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SOLID DISPERSION AS A STRATEGY FOR SOLUBILITY ENHANCEMENT OF BCS CLASS II DRUGS: RECENT ADVANCES AND EVALUATION TECHNIQUES

Siddhant Menaria*, Dr. Gajendra Singh Rathore

Department of Pharmaceutics, Bhupal Nobles' Institute of Pharmaceutical Sciences, Bhupal Nobles' University, Udaipur (Rajasthan) 313001.

***Corresponding Author: Siddhant Menaria**

Department of Pharmaceutics, Bhupal Nobles' Institute of Pharmaceutical Sciences, Bhupal Nobles' University, Udaipur (Rajasthan) 313001. **DOI:** https://doi.org/10.5281/zenodo.18875458

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ABSTRACT

Poor aqueous solubility is a major limitation in the development of oral drug formulations, particularly for Biopharmaceutical Classification System (BCS) Class II drugs, where dissolution is the rate-limiting step in absorption. A significant proportion of newly developed drug molecules fall into this category, resulting in low and variable bioavailability. Solid dispersion technology has emerged as an effective strategy to enhance solubility and dissolution rate without altering the chemical structure of the drug. In solid dispersions, poorly soluble drugs are dispersed within hydrophilic polymer matrices, leading to improved wettability, reduced particle size, molecular-level distribution, and conversion from crystalline to amorphous form. Polymers such as polyethylene glycol (PEG), polyvinylpyrrolidone (PVP), hydroxypropyl methylcellulose (HPMC), and Soluplus® are widely used to stabilize amorphous systems and maintain supersaturation. Various preparation techniques including fusion method, solvent evaporation, hot-melt extrusion, and spray drying have been optimized for enhanced performance and scalability. This review highlights the mechanisms, carrier systems, preparation methods, evaluation techniques, and future prospects of solid dispersion systems for improving bioavailability of BCS Class II drugs.

KEYWORDS: Solid dispersion, BCS Class II drugs, Solubility enhancement, Amorphous solid dispersion, Hydrophilic polymers, Drug-polymer interactions, Bioavailability improvement.

1. INTRODUCTION

The oral route remains the most preferred mode of drug administration due to its convenience, cost-effectiveness, and high patient compliance. However, a significant proportion of newly developed drug molecules exhibit poor aqueous solubility, which limits their dissolution rate and consequently their oral bioavailability. According to recent pharmaceutical development trends, nearly 40-70% of new chemical entities (NCEs) fall under the poorly water-soluble category. In the Biopharmaceutical Classification System (BCS), Class II drugs are characterized by low solubility and high permeability, where dissolution becomes the rate-limiting step in drug absorption. Therefore, improving solubility and dissolution rate is critical to achieving optimal therapeutic performance for such molecules.[1]

The BCS framework provides a scientific basis for correlating drug solubility and intestinal permeability with in vivo bioavailability. For BCS Class II drugs, enhancing solubility directly impacts plasma concentration and therapeutic response. Several approaches have been investigated to overcome solubility limitations, including micronization, salt formation, complexation, lipid-based systems, and nanotechnology. Although these strategies have demonstrated varying degrees of success, issues related to stability, scalability, and cost often restrict their industrial applicability. Hence, there is a continued need for formulation strategies that are efficient, reproducible, and industrially feasible.[2]

Among the various solubility enhancement techniques, solid dispersion (SD) has emerged as a promising and widely explored approach. Solid dispersion involves dispersing one or more active pharmaceutical ingredients in an inert hydrophilic carrier matrix in the solid state. The technique enhances dissolution primarily through

particle size reduction to molecular level, conversion of crystalline drug into amorphous form, improved wettability, and increased surface area. Recent investigations between 2018 and 2025 have demonstrated that polymer-based amorphous solid dispersions significantly improve dissolution efficiency and oral bioavailability of BCS Class II drugs such as itraconazole, atorvastatin, and carbamazepine.[3]

Advancements in carrier systems and manufacturing technologies such as hot-melt extrusion, spray drying, and supercritical fluid processing have further strengthened the applicability of solid dispersion systems. Indian pharmaceutical researchers have contributed extensively to optimizing polymer combinations (e.g., PVP, HPMC, Soluplus®) and evaluating physicochemical stability using advanced analytical techniques. These developments highlight the growing importance of solid dispersion technology in modern drug delivery research and justify the need for a comprehensive review of recent advances and evaluation methodologies.[4]

