Journal Homepage: www.ijarpr.com ISSN: 3049-0103 (Online)

International Journal of Advance Research Publication and Reviews

Vol 03, Issue 10, pp 104-114, October, 2026

Amorphous Solid Dispersions (ASDs): Thermodynamic Stability, In Vivo Performance, and Global Regulatory Expectations

Shraddha Vijay Jagtap [1]*, Shubham N. Kanawade [2], Uday Hitendra Mahajan [3], Gauri Bhausaheb Devgire, Sayali Vasant Gondkar [5]

[1-5] College of Pharmaceutical Sciences, Pravara Institute of Medical Sciences (DU), Loni, Ahilyanagar, Maharashtra, India-413736

Email: shraddhajagtap1283@gmail.com

ABSTRACT

Amorphous Solid Dispersions (ASDs) represent one of the most critical and robust formulation strategies developed within pharmaceutical sciences to address the major challenge of poorly water-soluble drug candidates classified under the Biopharmaceutics Classification System (BCS) Class II and Class IV. By dispersing a hydrophobic active pharmaceutical ingredient (API) inside a hydrophilic polymer matrix at a molecular level, the high lattice energy of the crystalline state is effectively bypassed, leading to substantial improvements in apparent solubility, dissolution rate, and subsequent oral bioavailability. However, the thermodynamic instability arising from the high free energy of amorphous systems remains a significant bottleneck, often leading to phase separation and recrystallization during storage or upon gastrointestinal fluid contact. This review article comprehensively covers the architectural and scientific milestones of ASD systems. It explores the key mechanisms underlying drug-polymer miscibility, physicochemical characterization techniques (such as DSC, XRPD, and spectroscopic assays), thermodynamic versus kinetic stabilization factors, and the vital phenomenon of supersaturation and precipitation control commonly described via the 'spring and parachute' model. Furthermore, this work bridges fundamental solid-state stability with real-world in vivo performance and pharmacokinetic translation. Finally, we discuss the evolving global regulatory landscapes, focusing on critical quality attributes (CQAs), Quality by Design (QbD) parameters, and validation standards defined by international regulatory authorities to ensure commercial feasibility, physical integrity, and batch-to-batch consistency.

Keywords: Amorphous solid dispersions; Thermodynamic stability; Drug-polymer interactions; Supersaturation; In vivo bioavailability; Regulatory expectations; Recrystallization kinetics.

1. Introduction

The development of modern high-throughput screening and combinatorial chemistry has significantly accelerated the discovery of highly potent therapeutic agents [1]. However, a major consequence of this paradigm shift is that a vast majority of newly synthesized chemical entities exhibit exceptionally low aqueous solubility [2]. According to the Biopharmaceutics Classification System (BCS), these compounds predominantly fall under Class II [3] and Class IV [4]. Poor aqueous solubility profoundly impairs the oral absorption of drugs [5], resulting in compromised bioavailability [6], inconsistent therapeutic outcomes [7], and high inter-patient variability [8]. To overcome these biopharmaceutical limitations, various formulation strategies have been formulated over the decades [9], including micronization [10], lipid-based delivery systems [11], salt formation [12], and cyclodextrin complexation [13]. Among these approaches, Amorphous Solid Dispersions (ASDs) have gained immense prominence as an exceptionally robust platform [14] capable of transforming low-solubility crystalline drugs into highly bioavailable entities [15]. By disrupting the long-range crystalline lattice and dispersing the drug at a molecular level [16] within an appropriate polymeric matrix [17], ASDs harness the high thermodynamic energy of the amorphous form [18]. This enables rapid dissolution and temporary supersaturation in the gastrointestinal fluids [19], unlocking therapeutic efficacy for challenging molecules [20]. Despite their commercial success, designing stable ASDs remains a delicate scientific challenge [21] due to the inherent tendency of amorphous forms to recrystallize over time [22].

2. Amorphous Solid Dispersions Overview

Amorphous Solid Dispersions are fundamentally defined as a solid-state system where at least two different components, usually a hydrophobic active pharmaceutical ingredient (API) and a hydrophilic polymer, are combined to create a single-phase amorphous mixture [23]. Unlike crystalline solids, which possess a highly ordered, repeating three-dimensional arrangement of molecules [24], amorphous materials exhibit a disordered molecular packing reminiscent of a liquid state [25], but with the mechanical properties of a solid [26]. This structural disorder imparts a much higher apparent solubility and rapid dissolution kinetics [27] because no energy is expended to break down a rigid crystal lattice during the dissolution process [28]. Structurally, solid dispersions can be classified into different generations depending on the carriers used [29]. The first generation utilized crystalline carriers like urea or PEG [30], which facilitated rate-limiting wetting but did not fully stabilize the amorphous state [31]. The second generation introduced amorphous polymeric carriers [32], establishing the true foundational framework of modern ASDs [33] where molecularly dispersed drug molecules are trapped in an immobilized matrix [34]. The third generation incorporates surfactant molecules or functional polymers [35] to enhance the solution-state stabilization and prevent precipitation upon dissolution [36]. Over the past decades, understanding the phase behavior—specifically whether a system exists as a homogeneous single-phase solid solution or a phase-separated amorphous-amorphous mixture—has become a cornerstone of solid-state pharmaceutical design [37].

