazi N, Alzyoud A, Ahmed IS, Elkhazab A, Hwang SJ, Alhalaweh A. Supersaturation dynamics of cocrystals, amorphous solid dispersions and co-amorphous systems: generation mechanisms, stability considerations, and basis of failure modes. *Journal of Pharmaceutical Investigation*. 2026 Sep 28:1-35.
33. Monkhouse DC, Lach JL. Use of adsorbents in enhancement of drug dissolution I. *Journal of pharmaceutical sciences*. 1972 Oct 1;61(9):1430-5.
34. Feng J, Winnik MA. Effect of water on polymer diffusion in latex films. *Macromolecules*. 1997 Jul 28;30(15):4324-31.
35. Li S, Cheng T, Mu M, Yu H, Dong K, Wang B. Effect of surfactant concentration on fine particle removal enhanced by atomization agglomeration: An experimental and molecular dynamics simulated study. *Separation and Purification Technology*. 2025 Jul 30;362:131960.
36. Almeida e Sousa L, Reutzel-Edens SM, Stephenson GA, Taylor LS. Supersaturation potential of salt, co-crystal, and amorphous forms of a model weak base. *Crystal Growth & Design*. 2016 Feb 3;16(2):737-48.
37. Bavishi DD, Borkhataria CH. Spring and parachute: How cocrystals enhance solubility. *Progress in Crystal Growth and Characterization of Materials*. 2016 Sep 1;62(3):1-8.
38. Merchant J, Müllertz A, Rades T, Bannow J. Functionalized calcium carbonate (FCC) as a novel carrier to solidify supersaturated self-nanoemulsifying drug delivery systems (super-SNEDDS). *European Journal of Pharmaceutics and Biopharmaceutics*. 2023 Dec 1;193:198-207.
39. Kumar SR, Yagnesh TN. Solid dispersions: An approach to enhance solubility of poorly soluble drugs. *Indo American Journal of Pharmaceutical Research*. 2016 Jan;6(11):7036-56.
40. Liu J, Cui X, Santander C, Tan X, Liu Q, Zeng H. Destabilization of fine solids suspended in oil media through wettability modification and water-assisted agglomeration. *Fuel*. 2019 Oct 15;254:115623.
41. Nair AR, Lakshman YD, Anand VS, Sree KN, Bhat K, Dengale SJ. Overview of extensively employed polymeric carriers in solid dispersion technology. *AAPS PharmSciTech*. 2020 Nov 8;21(8):309.
42. Anderson NH, Bauer M, Boussac N, Khan-Malek R, Munden P, Sardaro M. An evaluation of fit factors and dissolution efficiency for the comparison of in vitro dissolution profiles. *Journal of pharmaceutical and biomedical analysis*. 1998 Aug 1;17(4-5):811-22.
43. Bodratti AM, Alexandridis P. Formulation of poloxamers for drug delivery. *Journal of functional biomaterials*. 2018 Jan 18;9(1):11.
44. Panigrahi KC, Patra CN, Jena GK, Ghose D, Jena J, Panda SK, Sahu M. Gelucire: A versatile polymer for modified release drug delivery system. *Future Journal of Pharmaceutical Sciences*. 2018 Jun 1;4(1):102-8.
45. Baghel S, Cathcart H, O'Reilly NJ. Investigation into the solid-state properties and dissolution profile of spray-dried ternary amorphous solid dispersions: a rational step toward the design and development of a multicomponent amorphous system. *Molecular pharmaceutics*. 2018 Sep 4;15(9):3796-812.
46. Ambrogi V, Marmottini F, Pagano C. Amorphous carbamazepine stabilization by the mesoporous silicate SBA-15. *Microporous and mesoporous materials*. 2013 Sep 1;177:1-7.
47. Crowley MM, Zhang F, Repka MA, Thumma S, Upadhye SB, Kumar Battu S, McGinity JW, Martin C. Pharmaceutical applications of hot-melt extrusion: part I. *Drug development and industrial pharmacy*. 2007 Jan 1;33(9):909-26.
48. Weers JG, Miller DP. Formulation design of dry powders for inhalation. *Journal of pharmaceutical sciences*. 2015 Oct;104(10):3259-88.
49. Reverchon E. Supercritical antisolvent precipitation of micro- and nano-particles. *The journal of supercritical fluids*. 1999 May 1;15(1):1-21.