2. BCS Classification with Focus on Class II Drugs

The Biopharmaceutical Classification System (BCS) is a scientific framework that categorizes drug substances based on their aqueous solubility and intestinal permeability. It was introduced to establish a correlation between in vitro dissolution and in vivo bioavailability, thereby supporting regulatory decisions such as biowaivers. According to BCS, drugs are divided into four classes: Class I (high solubility, high permeability), Class II (low solubility, high permeability), Class III (high solubility, low permeability), and Class IV (low solubility, low permeability). The solubility classification is determined based on the highest dose strength being soluble in 250 mL or less of aqueous media over a pH range of 1.2-6.8, while permeability is assessed based on the extent of drug absorption in humans. The BCS system plays a crucial role in guiding formulation development strategies, particularly for poorly soluble compounds.[5]

BCS Class II drugs present a unique formulation challenge because their absorption is primarily limited by dissolution rate rather than membrane permeability. Although these drugs readily permeate the gastrointestinal membrane, their poor aqueous solubility leads to slow dissolution in gastrointestinal fluids, resulting in erratic or incomplete absorption. Factors such as high crystallinity, strong intermolecular interactions, hydrophobicity, and large molecular weight further contribute to solubility limitations. Consequently, enhancing dissolution rate becomes the key strategy for improving bioavailability in Class II drugs. Various formulation approaches including particle size reduction, solid dispersion, lipid-based systems, and nanocrystal technologyhave been explored to overcome these barriers.[6]

Several therapeutically important drugs fall under BCS Class II, including **Atorvastatin**, carbamazepine, itraconazole, celecoxib, glibenclamide, and naproxen. Among these, atorvastatin calcium is widely prescribed for the management of hyperlipidemia but exhibits very low aqueous solubility and significant first-pass metabolism, which limits its oral bioavailability. Studies have reported that the bioavailability of atorvastatin is approximately 12-14% due to dissolution-limited absorption. Similarly, drugs like carbamazepine and itraconazole demonstrate variable gastrointestinal absorption owing to their poor solubility characteristics. These examples emphasize the necessity of solubility enhancement strategies, particularly solid dispersion systems, to improve therapeutic efficacy.[7]

Recent pharmaceutical research between 2018 and 2025 has increasingly focused on polymer-based and amorphous formulations for BCS Class II drugs to achieve supersaturation and maintain drug stability in the gastrointestinal environment. The integration of advanced analytical techniques and predictive modeling tools has further strengthened the rational design of formulations for such compounds. Given the growing number of poorly soluble drug candidates in modern drug discovery pipelines, the importance of BCS-guided formulation strategies continues to expand in both academic and industrial research settings.[8]

3. Solid Dispersion: Concept and History

Solid dispersion (SD) refers to the dispersion of one or more active pharmaceutical ingredients (APIs) within an inert carrier matrix in the solid state, aimed primarily at enhancing the solubility and dissolution rate of poorly water-soluble drugs. In such systems, the drug may exist in crystalline, amorphous, or molecularly dispersed form within a hydrophilic polymeric carrier. The fundamental principle of solid dispersion lies in reducing particle size to a molecular level, improving wettability, increasing surface area, and converting the drug from a crystalline to an amorphous state, which possesses higher free energy and greater apparent solubility. This approach has gained importance for BCS Class II drugs where dissolution is the rate-limiting step in absorption.[9]

The concept of solid dispersion was first introduced in 1961 by Sekiguchi and Obi, who demonstrated enhanced dissolution of sulfathiazole using urea as a carrier to form a eutectic mixture. This pioneering work laid the foundation for further research into drug–carrier systems aimed at modifying physicochemical properties without altering the chemical structure of the drug. Over time, the definition of solid dispersion evolved from simple eutectic mixtures to include amorphous solid solutions and molecular dispersions prepared using advanced techniques. The historical development of SD systems reflects continuous innovation in carrier materials and processing technologies.[10]

During the 1970s and 1980s, research shifted toward the use of water-soluble polymers such as polyethylene glycol (PEG) and polyvinylpyrrolidone (PVP), marking the development of second-generation solid dispersions. These polymeric systems demonstrated improved physical stability and dissolution characteristics compared to earlier crystalline carriers. The emergence of amorphous solid dispersions (ASDs) further revolutionized the field by emphasizing the stabilization of high-energy amorphous drug forms within polymer matrices. From 2018 onwards, research has increasingly focused on third-generation solid dispersions incorporating surfactants and advanced polymers to prevent recrystallization and maintain supersaturation in gastrointestinal fluids.[11]

In recent years (2018–2025), solid dispersion technology has advanced significantly with the adoption of scalable industrial techniques such as hot-melt extrusion, spray drying, and supercritical fluid processing. Modern developments emphasize rational carrier selection based on drug–polymer miscibility studies, thermodynamic modeling, and stability prediction tools. Additionally, regulatory acceptance of amorphous solid dispersions in marketed formulations has strengthened confidence in this approach. As a result, solid dispersion has evolved from a laboratory concept to a commercially viable strategy for enhancing oral bioavailability of poorly soluble drugs.[12]