3. Need and Advantages of ASDs

The primary clinical and industrial driving force behind the adoption of ASD technology is the critical need to deliver brick-like hydrophobic drugs safely and effectively to the human body [38]. When a crystalline drug has an extremely high melting point and poor wetting properties [39], traditional formulations often fail because the transit time in the gastrointestinal tract is too short to allow complete dissolution [40]. ASDs elegantly circumvent this barrier by generating a high energetic state that provides an apparent solubility that is multiples higher than the crystalline equilibrium solubility [41]. The primary advantages of ASDs include: first, a drastic reduction in particle size down to the molecular level [42], which maximizes the effective surface area available for dissolution in accordance with the Noyes-Whitney equation [43]; second, a significant enhancement in wetability driven by the highly hydrophilic nature of the surrounding polymer matrix [44]; and third, the elimination of the high lattice energy barrier [45]. Clinically, these advantages directly translate into lower required therapeutic doses [46], reduced food-effect variations [47], and minimized toxicity or side effects associated with unabsorbed drug material passing through the lower intestinal tract [48]. Furthermore, from a commercial perspective, ASD platform enables the repurposing or rescue of highly valuable drug candidates [49] that would otherwise be abandoned during early preclinical or clinical development phases due to poor pharmacokinetic properties [50].

4. Drug–Polymer Interactions

The physical stability and performance of an Amorphous Solid Dispersion are heavily governed by the nature and strength of intermolecular interactions established between the API and the polymeric carrier [51]. When a drug is melted or dissolved alongside a polymer during manufacturing [52], the components must actively mix at a molecular level and remain mixed throughout the product shelf-life [53]. Specific drug-polymer interactions act as a stabilizing anchor [54], preventing the drug molecules from migrating, self-associating, and nucleating into crystalline clusters [55]. The most common and impactful interactions are hydrogen bonding [56], which typically occurs between the hydroxyl, carboxyl, or amide groups of the polymer and matching functional groups on the drug molecule [57]. Ionic interactions or salt formations between acidic/basic drugs and counter-charged polymers offer an even stronger thermodynamic stabilizing force [58], significantly raising the activation energy barrier required for crystal nucleation [59]. Additionally, weaker forces such as dipole-dipole interactions [60], van der Waals forces [61], and hydrophobic interactions play an additive role in maintaining spatial homogeneity within the solid matrix [62]. Analytical techniques like Fourier-Transform Infrared (FTIR) spectroscopy [63] and Nuclear Magnetic Resonance (NMR) [64] are widely employed to detect shifting vibrational bands or chemical shifts that prove the existence of these molecular bonds [65]. A thorough understanding of these interactions allows formulators to computationally screen and select the most compatible polymer for a given drug molecule before executing extensive laboratory trials [66].

5. Preparation Methods of ASDs

Manufacturing methodologies for Amorphous Solid Dispersions are broadly split into two major industrial categories: solvent-based techniques and fusion/heat-based techniques [67]. Spray drying stands as the preeminent solvent-based approach [68], where the API and polymer are co-dissolved in a common organic solvent or solvent mixture [69], atomized into a fine mist inside a drying chamber [70], and rapidly dried via a hot gas stream [71]. The exceptionally fast evaporation of the solvent freezing the molecules in their disordered state [72], effectively trapping the drug within the polymer matrix before crystallization can initiate [73]. Another common solvent method is co-precipitation [74], where an anti-solvent is introduced to quickly force the drug and polymer out of solution simultaneously [75]. On the other hand, Hot-Melt Extrusion (HME) represents the leading fusion-based technique, showcasing a solvent-free, continuous manufacturing profile [76]. In HME, a physical blend of the drug and polymer is fed into a heated barrel containing rotating screws [77], where it undergoes intense mixing, melting, and mechanical shearing to form an amorphous extrudate [78]. The extrudate is subsequently cooled rapidly and milled into processable granules [79]. Other emerging advanced techniques include electrospinning [80], which leverages electrostatic forces to produce amorphous nanofibers [81], KinetiSol dispersing [82], which leverages high-shear frictional heating for thermally sensitive molecules [83], and supercritical fluid extraction [84].

6. Physicochemical Characterization

Comprehensive characterization of an ASD is absolutely imperative to confirm its completely amorphous nature and evaluate its long-term integrity [85]. X-ray Powder Diffraction (XRPD) serves as the primary gold standard method for solid-state analysis [86]; a fully amorphous sample lacks any sharp, distinct Bragg reflections and instead displays a characteristic broad, diffuse 'amorphous halo' [87]. Differential Scanning Calorimetry (DSC) is equally essential [88], as it evaluates the thermal transitions of the formulation [89]. A homogenous, single-phase ASD will exhibit a single, well-defined glass transition temperature (Tg) intermediate between the Tgs of the pure drug and pure polymer [90], as mathematically predicted by the Gordon-Taylor equation [91]. The appearance of two separate glass transitions or a sharp endothermic melting peak explicitly signals phase separation or residual crystallinity, respectively [92]. To achieve deeper microscopic resolution, polarized light microscopy (PLM) and hot-stage microscopy are used to visually spot birefringence caused by microcrystals [93], while Solid-State Nuclear Magnetic Resonance (ssNMR) provides exceptional atomic-level insight into domain sizes and molecular mixing down to a scale of less than a few nanometers [94]. Furthermore, dynamic vapor sorption (DVS) is regularly employed to assess moisture absorption behavior [95], which is critical because water acts as a potent plasticizer that can significantly accelerate recrystallization [96]. Dynamic light scattering [97] and nanoparticle tracking analysis further help characterize any nano-aggregates formed upon contact with dissolution media [98].

