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Process Analytical Technology (PAT) Enabled Manufacturing of Amorphous Solid Dispersions: Advancing Process Control

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ABSTRACT

The therapeutic potential of drugs belonging to the Biopharmaceutics Classification System Class II and IV is limited by their severe solubility and bioavailability issues. Of the various solubility enhancement strategies explored, preparations of Amorphous Solid Dispersions (ASDs) are a potentially robust approach. When compared to crystalline dosage forms, ASDs provide better drug solubility and absorption, making them a useful strategy for bioavailability enhancement. This review examines a range of ASD manufacturing processes, including conventional approaches such as spray-drying and hot melt extrusion, as well as cutting-edge technologies like 3D printing and supercritical fluid processing. Furthermore, the article highlights the application of process analytical techniques (PAT), which are crucial for monitoring and controlling the manufacturing of ASDs. PAT-based analytical tools such as near infrared, mid infrared, and Raman spectroscopy offer important data about the solid-state characteristics, drug-polymer interaction, and other functional characteristics of ASDs. Enabling control over the manufacturing process via PAT-based analytical tools, assures better product quality and lower chances of product failure. Through the integration of manufacturing and analytical characterization improvements, this review provides a thorough framework for creating formulations based on ASDs.

Keywords: Amorphous Solid Dispersions; Solubility Enhancement; Hot-Melt Extrusion; Spray Drying; Supercritical Fluid Technology; Process Analytical Technology; Process control

1. INTRODUCTION

Recent reports suggest that most of the new drug moieties entering the research pipeline face lower bioavailability due to poor solubility and delayed dissolution rate. Exploring and executing strategies for improving the dissolution rate and bioavailability of such drugs deters the formulation development process. Numerous approaches have been investigated and researched for solubility enhancement, including, but not limited to, complexation with cyclodextrins, micellar systems, salt formation, particle size reduction, and micro/nano-emulsifying systems[1-5]. These strategies, though effective for multiple actives are often limited by drawbacks such as low drug-loading ability, use of organic solvents, and use of energy-intensive methods. One such solubility-enhancement method capable of overcoming most of the above-listed drawbacks is the development of Amorphous Solid Dispersions (ASDs) as documented in Table 1. The distortion of the crystal lattice generates a high-energy state analogous to the amorphous form, thereby enhancing the solubility and dissolution rate of the drugs incorporated in an ASD[6-8].

ASD system encapsulates the amorphous drug uniformly distributed throughout a lipid or polymer matrix. Amorphization enhances the solubility of a drug due to a rise in the Gibbs free energy and molecular mobility. The greater free energy drives the interaction of the drug with the dissolution media, thus enhancing the force that drives absorption by developing a transiently supersaturated solution during dissolution [9-10]. The molecular dispersion of the drugs in the ASD matrix also further improves the dissolution rate. Pharmaceutical compounds in their amorphous form tend to revert to their more stable crystalline form because they are thermodynamically metastable. In contrast to crystalline forms, amorphous forms often demonstrate higher degrees of supersaturation under aqueous conditions, resulting in increased solubility. Besides enhancing the solubility and dissolution rate, ASDs also improve the wettability of the drugs, thereby increasing membrane flux and improving oral bioavailability[11-12].

Drug characteristics can be customized with ASDs to accommodate a broad range of formulation possibilities. ASDs can be effectively reformulated to several formulations, such as conventional oral solid dosage forms, as well as immediate and controlled release formulations[13-14].

2. MANUFACTURING OF ASDs AND PAT

Numerous manufacturing techniques have been researched and documented for the preparation of ASDs, albeit the basic principle of their preparation remains the same. The crystal lattice matrix of the molecule is dismantled either by heating or solubilization in a solvent, followed by rapid cooling or drying as the case might be. The manufacturing techniques are classified into two distinct categories: 'Melting/Fusion-based methods' and 'Solvent Evaporation-based methods'. The former includes methods including 'Kinetisol' and 'Hot melt extrusion', while the latter principle is the basis for several techniques, such as 'fluidized bed technology', 'electrospraying', 'electrospinning', 'freeze-spray drying', 'spray-drying', and 'supercritical fluid technology'[15-17]. Besides these conventional methods, several cutting-edge techniques such as 3D printing are being investigated to address the shortcomings of the current production methods[18-20]. ASDs will invariably have diverse functional and physical characteristics depending on the production process chosen, hence the manufacturing methods must be carefully screened depending on the end-product characteristics[21, 22].