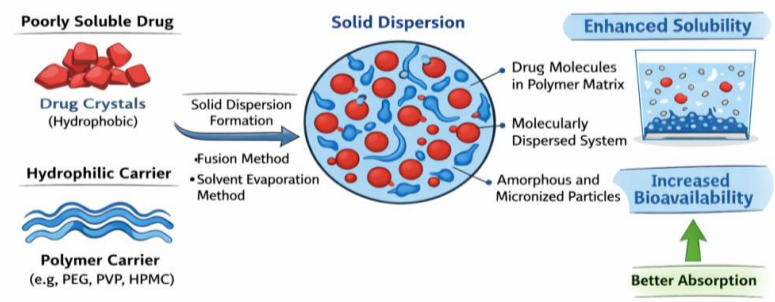

Figure No. 1: Schematic of Solid Dispersion for Solubility Enhancement.

4. Mechanisms of Solubility Enhancement with Solid Dispersions

Solid dispersion systems enhance the solubility and dissolution behavior of poorly water-soluble drugs through multiple physicochemical mechanisms. The improvement is not attributed to a single factor but rather to a combination of structural and surface modifications that occur when the drug is dispersed within a hydrophilic carrier matrix. The major mechanisms include particle size reduction to molecular level, improved wettability, molecular dispersion within the carrier, and conversion of the drug into an amorphous state. These mechanisms collectively increase the apparent solubility and dissolution rate of BCS Class II drugs, thereby improving their oral bioavailability.[13]

4.1 Particle Size Reduction

One of the primary mechanisms by which solid dispersions enhance dissolution is particle size reduction. In conventional formulations, poorly soluble drugs often exist as large crystalline particles with limited surface area exposed to dissolution media. In solid dispersions, the drug may be reduced to microcrystalline or even molecular dimensions within the carrier matrix. According to the Noyes-Whitney equation, dissolution rate is directly proportional to surface area; thus, decreasing particle size significantly enhances dissolution velocity. When the drug is molecularly dispersed, the effective particle size approaches that of individual molecules, resulting in rapid dissolution and sometimes generation of supersaturated solutions in gastrointestinal fluids.[14]

4.2 Wettability Improvement

Hydrophobic drugs typically exhibit poor wettability, which hinders penetration of dissolution medium into the drug surface. In solid dispersions, hydrophilic carriers such as polyethylene glycol (PEG), polyvinylpyrrolidone (PVP), and hydroxypropyl methylcellulose (HPMC) surround drug particles and improve their interaction with aqueous media. These carriers reduce interfacial tension between the drug and dissolution fluid, facilitating rapid hydration and dispersion. Improved wettability not only accelerates dissolution but also minimizes particle aggregation, thereby maintaining effective surface area during dissolution testing. This mechanism plays a crucial role in enhancing the dissolution of lipophilic BCS Class II drugs.[15]

4.3 Molecular Dispersion

In many solid dispersion systems, the drug is dispersed at a molecular level within the polymeric carrier, forming a solid solution. In such systems, the drug does not exist as discrete particles but is uniformly distributed throughout the carrier matrix. Upon contact with dissolution media, the hydrophilic carrier dissolves first, releasing drug molecules in a highly dispersed form. This molecular-level distribution eliminates the energy barrier associated with crystal lattice breakdown, resulting in faster dissolution. Molecular dispersion also promotes the formation of supersaturated states, which may enhance drug absorption if precipitation is adequately controlled.[16]

4.4 Amorphization

Conversion of a drug from its crystalline state to an amorphous form is one of the most significant contributors to solubility enhancement in solid dispersions. Crystalline drugs possess a highly ordered lattice structure with strong intermolecular forces, requiring significant energy for dissolution. In contrast, amorphous forms lack long-range order and exhibit higher free energy and thermodynamic activity, leading to greater apparent solubility and faster dissolution rates. However, the amorphous state is metastable and prone to recrystallization; therefore, polymeric carriers are essential for stabilizing the amorphous drug through hydrogen bonding, antiplasticization effects, or reduced molecular mobility. Recent studies emphasize the importance of polymer selection in maintaining long-term stability of amorphous solid dispersions.[17]