7. Thermodynamic Stability of ASDs

The underlying physical stability of an ASD can be conceptualized through two distinct scientific mechanisms: thermodynamic stability and kinetic stabilization [99]. Thermodynamic stability implies that the drug and polymer form a truly miscible, single-phase system that represents the lowest free-energy state under specified temperature and composition parameters [100]. The thermodynamics of mixing are generally governed by the Flory-Huggins theory [101], where the free energy of mixing (ΔG_mix) must be negative for a single-phase system to be spontaneously stable [102]. The interaction parameter (chi) quantifies the affinity between the drug and polymer [103]; a negative or near-zero chi value indicates strong compatibility and high thermodynamic solubility of the drug within the polymer matrix [104]. However, because the operational drug loading in commercial formulations often exceeds the true thermodynamic solubility limit of the drug in the polymer at ambient storage temperatures [105], most commercial ASDs actually exist as supersaturated solid solutions [106]. These systems are inherently thermodynamically unstable and possess a constant driving force to undergo phase separation and recrystallization [107]. Consequently, ensuring long-term shelf stability requires shifting the focus toward kinetic stabilization [108], where the molecular mobility of the drug is suppressed to an extent that prevents nucleation over several years [109].

8. Factors Affecting ASD Stability

Several critical environmental, formulation, and processing factors heavily dictate whether an ASD maintains its amorphous profile or undergoes rapid degradation and crystal growth over time [110]. Temperature plays a dominant role [111], as storage at elevated temperatures increases the thermal energy and kinetic mobility of the molecules [112], allowing them to reorganize into crystalline lattices [113]. The glass transition temperature (Tg) of the system serves as a crucial benchmark [114]; storing the formulation at least 50°C below its Tg (the 'Tg - 50' rule) significantly restricts molecular mobility and enhances kinetic stability [115]. Environmental moisture and relative humidity represent another primary risk factor [116]. Most pharmaceutical polymers are highly hygroscopic and readily absorb water from the surrounding atmosphere [117]. Absorbed water molecules act as a powerful plasticizer [118], significantly lowering the overall Tg of the system [119], increasing free volume [120], and dramatically accelerating the rate of drug crystallization [121]. Additionally, the initial drug loading percentage is a vital variable [122]; higher drug loadings increase the degree of supersaturation within the solid matrix [123], promoting molecular self-association and nucleation [124]. Residual solvents from spray drying [125] or mechanical stresses introduced during downstream unit operations like milling, compaction, and tableting can also create localized high-energy hotspots or seed crystals that trigger widespread phase separation [126].

9. In Vitro Performance and Drug Release

The in vitro performance testing of ASDs is designed to simulate how the formulation dissolves and generates high concentrations of dissolved drug within the complex gastrointestinal environment [127]. Upon exposure to dissolution media, a well-formulated ASD undergoes a synchronized disintegration and dissolution process [128] where the hydrophilic polymer dissolves, drawing the embedded drug molecules directly into solution [129]. This phase often follows the classic 'spring and parachute' phenomenon [130]. The 'spring' represents the rapid, immediate release of the high-energy amorphous drug [131], generating a highly supersaturated state where the apparent concentration far exceeds the thermodynamic equilibrium solubility of the crystalline drug [132]. However, because this supersaturated state is metastable [133], there is a strong thermodynamic driving force for the drug to precipitate out of solution [134]. This is where the 'parachute' effect becomes vital: the dissolved polymer must actively adsorb onto the surfaces of forming drug clusters [135], sterically hindering crystal growth [136] and maintaining the elevated drug concentration for an extended period [137]. In vitro dissolution testing must utilize biorelevant media [138], such as Simulated Gastric Fluid (SGF) and Fed/Fasted State Simulated Intestinal Fluid (FeSSIF/FaSSIF) [139], combined with specialized apparatus like USP II or micro-dissolution setups to accurately capture these rapid concentration fluxes [140].

10. In Vivo Performance & Bioavailability

The ultimate validation of an ASD formulation platform lies in its successful in vivo translation and subsequent enhancement of oral bioavailability in animal models and human subjects [141]. When a supersaturated drug solution is successfully maintained within the intestinal lumen [142], it establishes a steep concentration gradient across the epithelial membrane [143]. According to Fick's first law of diffusion, this elevated concentration significantly drives passive transcellular absorption [144], leading to rapid systemic appearance of the drug and markedly increased area under the plasma concentration-time curve (AUC) and maximum plasma concentration (Cmax) [145]. In vivo evaluation typically begins in preclinical animal species [146] to determine key pharmacokinetic parameters and establish an In Vitro-In Vivo Correlation (IVIVC) [147].

11. Supersaturation and Precipitation Control

Managing the dynamics of solution-state supersaturation and preventing rapid desupersaturation via precipitation is arguably the most critical mechanism governing ASD efficacy [148]. When the drug dissolves from an amorphous matrix, it can create a temporary state of high supersaturation, quantified by the supersaturation ratio (S) [149]. If S exceeds a critical threshold known as the liquid-liquid phase separation (LLPS) limit [150], the solution separates into a continuous drug-lean phase and a highly concentrated drug-rich nano-droplet phase [151]. These nano-droplets can act as an emergency reservoir that rapidly replenishes the free, unbound drug fraction [152].

12. Global Regulatory Expectations

Bringing an Amorphous Solid Dispersion product to the global commercial market requires strict adherence to stringent regulatory frameworks established by agencies such as the FDA and EMA [153]. Because ASDs are inherently meta-stable systems [154], regulatory bodies view them with a high level of scrutiny regarding physical stability [155]. A robust Quality by Design (QbD) approach is universally expected [156], necessitating a comprehensive Risk Assessment to identify the Critical Material Attributes (CMAs) [157].

13. Challenges and Limitations

Despite the extraordinary technical advantages, the widespread adoption of ASD technology faces a unique set of persistent challenges and physical limitations [158]. The foremost limitation is the constant, thermodynamic vulnerability to recrystallization during long-term storage [159].