The degree of crystallinity of a drug in an ASD has a significant impact on the stability and effectiveness of the final product since their solubility and bioavailability are dependent on its polymorphic form. Therefore, it is critical to characterize each product using solid state characterization methods like powder 'X-ray powder diffraction' (PXRD), 'Fourier Transform Infrared' (FTIR), and 'Differential Scanning Calorimetry' (DSC)[23-24]. Though imperative to the success of an ASD, these methods, however, are typically limited to offline measurements, requiring careful randomization of the sampling process, transport of samples to the appropriate laboratory, and complex sample preparation protocols that vary based on the analytical technique employed. Moreover, these measurements are time-consuming and costly[25].

In 2002, the United States Food and Drug Administration launched an initiative to upgrade the pharmaceutical manufacturing process and enhance the quality of the drug product. This initiative known as 'Pharmaceutical CGMPs for the 21st Century: A Risk-Based Approach' was announced with the intent of reducing consumer risk. This initiative complemented by the utilization of the latest advancement in manufacturing techniques, and concepts of 'quality management systems' and 'risk management' ensured a robust manufacturing process[26-28]. In conjunction with the publication of this guideline, the FDA's guidance document for industry, 'PAT—A Framework for Innovative Pharmaceutical Development, Manufacturing, and Quality Assurance', was issued with the goal of developing a designed to foster the adoption of advanced methodologies in pharmaceutical research, production processes, and quality management[29, 30]. Process Analytical Technology (PAT) is important for improving understanding of the process and product, as well as exerting more control over the production process[31].

While International Conference on Harmonization (ICH) Q8(R2) is often credited with the emergence of Quality by Design (QbD), the concept of QbD was first introduced with the PAT guideline. Designing and developing well-understood procedures that consistently ensure a predetermined quality of the manufactured product was a fundamental principle of QbD that was established in the PAT guidance and given as a desired goal of PAT. Establishing a relationship between the manufacturing process, material attributes, and quality characteristics of the drug product enables integration of process monitoring and control techniques, assuring that the finished product meets its predetermined quality standards[32, 33]. The objective of PAT is to constantly manufacture products with a predetermined level of quality and enable pharmaceutical manufacturers to switch from the tedious and empirical batch manufacturing methods that requires time-consuming and labor-intensive off-line sampling and analysis, to a more consistent and flexible method of manufacturing pharmaceuticals. Such PAT tools when incorporated in the manufacturing of ASDs can enable real-time monitoring and control of the polymorphic form of the drug that influence the stability and bioavailability of the formulation.

This review aims to present a brief overview of the various methodologies employed for the fabrication of ASDs, with emphasis on the application of PAT methodologies for exerting better control over the manufacturing process.

3. METHODS FOR MANUFACTURING ASDs

The manufacturing techniques are classified into two distinct categories: Melting/Fusion-based methods and Solvent Evaporation-based methods. The former includes methods such as Kinetisol and Hot melt extrusion, while the latter principle is the basis for several techniques, such as fluidized bed technology, electrospraying, electrospinning, freeze-spray drying, spray-drying, and supercritical fluid technology[15-17]. Solvent evaporation-based methods involve dissolving drug-polymer combinations in an organic solvent system, followed by evaporation of the solvent system. In Fusion-based methods, the drug-polymer matrix is heated to create molten dispersions and then cooled.

3.1 Solvent Evaporation-Based Methods

Spray Drying and Electrospraying

Spray drying is a conventional, continuous, scalable manufacturing technique to formulate ASDs that generates nano- to micron-sized particles with a narrow size-distribution in a very short time-frame[36,37]. Introducing variations in the construction and operating conditions of these established designs enable the control of the particle size distribution and density of the final product. Of particular importance for spray drying of amorphous systems is the need for strict inter-batch control of the temperature and humidity of the drying air[38-40]. The steps that have a crucial impact on the drying efficiency of the process and therefore can significantly impact the solid-state properties of ASD[41]. Analogous to the spray-drying process described earlier, electrospraying employs electrical energy to atomise feed liquid to produce low particle size (nanometre range) quasi-monodisperse products[43,44].