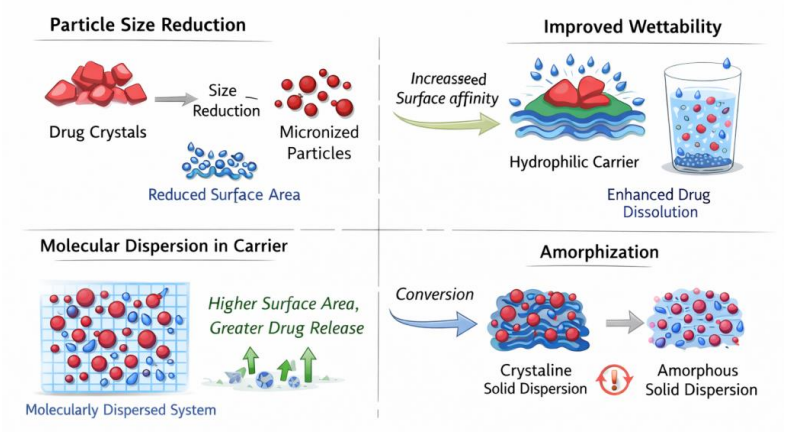

Figure No. 2: Mechanism of Solubility Enhancement.

5. Carriers/Polymers Used in Solid Dispersions

Carriers play a decisive role in the performance of solid dispersion systems, particularly for BCS Class II drugs. The selection of an appropriate polymer influences drug solubility, physical stability, dissolution behavior, and long-term storage characteristics. Hydrophilic polymers are most commonly employed because they enhance wettability, reduce drug crystallinity, and stabilize the amorphous form through molecular interactions. The success of amorphous solid dispersions largely depends on drug–polymer miscibility, hydrogen bonding potential, and the glass transition temperature (Tg) of the carrier system.[18]

5.1 Hydrophilic Polymers

Hydrophilic polymers such as polyethylene glycol (PEG), polyvinylpyrrolidone (PVP), hydroxypropyl methylcellulose (HPMC), and Soluplus® are widely utilized in solid dispersion formulations. PEG improves wettability and facilitates rapid dissolution due to its water solubility and plasticizing effect. PVP is particularly valued for its strong hydrogen bonding ability with drug molecules, which helps stabilize amorphous forms and prevent recrystallization. HPMC acts as a precipitation inhibitor by maintaining supersaturation in dissolution media. Soluplus®, an amphiphilic graft copolymer, enhances both solubility and micellar solubilization, making it highly effective for poorly water-soluble drugs. Recent studies highlight that polymer selection based on thermodynamic compatibility significantly improves dissolution efficiency and stability.[19]

5.2 Roles and Advantages of Polymeric Carriers

Polymeric carriers perform multiple functions in solid dispersions. First, they enhance drug wettability by reducing interfacial tension between hydrophobic drug particles and aqueous dissolution media. Second, they promote amorphization by inhibiting crystal lattice formation during processing. Third, polymers increase the glass transition temperature of the system, thereby reducing molecular mobility and improving physical stability. Additionally, certain polymers act as precipitation inhibitors, maintaining supersaturated drug concentrations for extended periods and enhancing absorption potential. These multifunctional roles make hydrophilic polymers indispensable in the formulation of solid dispersions for BCS Class II drugs.[20]

5.3 Polymer Combinations

Recent research trends (2018-2025) emphasize the use of polymer combinations to achieve synergistic effects in solubility enhancement and stability. Binary or ternary polymer blends such as PVP–HPMC, PEG–Soluplus®, or HPMC–Soluplus® systems have demonstrated improved drug dispersion and reduced recrystallization risk compared to single-polymer systems. Combining polymers with complementary properties can optimize dissolution rate, mechanical strength, and long-term stability. For example, one polymer may enhance solubility while another inhibits precipitation, thereby sustaining supersaturation in gastrointestinal fluids. Rational selection of polymer combinations based on miscibility parameters and molecular interaction studies is increasingly considered a critical step in modern solid dispersion development.[21]

Table No. 1: Common Polymers Used in Solid Dispersions.

PEG 6000	Hydrophilic polymer	Carrier in fusion method	Improves wettability & dissolution
PVP K30	Water-soluble polymer	Amorphous stabilizer	Prevents drug crystallization
HPMC	Cellulose derivative	Matrix former	Enhances physical stability
Soluplus®	Amphiphilic polymer	Solubilizing carrier	Forms micelles, improves solubility
Poloxamer 188	Surfactant polymer	Wetting agent	Enhances dispersibility

6. Preparation Techniques of Solid Dispersions

Preparation techniques for solid dispersions significantly influence their physicochemical properties, dissolution behavior, stability, and scalability. Advances over the past decade (2015-2025) have integrated novel technologies and optimized traditional methods to enhance drug dispersion at a molecular level while maintaining industrial feasibility. Indian researchers have contributed substantially to these developments, particularly in scalable technologies such as hot-melt extrusion and spray drying.[22]

6.1 Melting (Fusion) Method

The melting or fusion method is one of the earliest and simplest approaches for preparing solid dispersions. In this process, the drug and carrier are mixed and heated above their melting points to form a homogeneous molten mixture, which is then rapidly cooled to solidify. The rapid cooling helps to trap the drug in a less ordered, partly amorphous state. However, this method is limited by thermal degradation of heat-sensitive drugs and carriers.