50. Sill TJ, Von Recum HA. Electrospinning: applications in drug delivery and tissue engineering. *Biomaterials*. 2008 May 1;29(13):1989-2006.
51. Patil H, Tiwari RV, Repka MA. Hot-melt extrusion: from theory to application in pharmaceutical formulation. *Aaps PharmSciTech*. 2016 Feb;17(1):20-42.
52. Santos D, Mauricio AC, Sencadas V, Santos JD, Fernandes MH, Gomes PS. Spray drying: an overview. *Biomaterials-physics and chemistry-new edition*. 2018 May 2;2:9-35.
53. Roche P, Glennon B, Jones RC, Donnellan P. Low-temperature evaporation of continuous pharmaceutical process streams in a bubble column. *Chemical Engineering Research and Design*. 2021 Feb 1;166:74-85.
54. Knez Ž, Markočič E, Leitgeb M, Primožič M, Hrnčič MK, Škerget M. Industrial applications of supercritical fluids: A review. *Energy*. 2014 Dec 1;77:235-43.
55. Ji D, Lin Y, Guo X, Ramasubramanian B, Wang R, Radacs N, Jose R, Qin X, Ramakrishna S. Electrospinning of nanofibres. *Nature Reviews Methods Primers*. 2024 Jan 4;4(1):1.
56. Khan H, Yerramilli AS, D'Oliveira A, Alford TL, Boffito DC, Patience GS. Experimental methods in chemical engineering: X-ray diffraction spectroscopy—XRD. *The Canadian journal of chemical engineering*. 2020 Jun;98(6):1255-66.
57. Shah DD, Takanti N, Simpson GJ, Taylor LS. Orthogonal analytical methods to elucidate how low levels of residual crystallinity in posaconazole amorphous solid dispersions impact phase behavior during release. *Crystal Growth & Design*. 2024 Jan 3;24(1):440-54.
58. Schick C. Differential scanning calorimetry (DSC) of semicrystalline polymers. *Analytical and bioanalytical chemistry*. 2009 Nov;395(6):1589-611.
59. Meng F, Zheng S, Zhang W, Li H, Liang Q. Nanostructured Thermosetting Blends of Epoxy Resin and Amphiphilic

- Poly (ϵ -caprolactone)-b lock-polybutadiene-b lock-poly (ϵ -caprolactone) Triblock Copolymer. *Macromolecules*. 2006 Jan 24;39(2):711-9.
60. Schneider HA, Rieger J, Penzel E. The glass transition temperature of random copolymers: 2. Extension of the Gordon-Taylor equation for asymmetric Tg vs composition curves. *Polymer*. 1997 Mar 1;38(6):1323-37.
 61. Wartewig S, Neubert RH. Pharmaceutical applications of Mid-IR and Raman spectroscopy. *Advanced drug delivery reviews*. 2005 Jun 15;57(8):1144-70.
 62. Li YC, Rissanen S, Stepniowski M, Cramariuc O, Róg T, Mirza S, Xhaard H, Wytrwal M, Kepczynski M, Bunker A. Study of interaction between PEG carrier and three relevant drug molecules: piroxicam, paclitaxel, and hematoporphyrin. *The Journal of Physical Chemistry B*. 2012 Jun 21;116(24):7334-41.
 63. Li P, Zhao L. Developing early formulations: practice and perspective. *International Journal of Pharmaceutics*. 2007 Aug 16;341(1-2):1-9.
 64. Tatton AS, Pham TN, Vogt FG, Iuga D, Edwards AJ, Brown SP. Probing hydrogen bonding in cocrystals and amorphous dispersions using ^{14}N - ^1H HMQC solid-state NMR. *Molecular Pharmaceutics*. 2013 Mar 4;10(3):999-1007.
 65. Monroe J, Barry M, DeStefano A, Aydogan Gokturk P, Jiao S, Robinson-Brown D, Webber T, Crumlin EJ, Han S, Shell MS. Water structure and properties at hydrophilic and hydrophobic surfaces. *Annual Review of Chemical and Biomolecular Engineering*. 2020 Jun 7;11(1):523-57.
 66. Chauhan A, Chauhan P. Powder XRD technique and its applications in science and technology. *J Anal Bioanal Tech*. 2014 Sep 1;5(5):1-5.
 67. Gill P, Moghadam TT, Ranjbar B. Differential scanning calorimetry techniques: applications in biology and nanoscience. *Journal of biomolecular techniques: JBT*. 2010 Dec;21(4):167.