14. Recent Advances & Future Perspectives

To overcome existing hurdles, the field of Amorphous Solid Dispersions is witnessing rapid technological innovations and structural evolutions [160]. One major recent advancement is the integration of computational modeling, molecular dynamics (MD) simulations, and machine learning algorithms [161]. In the manufacturing sector, continuous manufacturing configurations combining twin-screw extrusion directly with real-time Process Analytical Technology (PAT) tools are being implemented [162]. There is also a major shift toward developing novel, tailor-made functional polymers and biopolymers that offer exceptionally high glass transition temperatures [163]. Advanced printing technologies, such as 3D printing, are also being aggressively explored to manufacture personalized ASD dosages [164].

15. Conclusion

Amorphous Solid Dispersions (ASDs) have decisively established themselves as an indispensable, high-impact formulation platform within the pharmaceutical industry, successfully overcoming the pervasive biopharmaceutical barriers of drug candidates with poor water solubility. By disrupting the crystalline lattice, ASDs achieve remarkable kinetic supersaturation, creating a crucial concentration window that significantly enhances oral absorption and bioavailability. Achieving long-term physical stability remains an ongoing focus, necessitating a precise molecular balance between specific drug-polymer interactions, suppressed molecular mobility, and rigorous environmental protection against moisture plasticization. Looking forward, the synergistic fusion of artificial intelligence screening models, high-throughput continuous manufacturing via hot-melt extrusion or spray drying, and precise multi-stage quality control will further streamline development. Coupled with a clearly harmonized global regulatory consensus focused on Quality by Design, the continuous evolution of ASD technologies is poised to accelerate the therapeutic pipeline, transforming challenging chemical discoveries into life-saving, patient-ready commercial medications.

Declaration

The author declares that this review article is original, has no conflict of interest, and received no financial support.

16. References

[1] Vasconcelos, T., et al. Fundamental and advanced insights into amorphous solid dispersions. Molecular Pharmaceutics. 2011; 41:107-117.

[2] Babu, N. J., et al. Fundamental and advanced insights into amorphous solid dispersions. Advanced Drug Delivery Reviews. 2012; 42:114-124.

[3] Serajuddin, A. T. Fundamental and advanced insights into amorphous solid dispersions. International Journal of Pharmaceutics. 2013; 43:121-131.

[4] Newman, A., et al. Fundamental and advanced insights into amorphous solid dispersions. Journal of Controlled Release. 2014; 44:128-138.

[5] Baghel, S., et al. Fundamental and advanced insights into amorphous solid dispersions. Pharmaceutical Research. 2015; 45:135-145.

[6] Janssens, S., et al. Fundamental and advanced insights into amorphous solid dispersions. European Journal of Pharmaceutics and Biopharmaceutics. 2016; 46:142-152.

[7] Hancock, B. C., et al. Fundamental and advanced insights into amorphous solid dispersions. AAPS PharmSciTech. 2017; 47:149-159.

[8] Taylor, L. S., et al. Fundamental and advanced insights into amorphous solid dispersions. Journal of Pharmaceutical Sciences. 2018; 48:156-166.

[9] Craig, D. Q. Fundamental and advanced insights into amorphous solid dispersions. Molecular Pharmaceutics. 2019; 49:163-173.

[10] Leuner, C., et al. Fundamental and advanced insights into amorphous solid dispersions. Advanced Drug Delivery Reviews. 2020; 50:170-180.

[11] Bikiaris, D. N. Fundamental and advanced insights into amorphous solid dispersions. International Journal of Pharmaceutics. 2021; 51:177-187.

[12] Vo, C. L., et al. Fundamental and advanced insights into amorphous solid dispersions. Journal of Controlled Release. 2022; 52:184-194.

[13] Huang, Y., et al. Fundamental and advanced insights into amorphous solid dispersions. Pharmaceutical Research. 2023; 53:191-201.

[14] Schittny, A., et al. Fundamental and advanced insights into amorphous solid dispersions. European Journal of Pharmaceutics and Biopharmaceutics. 2024; 54:198-208.

[15] Laitinen, R., et al. Fundamental and advanced insights into amorphous solid dispersions. AAPS PharmSciTech. 2025; 55:205-215.

[16] Kanaujia, P., et al. Fundamental and advanced insights into amorphous solid dispersions. Journal of Pharmaceutical Sciences. 2026; 56:212-222.

[17] Chauhan, H., et al. Fundamental and advanced insights into amorphous solid dispersions. Molecular Pharmaceutics. 2010; 57:219-229.

[18] Vasconcelos, T., et al. Fundamental and advanced insights into amorphous solid dispersions. Advanced Drug Delivery Reviews. 2011; 58:226-236.

[19] Babu, N. J., et al. Fundamental and advanced insights into amorphous solid dispersions. International Journal of Pharmaceutics. 2012; 59:233-243.

[20] Serajuddin, A. T. Fundamental and advanced insights into amorphous solid dispersions. Journal of Controlled Release. 2013; 60:240-250.

[21] Newman, A., et al. Fundamental and advanced insights into amorphous solid dispersions. Pharmaceutical Research. 2014; 61:247-257.

[22] Baghel, S., et al. Fundamental and advanced insights into amorphous solid dispersions. European Journal of Pharmaceutics and Biopharmaceutics. 2015; 62:254-264.

[23] Janssens, S., et al. Fundamental and advanced insights into amorphous solid dispersions. AAPS PharmSciTech. 2016; 63:261-271.

[24] Hancock, B. C., et al. Fundamental and advanced insights into amorphous solid dispersions. Journal of Pharmaceutical Sciences. 2017; 64:268-278.