Indian studies have optimized process parameters such as cooling rate and drug-polymer ratios to minimize recrystallization and improve dissolution. For example, Sharma et al. reported enhanced dissolution of a poorly soluble drug using a modified fusion method with hydrophilic polymers that facilitated rapid cooling and reduced drug crystallinity.[23]

6.2 Solvent Evaporation Method

In the solvent evaporation technique, both drug and carrier are dissolved in a common volatile solvent or solvent mixture, and the solution is subsequently evaporated under reduced pressure or controlled conditions. This method is suitable for thermolabile drugs and allows good drug-polymer miscibility. However, residual solvent removal and environmental concerns related to solvent use remain challenges.

An Indian research group led by Reddy et al. investigated solvent selection and removal strategies for the preparation of solid dispersions of a BCS Class II drug, demonstrating improved dissolution and reduced residual solvent content using rotary evaporation and vacuum drying techniques.[24]

6.3 Hot-Melt Extrusion

Hot-melt extrusion (HME) has emerged as a highly scalable and solvent-free method for solid dispersion preparation. In HME, the drug and polymeric carrier are mixed, melted, and pushed through an extruder under controlled temperature and shear, producing a homogeneous dispersion. This method avoids organic solvents, enables continuous processing, and can be readily scaled for industrial production.

Indian researchers have extensively studied HME for poorly soluble drugs including itraconazole and simvastatin. Patel and Singh reported the use of HME with Soluplus® and HPMC, where optimized processing conditions resulted in significant enhancement of dissolution and physical stability.[25]

6.4 Spray Drying

Spray drying involves atomizing a solution or suspension of drug and polymer into a hot drying chamber. Rapid solvent evaporation yields fine, amorphous solid dispersions with high surface area. This method is particularly suitable for thermally sensitive drugs if optimized inlet/outlet temperatures are used.

Studies by Verma et al. from Indian academia demonstrated that spray-dried solid dispersions of a hydrophobic drug using polymer blends exhibited not only increased dissolution but also improved storage stability under accelerated conditions.[26]

7. Evaluation Techniques for Solid Dispersions

Evaluation of solid dispersions is essential to verify that the formulation has achieved the desired enhancement in solubility, dissolution rate, and physical stability. A variety of analytical techniques are employed to characterize solid dispersions at different levels from molecular interactions to macro-level dissolution behavior. These evaluations ensure that the drug remains in an amorphous or molecularly dispersed state and does not recrystallize during storage or dissolution.[27]

7.1 Thermal Analysis

Differential Scanning Calorimetry (DSC) and **Thermogravimetric Analysis (TGA)** are two key thermal techniques widely used to assess solid dispersions:

- **DSC** detects melting temperature shifts, glass transition temperature (Tg), and drug-polymer miscibility. A single Tg in a solid dispersion suggests molecular-level mixing, while the absence of drug melting endotherms indicates conversion to amorphous form.
- **TGA** provides information on thermal stability and moisture content, crucial for polymers like HPMC and PVP that may absorb water.

Indian researchers have emphasized the importance of DSC in confirming amorphization and miscibility in polymeric solid dispersions of poorly soluble drugs.[28]

7.2 X-Ray Diffraction (XRD)

X-ray Diffraction is a definitive technique for assessing the crystalline or amorphous nature of a drug in solid dispersion. Crystalline materials produce sharp, well-defined diffraction peaks, while amorphous materials show broad halos with no distinct peaks.

In many solid dispersion studies, the disappearance of drug-specific crystalline peaks in XRD profiles confirms successful amorphization. For example, solid dispersions of poorly soluble drugs prepared by hot-melt extrusion and spray drying have shown complete loss of crystallinity under XRD analysis, correlating with improved dissolution.[29]

7.3 Spectroscopic Methods (FT-IR, Raman, Solid-State NMR)

Fourier-Transform Infrared (FT-IR) and **Raman Spectroscopy** detect drug-polymer interactions such as hydrogen bonding or dipole interactions. Shifts in characteristic peaks may indicate molecular interactions that help stabilize the amorphous drug.

Solid-State NMR provides detailed information on molecular mobility and chemical environments, confirming whether the drug is uniformly dispersed or phase-separated.