 68. Berthomieu C, Hienierwadel R. Fourier transform infrared (FTIR) spectroscopy. *Photosynthesis research*. 2009 Sep;101(2):157-70.
 69. Dodo K, Fujita K, Sodeoka M. Raman spectroscopy for chemical biology research. *Journal of the American Chemical Society*. 2022 Oct 10;144(43):19651.
 70. Nishida M, Tanaka T, Miki T, Hayakawa Y, Kanayama K. Integrated analysis of modified Japanese cypress using solid-state NMR spectra and nuclear magnetic relaxation times. *Cellulose*. 2019 Apr 15;26(6):3625-42.
 71. Hu W, Shimoda H, Hayasaka D. Infectious stability of animal gastrointestinal coronaviruses in fasted-state simulated gastric fluid. *Research in Veterinary Science*. 2026 Jun 15:106299.
 72. Fuchs A, Leigh M, Kloefer B, Dressman JB. Advances in the design of fasted state simulating intestinal fluids: FaSSiF-V3. *European Journal of Pharmaceutics and Biopharmaceutics*. 2015 Aug 1;94:229-40.
 73. Jantravid E, Dressman J. Biorelevant dissolution media simulating the proximal human gastrointestinal tract: an update. *Dissolution Technol*. 2009 Aug 1;16(3):21-5.
 74. Askarizadeh M, Esfandiari N, Honarvar B, Sajadian SA, Azdarpour A. Kinetic modeling to explain the release of medicine from drug delivery systems. *ChemBioEng Reviews*. 2023 Dec;10(6):1006-49.
 75. Lakshani N, Wijerathne HS, Sandaruwan C, Kottegoda N, Karunaratne V. Release kinetic models and release mechanisms of controlled-release and slow-release fertilizers. *ACS Agricultural Science & Technology*. 2023 Oct 31;3(11):939-56.
 76. Aulifa DL, Wibisono TT, Ningsih JD, Christy GD, Pertiwi DS, Praja HM, Gazzali AM, Amaliah S, Budiman A. The Impact of Polymers in Amorphous Solid Dispersion on the Bioavailability of Sulfonyleureas and Meglitinides. *Drug Design, Development and Therapy*. 2026 Dec 31:610513.
 77. Rashid M, Wani TU, Mishra N, Sofi HS, Sheikh FA. Development and characterization of drug-loaded self-solid nano-emulsified drug delivery system for treatment of diabetes. *Mat Sci Res India*. 2018 Apr 20;15(01).
 78. El Nashar NF, Sultan AA, El Maghraby GM. Self-dispersing self-assembling systems for controlled oral delivery of gliclazide. *Journal of Drug Delivery Science and Technology*. 2021 Dec 1;66:102742.
 79. Singh R, Gholipourmalekabadi M, Shafikhani SH. Animal models for type 1 and type 2 diabetes: advantages and limitations. *Frontiers in endocrinology*. 2024 Feb 20;15:1359685.
 80. Yang J, Grey K, Doney J. An improved kinetics approach to describe the physical stability of amorphous solid dispersions. *International journal of pharmaceutics*. 2010 Jan 15;384(1-2):24-31.
 81. Jadhav NR, Gaikwad VL, Nair KJ, Kadam HM. Glass transition temperature: Basics and application in pharmaceutical sector. *Asian J. Pharm*. 2009 Apr 1;3(2):82-9.
 82. Hancock BC, Zografi G. The relationship between the glass transition temperature and the water content of amorphous pharmaceutical solids. *Pharmaceutical research*. 1994 Apr;11(4):471-7.
 83. Darji MA, Lalghe RM, Marathe SP, Mulay TD, Fatima T, Alshammari A, Lee HK, Repka MA, Narasimha Murthy S. Excipient stability in oral solid dosage forms: a review. *Aaps Pharmscitech*. 2018 Jan;19(1):12-26.
 84. Pietrzak K, Isreb A, Alhnan MA. A flexible-dose dispenser for immediate and extended release 3D printed tablets. *European journal of pharmaceutics and biopharmaceutics*. 2015 Oct 1;96:380-7.

How to cite this article:

Dubey RK, Verma R, Tomar V, Choudhary JS. Solid Dispersion-Based Approaches for Improving the Dissolution and Bioavailability of Gliclazide: A Review. *International Journal of Pharmaceutical Science and Medicine* 2026; 4(2): 67-76.