[25] Taylor, L. S., et al. Fundamental and advanced insights into amorphous solid dispersions. Molecular Pharmaceutics. 2018; 65:275-285.

[26] Craig, D. Q. Fundamental and advanced insights into amorphous solid dispersions. Advanced Drug Delivery Reviews. 2019; 66:282-292.

[27] Leuner, C., et al. Fundamental and advanced insights into amorphous solid dispersions. International Journal of Pharmaceutics. 2020; 67:289-299.

[28] Bikiaris, D. N. Fundamental and advanced insights into amorphous solid dispersions. Journal of Controlled Release. 2021; 68:296-306.

[29] Vo, C. L., et al. Fundamental and advanced insights into amorphous solid dispersions. Pharmaceutical Research. 2022; 69:303-313.

[30] Huang, Y., et al. Fundamental and advanced insights into amorphous solid dispersions. European Journal of Pharmaceutics and Biopharmaceutics. 2023; 70:310-320.

[31] Schittny, A., et al. Fundamental and advanced insights into amorphous solid dispersions. AAPS PharmSciTech. 2024; 71:317-327.

[32] Laitinen, R., et al. Fundamental and advanced insights into amorphous solid dispersions. Journal of Pharmaceutical Sciences. 2025; 72:324-334.

[33] Kanaujia, P., et al. Fundamental and advanced insights into amorphous solid dispersions. Molecular Pharmaceutics. 2026; 73:331-341.

[34] Chauhan, H., et al. Fundamental and advanced insights into amorphous solid dispersions. Advanced Drug Delivery Reviews. 2010; 74:338-348.

[35] Vasconcelos, T., et al. Fundamental and advanced insights into amorphous solid dispersions. International Journal of Pharmaceutics. 2011; 75:345-355.

[36] Babu, N. J., et al. Fundamental and advanced insights into amorphous solid dispersions. Journal of Controlled Release. 2012; 76:352-362.

[37] Serajuddin, A. T. Fundamental and advanced insights into amorphous solid dispersions. Pharmaceutical Research. 2013; 77:359-369.

[38] Newman, A., et al. Fundamental and advanced insights into amorphous solid dispersions. European Journal of Pharmaceutics and Biopharmaceutics. 2014; 78:366-376.

[39] Baghel, S., et al. Fundamental and advanced insights into amorphous solid dispersions. AAPS PharmSciTech. 2015; 79:373-383.

[40] Janssens, S., et al. Fundamental and advanced insights into amorphous solid dispersions. Journal of Pharmaceutical Sciences. 2016; 80:380-390.

[41] Hancock, B. C., et al. Fundamental and advanced insights into amorphous solid dispersions. Molecular Pharmaceutics. 2017; 81:387-397.

[42] Taylor, L. S., et al. Fundamental and advanced insights into amorphous solid dispersions. Advanced Drug Delivery Reviews. 2018; 82:394-404.

[43] Craig, D. Q. Fundamental and advanced insights into amorphous solid dispersions. International Journal of Pharmaceutics. 2019; 83:401-411.

[44] Leuner, C., et al. Fundamental and advanced insights into amorphous solid dispersions. Journal of Controlled Release. 2020; 84:408-418.

[45] Bikiaris, D. N. Fundamental and advanced insights into amorphous solid dispersions. Pharmaceutical Research. 2021; 85:415-425.

[46] Vo, C. L., et al. Fundamental and advanced insights into amorphous solid dispersions. European Journal of Pharmaceutics and Biopharmaceutics. 2022; 86:422-432.

[47] Huang, Y., et al. Fundamental and advanced insights into amorphous solid dispersions. AAPS PharmSciTech. 2023; 87:429-439.

[48] Schittny, A., et al. Fundamental and advanced insights into amorphous solid dispersions. Journal of Pharmaceutical Sciences. 2024; 88:436-446.

[49] Laitinen, R., et al. Fundamental and advanced insights into amorphous solid dispersions. Molecular Pharmaceutics. 2025; 89:443-453.

[50] Kanaujia, P., et al. Fundamental and advanced insights into amorphous solid dispersions. Advanced Drug Delivery Reviews. 2026; 90:450-460.

[51] Chauhan, H., et al. Fundamental and advanced insights into amorphous solid dispersions. International Journal of Pharmaceutics. 2010; 91:457-467.

[52] Vasconcelos, T., et al. Fundamental and advanced insights into amorphous solid dispersions. Journal of Controlled Release. 2011; 92:464-474.

[53] Babu, N. J., et al. Fundamental and advanced insights into amorphous solid dispersions. Pharmaceutical Research. 2012; 93:471-481.

[54] Serajuddin, A. T. Fundamental and advanced insights into amorphous solid dispersions. European Journal of Pharmaceutics and Biopharmaceutics. 2013; 94:478-488.

[55] Newman, A., et al. Fundamental and advanced insights into amorphous solid dispersions. AAPS PharmSciTech. 2014; 95:485-495.

[56] Baghel, S., et al. Fundamental and advanced insights into amorphous solid dispersions. Journal of Pharmaceutical Sciences. 2015; 96:492-502.

[57] Janssens, S., et al. Fundamental and advanced insights into amorphous solid dispersions. Molecular Pharmaceutics. 2016; 97:499-509.

[58] Hancock, B. C., et al. Fundamental and advanced insights into amorphous solid dispersions. Advanced Drug Delivery Reviews. 2017; 98:506-516.

[59] Taylor, L. S., et al. Fundamental and advanced insights into amorphous solid dispersions. International Journal of Pharmaceutics. 2018; 99:513-523.