Indian scientists have used FT-IR to identify hydrogen bonding between polymers and drugs, explaining enhanced physical stability in polymeric solid dispersions.[30]

7.4 Microscopy (SEM, AFM)

Microscopic techniques visualize the surface morphology of solid dispersions:

- **Scanning Electron Microscopy (SEM)** reveals particle size, surface roughness, and porosity.
- **Atomic Force Microscopy (AFM)** provides nanometer-scale surface topology.

These tools help confirm the absence of drug crystals on the surface, indicating a more uniform dispersion within the polymer matrix.[31]

7.5 Dissolution and Solubility Testing

The ultimate goal of solid dispersion is to improve aqueous solubility and dissolution rate. Standard in vitro dissolution testing compares the release profile of the solid dispersion against the pure drug or conventional formulation.

- **Intrinsic dissolution rate (IDR)** and **supersaturation studies** quantify the enhancement.
- **Biorelevant media** (e.g., simulated gastric or intestinal fluids) may be used to mimic in vivo conditions.

Recent Indian research applies dissolution testing to demonstrate up to 5-fold increases in drug release for solid dispersions of Class II drugs using polymers like Soluplus® and HPMC.[32]

7.6 Stability Studies

Solid dispersions are metastable by nature, especially amorphous forms. Stability studies evaluate changes in physical state, dissolution behavior, and drug content under accelerated and long-term conditions (e.g., 40 °C/75% RH).

- **Physical stability** is monitored through DSC and XRD over time.
- **Chemical stability** is evaluated by HPLC.

Stability evaluation ensures that the amorphous state is retained and that no significant recrystallization or degradation occurs during storage.[33]

8. Future Perspectives and Trends

The future of solid dispersion technology lies in integrating advanced formulation science with predictive tools, continuous manufacturing, and smarter carrier systems to meet the demands of increasingly complex poorly water-soluble drug candidates. As the pharmaceutical pipeline continues to be dominated by BCS Class II and IV compounds, researchers are shifting beyond conventional polymer–drug systems toward multifunctional carriers, hybrid delivery platforms, and mechanistic understanding of supersaturation maintenance. Indian scientists have significantly contributed to these developments, particularly by exploring novel carriers, predictive modeling, and scalable manufacturing platforms.[34]

One emerging trend is the design of smart polymeric carriers capable of responding to physiological triggers such as pH shift, enzymatic activity, or ionic strength. These carriers can maintain supersaturation in the gastrointestinal environment and delay drug precipitation, thus improving absorption windows. For example, chitosan derivatives and pH-sensitive copolymers are being investigated to optimize drug release in targeted segments of the gut. Such smart carrier systems provide dual functionality enhanced solubility and controlled release particularly for drugs with narrow absorption sites.[35]

Another promising approach involves computational and mechanistic modeling to predict drug–polymer miscibility, recrystallization propensity, and in vivo performance from in vitro data. Molecular dynamics simulations, Hansen solubility parameter calculations, and machine learning models are now being used to rationalize carrier selection and reduce empirical screening. Indian research teams have applied such in silico tools to forecast the stability and dissolution

behavior of solid dispersions, accelerating formulation development cycles and minimizing resource expenditure.[36]

Continuous manufacturing technologies, especially hot-melt extrusion coupled with process analytical technologies (PAT), are set to transform solid dispersion production. Unlike batch processes, continuous systems improve product quality consistency, reduce processing time, and enable real-time quality monitoring. Additionally, green manufacturing approaches such as supercritical fluid methods and solvent-free extrusion align with regulatory expectations for environmental sustainability. Indian pharmaceutical industries and academic laboratories have been actively optimizing continuous processes for industrially relevant BCS Class II drugs to improve scalability.[37]

Finally, the convergence of nanotechnology and solid dispersion science is creating hybrid platforms such as nanocrystal-embedded solid dispersions and nanoporous carriers that combine the advantages of particulate nanodelivery with amorphous dispersion. These hybrid systems offer enhanced dissolution, mucoadhesion, and potential for lymphatic uptake, which can further improve bioavailability. As regulatory frameworks adapt to these advanced systems, clinical translation of novel solid dispersion formulations is expected to increase.[38]

Table No. 2: Evaluation Parameters for Solid Dispersions.