Fluidized Bed Technology

The fluidized bed technology, commonly known as the Wurster process has also been explored for the manufacturing of ASDs using granulators and fluidised bed coaters wherein a homogenous solution of drug and carriers is sprayed onto the surface of inert excipients or beads[46].

Supercritical fluid technology

Supercritical fluid technology (SFT) for the preparation of ASDs uses carbon dioxide (CO_2) as a solvent or anti-solvent. The matrix-former and drug are dissolved in supercritical CO_2 and sprayed via a nozzle into a lower-pressure expansion vessel, where ASD particles are spontaneously generated. The mixture cools quickly due to adiabatic expansion[53-55]. Supercritical fluid technology (SFT) is a safe, environmentally friendly, green, and sustainable technique. SFT-CO_2-assisted impregnation, which delivers pharmaceuticals into polymeric materials, is a viable substitute for traditional techniques, which normally ask for the use of appropriate solvents[56].

3.2 Fusion/ Melting-Based Methods

Hot-Melt Extrusion

Hot melt extrusion (HME) is a versatile technique used for the formulation of ASDs to improve the dissolution rate and the bioavailability of poorly soluble drugs. HME involved circulating a blend of drug and polymeric materials with a rotating screw at temperatures above their melting temperature to achieve molecular-level mixing of the active compounds and thermoplastic binders or polymers. This molecular mixing converts the components into an amorphous product with a uniform shape and density, thereby increasing the dissolution profile of the poorly water-soluble drug[62-65].

KinetiSol

This is a relatively recent fusion-based technique that produces an ASD by applying high shear force and heat to a molten blend of drug and polymer. Frictional and shear energy are produced in huge quantities by spinning of paddles in a cylindrical tank and the shaft having mixing blades of high speed. Without the need for external heating, the temperature of the material rises because of this mechanical force[70,71].

3.3 Novel Methods for Fabrication of ASDs

Three-dimensional printing (3DP)

Three-dimensional printing (3DP) is a cutting-edge additive manufacturing (AM) process that has revolutionized the fabrication of customised dosage forms and developed a new approach to individualized treatment. The technique uses layer-by-layer sequential material deposition to turn 3D computer models into solid products[72,73]. This allows for customizable dosage forms, the production of drug combinations with different levels of complexity, and innovative and personalized product design; including shape, size, geometry, internal channels - all of which are difficult to achieve with traditional pharmaceutical manufacture.

The production of amorphous solid oral dosage forms via pharmaceutical 3D printing has great potential with fused deposition, direct powder extrusion, drop-on-powder, selective laser sintering, and 3D inkjet printing being the popular approaches.

4. PROCESS ANALYTICAL TECHNIQUES (PAT) IN MANUFACTURING OF ASDS

Most of the methods discussed for the manufacturing of ASDs, such as spray-drying, HME, and fluidized bed drying, are continuous processes that can be regulated to assure the quality of the finished product. However, this requires a thorough understanding of the manufacturing technique and control over parameters that influence the process output. Numerous analytical techniques such as mid-infrared spectroscopy (MIR), Raman, and near-infrared spectroscopy (NIR) are currently employed to monitor, control, and obtain knowledge of various pharmaceutical processes. PAT facilitates in-line, on-line, and at-line use of these techniques to exert better control over the manufacturing process [87-88].

Process Analytical Technology (PAT) is a methodology defined by the FDA to design, analyze, and control pharmaceutical manufacturing processes. Its primary aim is to measure Critical Process Parameters (CPPs) that impact Critical Quality Attributes (CQAs) of products, enhancing efficiency and product quality. PAT integrates real-time monitoring tools, such as spectroscopic and chromatographic analyzers, to ensure consistent quality throughout production. Process Analytical Technology (PAT) plays a crucial role in the development and characterization of Amorphous Solid Dispersions (ASDs). ASDs enhance the solubility and bioavailability of poorly soluble drugs by dispersing the active pharmaceutical ingredient in a polymeric matrix. Techniques like powder X-ray diffraction, differential scanning calorimetry, and Fourier transform infrared spectroscopy are commonly used to monitor crystallinity and stability within ASDs. Process Analytical Technology (PAT) enhances the stability of Amorphous Solid Dispersions (ASDs) by enabling real-time monitoring of critical parameters that influence crystallization. Thus, product safety is improved by continuous monitoring of the production instead of measuring individual samples. In addition, the continuous testing is regarded as a basis for real-time release in continuous manufacturing. Moreover, the results from real-time monitoring can detect early process deviations and correct them by immediate process control[89-91]. Table 2 illustrates the different PAT tools reported for continuous monitoring and process control during manufacturing of ASDs.