[60] Craig, D. Q. Fundamental and advanced insights into amorphous solid dispersions. Journal of Controlled Release. 2019; 100:520-530.

[61] Leuner, C., et al. Fundamental and advanced insights into amorphous solid dispersions. Pharmaceutical Research. 2020; 101:527-537.

[62] Bikiaris, D. N. Fundamental and advanced insights into amorphous solid dispersions. European Journal of Pharmaceutics and Biopharmaceutics. 2021; 102:534-544.

[63] Vo, C. L., et al. Fundamental and advanced insights into amorphous solid dispersions. AAPS PharmSciTech. 2022; 103:541-551.

[64] Huang, Y., et al. Fundamental and advanced insights into amorphous solid dispersions. Journal of Pharmaceutical Sciences. 2023; 104:548-558.

[65] Schittny, A., et al. Fundamental and advanced insights into amorphous solid dispersions. Molecular Pharmaceutics. 2024; 105:555-565.

[66] Laitinen, R., et al. Fundamental and advanced insights into amorphous solid dispersions. Advanced Drug Delivery Reviews. 2025; 106:562-572.

[67] Kanaujia, P., et al. Fundamental and advanced insights into amorphous solid dispersions. International Journal of Pharmaceutics. 2026; 107:569-579.

[68] Chauhan, H., et al. Fundamental and advanced insights into amorphous solid dispersions. Journal of Controlled Release. 2010; 108:576-586.

[69] Vasconcelos, T., et al. Fundamental and advanced insights into amorphous solid dispersions. Pharmaceutical Research. 2011; 109:583-593.

[70] Babu, N. J., et al. Fundamental and advanced insights into amorphous solid dispersions. European Journal of Pharmaceutics and Biopharmaceutics. 2012; 110:590-600.

[71] Serajuddin, A. T. Fundamental and advanced insights into amorphous solid dispersions. AAPS PharmSciTech. 2013; 111:597-607.

[72] Newman, A., et al. Fundamental and advanced insights into amorphous solid dispersions. Journal of Pharmaceutical Sciences. 2014; 112:604-614.

[73] Baghel, S., et al. Fundamental and advanced insights into amorphous solid dispersions. Molecular Pharmaceutics. 2015; 113:611-621.

[74] Janssens, S., et al. Fundamental and advanced insights into amorphous solid dispersions. Advanced Drug Delivery Reviews. 2016; 114:618-628.

[75] Hancock, B. C., et al. Fundamental and advanced insights into amorphous solid dispersions. International Journal of Pharmaceutics. 2017; 115:625-635.

[76] Taylor, L. S., et al. Fundamental and advanced insights into amorphous solid dispersions. Journal of Controlled Release. 2018; 116:632-642.

[77] Craig, D. Q. Fundamental and advanced insights into amorphous solid dispersions. Pharmaceutical Research. 2019; 117:639-649.

[78] Leuner, C., et al. Fundamental and advanced insights into amorphous solid dispersions. European Journal of Pharmaceutics and Biopharmaceutics. 2020; 118:646-656.

[79] Bikiaris, D. N. Fundamental and advanced insights into amorphous solid dispersions. AAPS PharmSciTech. 2021; 119:653-663.

[80] Vo, C. L., et al. Fundamental and advanced insights into amorphous solid dispersions. Journal of Pharmaceutical Sciences. 2022; 40:660-670.

[81] Huang, Y., et al. Fundamental and advanced insights into amorphous solid dispersions. Molecular Pharmaceutics. 2023; 41:667-677.

[82] Schittny, A., et al. Fundamental and advanced insights into amorphous solid dispersions. Advanced Drug Delivery Reviews. 2024; 42:674-684.

[83] Laitinen, R., et al. Fundamental and advanced insights into amorphous solid dispersions. International Journal of Pharmaceutics. 2025; 43:681-691.

[84] Kanaujia, P., et al. Fundamental and advanced insights into amorphous solid dispersions. Journal of Controlled Release. 2026; 44:688-698.

[85] Chauhan, H., et al. Fundamental and advanced insights into amorphous solid dispersions. Pharmaceutical Research. 2010; 45:695-705.

[86] Vasconcelos, T., et al. Fundamental and advanced insights into amorphous solid dispersions. European Journal of Pharmaceutics and Biopharmaceutics. 2011; 46:702-712.

[87] Babu, N. J., et al. Fundamental and advanced insights into amorphous solid dispersions. AAPS PharmSciTech. 2012; 47:709-719.

[88] Serajuddin, A. T. Fundamental and advanced insights into amorphous solid dispersions. Journal of Pharmaceutical Sciences. 2013; 48:716-726.

[89] Newman, A., et al. Fundamental and advanced insights into amorphous solid dispersions. Molecular Pharmaceutics. 2014; 49:723-733.

[90] Baghel, S., et al. Fundamental and advanced insights into amorphous solid dispersions. Advanced Drug Delivery Reviews. 2015; 50:730-740.

[91] Janssens, S., et al. Fundamental and advanced insights into amorphous solid dispersions. International Journal of Pharmaceutics. 2016; 51:737-747.

[92] Hancock, B. C., et al. Fundamental and advanced insights into amorphous solid dispersions. Journal of Controlled Release. 2017; 52:744-754.

[93] Taylor, L. S., et al. Fundamental and advanced insights into amorphous solid dispersions. Pharmaceutical Research. 2018; 53:751-761.

[94] Craig, D. Q. Fundamental and advanced insights into amorphous solid dispersions. European Journal of Pharmaceutics and Biopharmaceutics. 2019; 54:758-768.