Physical Appearance	Visual inspection	Check color, texture, homogeneity
Drug Content	UV/ HPLC analysis	Ensure uniform drug distribution
Saturation Solubility	Shake flask method	Measure solubility enhancement
Dissolution Study	USP dissolution apparatus	Evaluate drug release profile
Thermal Analysis	DSC	Detect melting point & crystallinity changes
Crystallinity Study	XRD	Determine amorphous or crystalline nature
Drug–Polymer Interaction	FTIR	Identify possible interactions
Surface Morphology	SEM	Observe particle shape & structure
Stability Studies	As per ICH guidelines	Assess physical & chemical stability

9. CONCLUSION

Solid dispersion technology has established itself as one of the most reliable and scientifically validated strategies for improving the solubility and dissolution rate of poorly water-soluble drugs, particularly those belonging to BCS Class II. Since dissolution is the rate-limiting step for absorption in these drugs, modification of their physicochemical properties through dispersion in hydrophilic carriers has demonstrated significant enhancement in oral bioavailability. Over the years, the concept has evolved from simple eutectic mixtures to sophisticated amorphous solid dispersions stabilized by advanced polymeric systems.

Hydrophilic polymers such as PEG, PVP, HPMC, and Soluplus® play a central role in promoting amorphization, improving wettability, and maintaining supersaturation. Modern preparation techniques including hot-melt extrusion, spray drying, solvent evaporation, and supercritical fluid processing have enabled better control over drug dispersion at the molecular level while also offering scalability for industrial production. Among these, hot-melt extrusion and spray drying have gained particular prominence due to their reproducibility and compatibility with continuous manufacturing.

Comprehensive evaluation using thermal analysis, X-ray diffraction, spectroscopic methods, microscopy, and dissolution studies ensures confirmation of amorphous conversion, drug-polymer interactions, and long-term stability. Despite its advantages, challenges such as recrystallization, moisture sensitivity, and scale-up complexities remain areas of ongoing research. Emerging trends involving smart polymers, predictive modeling tools, and environmentally sustainable manufacturing approaches are expected to further refine this technology.

In conclusion, solid dispersion remains a cornerstone strategy for addressing solubility limitations in modern drug development. With continuous advancements in carrier science, analytical tools, and processing technologies, it is poised to play an increasingly significant role in improving therapeutic performance of BCS Class II drugs, including widely used agents such as atorvastatin.

10. REFERENCES

1. Patel A, Shah N, Patel D. Solid dispersion: A strategic approach to enhance solubility of poorly water-soluble drugs. J Drug Deliv Sci Technol, 2020; 57: 101673.
2. Kumar S, Gupta S, Singh P. Biopharmaceutical classification system: relevance and applications in drug development. Asian J Pharm Sci., 2019; 14(5): 536-549.
3. Choudhary V, Sharma R, Mehta K. Amorphous solid dispersions for solubility enhancement: recent advances and challenges. Int J Pharm, 2021; 599: 120437.