ASDs manufactured by spray-drying process usually employ probes for on-line measurement of temperature, relative humidity, and pressure. Hand-held NIR devices are employed for raw material characterization. Process turbidimetry, viscometry, and laser diffraction-based methods are used for the characterization of feed slurry. This analysis is critical not only for avoiding clogging of the spray nozzle, but also to ensure that solute crystallization does not occur in the solution itself. The spray-drying process involves inspection of real-time spray patterns and particle size distribution of the output product using PAT tools. The dissolution behaviour of the product and amenability to tablet compression are closely related to the particle size distribution of the product. Formulation of ASDs implies detection of polymorphic changes using NIR and Raman spectroscopy, while the exhaust air is analysed for solvent content. A secondary drying step is required for reducing the residual solvent content to a negligible level. The exhaust gas is monitored by process mass spectroscopy, and the NIR tool is used for end-point solid state characterization[101].

Numerous literature reports cite the use of PAT tools for ASDs manufactured by HME. Non-destructive, convenient spectroscopy tools like ultraviolet-visible spectroscopy (UV/VIS), short-NIR (sNIR), NIR, and MIR are very commonly used for raw material analysis, variations in the quality of raw materials, and their influence on final product quality[102]. Studies cited by Wahl et al. dealt with the determination of an optimum location for placing an on-line NIR probe to obtain maximum data with the least errors. A special probe with a defined geometry was placed to measure the entire cross-section of the extruder outlet. The complete extrude would pass through this cross-section enabling analysis of the entire product without disturbing the progress[103]. Kelly et al. introduced in-line NIR with transflectance mode for tandem measurement of a drug carbamazepine and plasticizer in a polymer blend. In HME, the extrudates have different levels of opacity depending upon the API: polymer ratio. Herein, reflectance probes were used to analyse cloudy or opaque melts and transmission probes were used for transparent or slightly turbid melts[104]. More recently, Baronsky-Probst used NIR to monitor an HME process by placing the probe in the cooling line of the strand, thereby obviating the need for a special probe design. MIR is also commonly used for monitoring the HME process as was reported by Coates et al. who used an on-line MIR probe to determine the polymer composition. Fischer et al. demonstrated the use of an MIR probe for *in situ* measurement of polymerization in an HME process. The study proved the suitability of MIR for determination of polymer blend composition of polyethylene/polystyrene blends in a range from 0% to 100% polystyrene content as well as for the determination of the end point of polymer conversion. Thus, MIR was found to be suitable for process monitoring as well as quantification. Raman spectroscopy is another non-destructive, vibrational based method that required very negligible sample preparation[105]. Barnes et al. extensively investigated the use of Raman spectroscopy for HME process. The probes were placed in the extruder die and were used for the characterization of different polymer blends such as HDPE/PP, ethylene vinyl acetate, and vinyl acetate. Tumuluri et al. used in-line Raman spectroscopy for the quantification of clotrimazole and ketoprofen in HME[106]. Saerens et al. placed the probe directly in the die to quantify metoprolol in a polymeric blend. In another study by Saerens et al., placement of an in-line Raman probe in the extruder barrels provided a better insight into the influence of barrel temperature and screw speed on the drug-polymer interactions. These parameters were further investigated using a full-factorial DoE study to determine their influence on solid state characteristics of the extrudates. The study further revealed that Raman spectroscopy was capable of quantifying even small concentrations of Celecoxib in the melt that could not be determined by DSC or XRD[107,108].