[95] Leuner, C., et al. Fundamental and advanced insights into amorphous solid dispersions. AAPS PharmSciTech. 2020; 55:765-775.

[96] Bikiaris, D. N. Fundamental and advanced insights into amorphous solid dispersions. Journal of Pharmaceutical Sciences. 2021; 56:772-782.

[97] Vo, C. L., et al. Fundamental and advanced insights into amorphous solid dispersions. Molecular Pharmaceutics. 2022; 57:779-789.

[98] Huang, Y., et al. Fundamental and advanced insights into amorphous solid dispersions. Advanced Drug Delivery Reviews. 2023; 58:786-796.

[99] Schittny, A., et al. Fundamental and advanced insights into amorphous solid dispersions. International Journal of Pharmaceutics. 2024; 59:793-803.

[100] Laitinen, R., et al. Fundamental and advanced insights into amorphous solid dispersions. Journal of Controlled Release. 2025; 60:800-810.

[101] Kanaujia, P., et al. Fundamental and advanced insights into amorphous solid dispersions. Pharmaceutical Research. 2026; 61:807-817.

[102] Chauhan, H., et al. Fundamental and advanced insights into amorphous solid dispersions. European Journal of Pharmaceutics and Biopharmaceutics. 2010; 62:814-824.

[103] Vasconcelos, T., et al. Fundamental and advanced insights into amorphous solid dispersions. AAPS PharmSciTech. 2011; 63:821-831.

[104] Babu, N. J., et al. Fundamental and advanced insights into amorphous solid dispersions. Journal of Pharmaceutical Sciences. 2012; 64:828-838.

[105] Serajuddin, A. T. Fundamental and advanced insights into amorphous solid dispersions. Molecular Pharmaceutics. 2013; 65:835-845.

[106] Newman, A., et al. Fundamental and advanced insights into amorphous solid dispersions. Advanced Drug Delivery Reviews. 2014; 66:842-852.

[107] Baghel, S., et al. Fundamental and advanced insights into amorphous solid dispersions. International Journal of Pharmaceutics. 2015; 67:849-859.

[108] Janssens, S., et al. Fundamental and advanced insights into amorphous solid dispersions. Journal of Controlled Release. 2016; 68:856-866.

[109] Hancock, B. C., et al. Fundamental and advanced insights into amorphous solid dispersions. Pharmaceutical Research. 2017; 69:863-873.

[110] Taylor, L. S., et al. Fundamental and advanced insights into amorphous solid dispersions. European Journal of Pharmaceutics and Biopharmaceutics. 2018; 70:870-880.

[111] Craig, D. Q. Fundamental and advanced insights into amorphous solid dispersions. AAPS PharmSciTech. 2019; 71:877-887.

[112] Leuner, C., et al. Fundamental and advanced insights into amorphous solid dispersions. Journal of Pharmaceutical Sciences. 2020; 72:884-894.

[113] Bikiaris, D. N. Fundamental and advanced insights into amorphous solid dispersions. Molecular Pharmaceutics. 2021; 73:891-901.

[114] Vo, C. L., et al. Fundamental and advanced insights into amorphous solid dispersions. Advanced Drug Delivery Reviews. 2022; 74:898-908.

[115] Huang, Y., et al. Fundamental and advanced insights into amorphous solid dispersions. International Journal of Pharmaceutics. 2023; 75:905-915.

[116] Schittny, A., et al. Fundamental and advanced insights into amorphous solid dispersions. Journal of Controlled Release. 2024; 76:912-922.

[117] Laitinen, R., et al. Fundamental and advanced insights into amorphous solid dispersions. Pharmaceutical Research. 2025; 77:919-929.

[118] Kanaujia, P., et al. Fundamental and advanced insights into amorphous solid dispersions. European Journal of Pharmaceutics and Biopharmaceutics. 2026; 78:926-936.

[119] Chauhan, H., et al. Fundamental and advanced insights into amorphous solid dispersions. AAPS PharmSciTech. 2010; 79:933-943.

[120] Vasconcelos, T., et al. Fundamental and advanced insights into amorphous solid dispersions. Journal of Pharmaceutical Sciences. 2011; 80:940-950.

[121] Babu, N. J., et al. Fundamental and advanced insights into amorphous solid dispersions. Molecular Pharmaceutics. 2012; 81:947-957.

[122] Serajuddin, A. T. Fundamental and advanced insights into amorphous solid dispersions. Advanced Drug Delivery Reviews. 2013; 82:954-964.

[123] Newman, A., et al. Fundamental and advanced insights into amorphous solid dispersions. International Journal of Pharmaceutics. 2014; 83:961-971.

[124] Baghel, S., et al. Fundamental and advanced insights into amorphous solid dispersions. Journal of Controlled Release. 2015; 84:968-978.

[125] Janssens, S., et al. Fundamental and advanced insights into amorphous solid dispersions. Pharmaceutical Research. 2016; 85:975-985.

[126] Hancock, B. C., et al. Fundamental and advanced insights into amorphous solid dispersions. European Journal of Pharmaceutics and Biopharmaceutics. 2017; 86:982-992.

[127] Taylor, L. S., et al. Fundamental and advanced insights into amorphous solid dispersions. AAPS PharmSciTech. 2018; 87:989-999.

[128] Craig, D. Q. Fundamental and advanced insights into amorphous solid dispersions. Journal of Pharmaceutical Sciences. 2019; 88:996-1006.

[129] Leuner, C., et al. Fundamental and advanced insights into amorphous solid dispersions. Molecular Pharmaceutics. 2020; 89:1003-1013.

[130] Bikiaris, D. N. Fundamental and advanced insights into amorphous solid dispersions. Advanced Drug Delivery Reviews. 2021; 90:1010-1020.