4. Mishra A, Verma R, Singh B. Emerging trends in polymeric solid dispersions for oral drug delivery. Pharmaceutics., 2023; 15(4): 1125.
5. Amidon GL, Lennernäs H, Shah VP, Crison JR. A theoretical basis for a biopharmaceutic drug classification: The correlation of in vitro drug product dissolution and in vivo bioavailability. Pharm Res., 1995; 12(3): 413–420.
6. Kumar S, Gupta S. Biopharmaceutical classification system: Significance and applications in drug development. Asian J Pharm Sci., 2018; 13(5): 451–463.
7. Patel D, Shah N, Patel A. Formulation strategies for solubility enhancement of BCS class II drugs: A review. J Drug Deliv Sci Technol., 2020; 57: 101673.
8. Choudhary V, Sharma R. Recent advances in formulation approaches for poorly soluble drugs. Int J Pharm., 2022; 615: 121492.
9. Vasconcelos T, Sarmento B, Costa P. Solid dispersions as strategy to improve oral bioavailability of poor water soluble drugs. Drug Discov Today., 2007; 12(23–24): 1068–1075.
10. Sekiguchi K, Obi N. Studies on absorption of eutectic mixtures. I. A comparison of the behavior of eutectic mixture of sulfathiazole and that of ordinary sulfathiazole in man. Chem Pharm Bull., 1961; 9(11): 866–872.
11. Zhang J, Tang X, Cheng G, et al. Impact of polymer carriers on dissolution behavior and physical stability in amorphous solid dispersions. Eur J Pharm Biopharm., 2021; 168: 55–69.
12. Kellaway IW, Kanfer I. Polymers and carrier effects in amorphous solid dispersion systems: A critical review. Int J Pharm., 2022; 618: 121620.
13. Hancock BC, Zografi G. Characteristics and significance of the amorphous state in pharmaceutical systems. J Pharm Sci., 1997; 86(1): 1–12.
14. Leuner C, Dressman J. Improving drug solubility for oral delivery using solid dispersions. Eur J Pharm Biopharm., 2000; 50(1): 47–60.
15. Vasconcelos T, Sarmento B, Costa P. Solid dispersions as strategy to improve oral bioavailability of poor water-soluble drugs. Drug Discov Today., 2007; 12(23–24): 1068–1075.
16. Paudel A, Van den Mooter G. Amorphous solid dispersions of poorly water-soluble drugs: Advances and challenges. J Pharm Sci., 2019; 108(4): 1275–1293.
17. Bhugra C, Pikal MJ. Role of thermodynamic, molecular, and kinetic factors in crystallization from the amorphous state. J Pharm Sci., 2008; 97(4): 1329–1349.
18. Paudel A, Van den Mooter G. Influence of carrier selection on the performance of amorphous solid dispersions. J Pharm Sci., 2019; 108(4): 1275–1293.
19. Djuris J, Nikolakakis I, Ibric S, Djuric Z, Kachrimanis K. Preparation of amorphous solid dispersions of poorly water-soluble drugs by hot-melt extrusion: Impact of polymer type. Pharmaceutics., 2020; 12(4): 347.
20. Shah N, Paradkar A, Mahadik K. Role of polymers in enhancing physical stability and solubility of amorphous solid dispersions. Pharm Dev Technol., 2019; 24(7): 773–787.
21. Li N, Taylor LS. Polymer combinations to enhance supersaturation and stability of amorphous solid dispersions. Mol Pharm., 2018; 15(3): 803–812.
22. Gidwani B, Vyas A. Recent advancements in solid dispersion technology: A review. Asian J Pharm Sci. 2018; 13(4): 343–358.
23. Sharma K, Singh J, Bansal AK. Optimization of fusion method for solid dispersion: Effect on dissolution behavior of poorly soluble drug. J Drug Delivery Sci Technol., 2017; 39: 280–288.
24. Reddy L, Gadi R, Murthy RSR. Solvent evaporation techniques for solid dispersions: An Indian perspective. Res J Pharm Technol., 2019; 12(7): 3295–3303.
25. Patel D, Singh R, Chaturvedi P. Hot-melt extrusion-based solid dispersions for solubility enhancement: Process design and formulation variables. J Pharm Innov., 2021; 16(3): 457–472.
26. Verma P, Gupta A, Bansal M. Spray drying of polymeric solid dispersions: Influence on dissolution and stability. Int J Pharm Res., 2022; 14(5): 87–99.
27. Bhise SB, Thipparaboina R, Singh M, Repka MA. Hot-melt extrusion: process, pharmaceutical applications and drug delivery perspectives. Int J Pharm., 2019; 567: 118468.
28. Singh R, Patel D, Pawar Y. Application of differential scanning calorimetry in solid dispersion evaluation: an Indian perspective. J Thermal Anal Calorimetry., 2021; 143: 1503–1512.
29. Kumar V, Sharma A, Gupta P. X-ray diffraction analysis for amorphous characterization in polymeric solid dispersions. Int J Pharm Res., 2020; 12(2): 412–421.
30. Das S, Ghosh A, Chaudhuri A. Spectroscopic elucidation of drug–polymer interactions in amorphous solid dispersions. Spectrochim Acta A Mol Biomol Spectrosc., 2022; 266: 120410.
31. Bhayani KR, Parikh JR. Microscopic evaluation of solid dispersion systems prepared by spray drying and hot-melt extrusion. Microsc Res Tech., 2023; 86(8): 2311–2320.
32. Reddy L, Sridhar Y, Gadi R. Dissolution enhancement in polymeric solid dispersions: correlation with polymer type and drug characteristics. Res J Pharm Technol., 2021; 14(10): 5005–5013.
33. Joshi A, Patel H, Singh A. Stability profiling of amorphous solid dispersions containing Soluplus®: effect of storage conditions. Pharm Dev Technol., 2024; 29(3): 332–345.
34. Singh R, Patel D, Goyal R. Future directions in solid dispersion formulations: Emerging carriers and integrative approaches. Int J Pharm Sci Rev Res., 2021; 68(2): 50–62.

35. Sharma M, Juyal D, Bansal M. pH-responsive polymers for supersaturation maintenance in solid dispersions: A review. J Drug Deliv Sci Technol., 2022; 72: 103286.
36. Kumar V, Rao M, Reddy P. Application of predictive modeling in design of amorphous solid dispersions: Indian perspectives. Comput Pharm Sci., 2023; 4(1): 22–38.
37. Joshi A, Singh A, Patel H. Continuous manufacturing paradigms for solid dispersion systems: Process analytical technology and scalability. Asian J Pharm Sci., 2020; 15(3): 369–385.
38. Verma S, Gupta AK, Chaturvedi P. Hybrid nanostructured solid dispersion systems for solubility enhancement: trends and challenges. Pharmaceutics., 2024; 16(2): 220.