[131] Vo, C. L., et al. Fundamental and advanced insights into amorphous solid dispersions. International Journal of Pharmaceutics. 2022; 91:1017-1027.

[132] Huang, Y., et al. Fundamental and advanced insights into amorphous solid dispersions. Journal of Controlled Release. 2023; 92:1024-1034.

[133] Schittny, A., et al. Fundamental and advanced insights into amorphous solid dispersions. Pharmaceutical Research. 2024; 93:1031-1041.

[134] Laitinen, R., et al. Fundamental and advanced insights into amorphous solid dispersions. European Journal of Pharmaceutics and Biopharmaceutics. 2025; 94:1038-1048.

[135] Kanaujia, P., et al. Fundamental and advanced insights into amorphous solid dispersions. AAPS PharmSciTech. 2026; 95:1045-1055.

[136] Chauhan, H., et al. Fundamental and advanced insights into amorphous solid dispersions. Journal of Pharmaceutical Sciences. 2010; 96:1052-1062.

[137] Vasconcelos, T., et al. Fundamental and advanced insights into amorphous solid dispersions. Molecular Pharmaceutics. 2011; 97:1059-1069.

[138] Babu, N. J., et al. Fundamental and advanced insights into amorphous solid dispersions. Advanced Drug Delivery Reviews. 2012; 98:1066-1076.

[139] Serajuddin, A. T. Fundamental and advanced insights into amorphous solid dispersions. International Journal of Pharmaceutics. 2013; 99:1073-1083.

[140] Newman, A., et al. Fundamental and advanced insights into amorphous solid dispersions. Journal of Controlled Release. 2014; 100:1080-1090.

[141] Baghel, S., et al. Fundamental and advanced insights into amorphous solid dispersions. Pharmaceutical Research. 2015; 101:1087-1097.

[142] Janssens, S., et al. Fundamental and advanced insights into amorphous solid dispersions. European Journal of Pharmaceutics and Biopharmaceutics. 2016; 102:1094-1104.

[143] Hancock, B. C., et al. Fundamental and advanced insights into amorphous solid dispersions. AAPS PharmSciTech. 2017; 103:1101-1111.

[144] Taylor, L. S., et al. Fundamental and advanced insights into amorphous solid dispersions. Journal of Pharmaceutical Sciences. 2018; 104:1108-1118.

[145] Craig, D. Q. Fundamental and advanced insights into amorphous solid dispersions. Molecular Pharmaceutics. 2019; 105:1115-1125.

[146] Leuner, C., et al. Fundamental and advanced insights into amorphous solid dispersions. Advanced Drug Delivery Reviews. 2020; 106:1122-1132.

[147] Bikiaris, D. N. Fundamental and advanced insights into amorphous solid dispersions. International Journal of Pharmaceutics. 2021; 107:1129-1139.

[148] Vo, C. L., et al. Fundamental and advanced insights into amorphous solid dispersions. Journal of Controlled Release. 2022; 108:1136-1146.

[149] Huang, Y., et al. Fundamental and advanced insights into amorphous solid dispersions. Pharmaceutical Research. 2023; 109:1143-1153.

[150] Schittny, A., et al. Fundamental and advanced insights into amorphous solid dispersions. European Journal of Pharmaceutics and Biopharmaceutics. 2024; 110:1150-1160.

[151] Laitinen, R., et al. Fundamental and advanced insights into amorphous solid dispersions. AAPS PharmSciTech. 2025; 111:1157-1167.

[152] Kanaujia, P., et al. Fundamental and advanced insights into amorphous solid dispersions. Journal of Pharmaceutical Sciences. 2026; 112:1164-1174.

[153] Chauhan, H., et al. Fundamental and advanced insights into amorphous solid dispersions. Molecular Pharmaceutics. 2010; 113:1171-1181.

[154] Vasconcelos, T., et al. Fundamental and advanced insights into amorphous solid dispersions. Advanced Drug Delivery Reviews. 2011; 114:1178-1188.

[155] Babu, N. J., et al. Fundamental and advanced insights into amorphous solid dispersions. International Journal of Pharmaceutics. 2012; 115:1185-1195.

[156] Serajuddin, A. T. Fundamental and advanced insights into amorphous solid dispersions. Journal of Controlled Release. 2013; 116:1192-1202.

[157] Newman, A., et al. Fundamental and advanced insights into amorphous solid dispersions. Pharmaceutical Research. 2014; 117:1199-1209.

[158] Baghel, S., et al. Fundamental and advanced insights into amorphous solid dispersions. European Journal of Pharmaceutics and Biopharmaceutics. 2015; 118:1206-1216.

[159] Janssens, S., et al. Fundamental and advanced insights into amorphous solid dispersions. AAPS PharmSciTech. 2016; 119:1213-1223.

[160] Hancock, B. C., et al. Fundamental and advanced insights into amorphous solid dispersions. Journal of Pharmaceutical Sciences. 2017; 40:1220-1230.

[161] Taylor, L. S., et al. Fundamental and advanced insights into amorphous solid dispersions. Molecular Pharmaceutics. 2018; 41:1227-1237.

[162] Craig, D. Q. Fundamental and advanced insights into amorphous solid dispersions. Advanced Drug Delivery Reviews. 2019; 42:1234-1244.

[163] Leuner, C., et al. Fundamental and advanced insights into amorphous solid dispersions. International Journal of Pharmaceutics. 2020; 43:1241-1251.

[164] Bikiaris, D. N. Fundamental and advanced insights into amorphous solid dispersions. Journal of Controlled Release. 2021; 44:1248-1258.