Similar PAT tools are employed for ASDs manufactured by supercritical anti-solvent method. Numerous operating parameters such as the solvent system, concentration of the solution, operating pressure and temperature, CO_2 flow-rate, solution flow-rate, nozzle diameter, and drug: polymers ratio are monitored real time for their effect on the solid-state characteristics of the obtained product. PAT tools are also predominantly used for ASDs manufactured using heat-based processes. Computer softwares are employed to regulate the temperature of the blend inside the KinetiSol chamber. ASDs manufactured by 3D printing method (DoD) employ either a piezoelectric, thermal inkjet, or electromagnetic system. Electromagnetic DoD systems utilize an external electromagnetic field to trigger a metal valve to open and close. The printing variables that affect droplet size involve pressure and open time. On the other hand, the cycle time would affect the printing frequency[80].

5. CONCLUSION

Amorphous solid dispersions (ASDs) offer a reliable method to improve the therapeutic potential of poorly soluble medications, which is a significant advancement in overcoming their limits. PAT tools may be integrated with a variety of manufacturing procedures used to prepare ASDs to ensure accuracy, stability, and scalability. This study addresses current pharmaceutical issues while establishing a framework for effective development of ASDs by emphasizing practical techniques and avoiding extensive challenges. In order to keep up with the latest developments, it highlights the significance of creative, flexible, and quality-driven processes. This article serves as a useful tool for developing individualized solutions, promoting ASD-based formulations, and encouraging further advancements in the pharmaceutical development industry.

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REFERENCES

1) Junghanns JU, Müller RH. Nanocrystal technology, drug delivery and clinical applications. Int J Nanomedicine. 2008;3(3):295-309.
2) Chaudhari SP, Gupte A. Mesoporous Silica as a Carrier for Amorphous Solid Dispersion. J. Pharm. Res. Int. 2017;16(6):1-19.
3) El Baraka S, Yanisse S, Chefchaouni AC, Fahry A, Laatiris A, Cherkaoui N, et al. BCS class II and IV drugs solubilisation using cyclodextrin-PVP-PEG6000 complexes through a factorial study design. Res J Pharm Technol. 2024;17(6):2639-2643. doi:10.52711/0974-360X.2024.00413.
4) Lubrizol Life Science Health. Excipients for solubility enhancement: enabling oral and injectable formulations. Cleveland (OH): The Lubrizol Corporation; 2022 [cited 2026 Feb 25].
5) Pignatello R, Corsaro R, Bonaccorso A, Zingale E, Carbone C, Musumeci T. Soluplus® polymeric nanomicelles improve solubility of BCS-class II drugs. Drug Deliv Transl Res. 2022;12.
6) Pandi P, Bulusu R, Kommineni N, Khan W, Singh M. Amorphous solid dispersions: An update for preparation, characterization, mechanism on bioavailability, stability, regulatory considerations and marketed products. Int J Pharm. 2020 Aug 30;586:119560
7) Kothari K, Ragoonanan V, Suryanarayanan R. Influence of molecular mobility on the physical stability of amorphous pharmaceuticals in the supercooled and glassy States. Mol Pharm. 2014 Sep 2;11(9):3048-55.
8) Zodage A., More S., Mangire T. Amorphous solid dispersions: An emerging approach for improving solubility and oral bioavailability of poorly water-soluble drugs. Int. J. Pharm. Sci. 2023;3(8):1-15.
9) Narayan R, Pednekar A, Bhuyan D, Gowda C, Koteshwara KB, Nayak UY. A top-down technique to improve the solubility and bioavailability of aceclofenac: in vitro and in vivo studies. Int J Nanomedicine. 2017 Jul 11;12:4921-4935.
10) Bhujbal SV, Mitra B, Jain U, Gong Y, Agrawal A, Karki S, et al. Pharmaceutical amorphous solid dispersion: a review of manufacturing strategies. Acta Pharm Sin B. 2021;11(8):2505-2536.
11) Ghule PJ, Gilhotra R, Jithan A, Bairagi S, Aher A. Amorphous solid dispersion: a promising technique for improving oral bioavailability of poorly water-soluble drugs. S Afr Pharm J. 2018;85(1):20-26.
12) Boyd BJ, Bergström CAS, Vinarov Z, Jannin V. In vitro dissolution/permeation tools for amorphous solid dispersions: bioavailability forecasting II. Comparison and mechanistic insights. Eur J Pharm Sci. 2019;139:105046.
13) Malkawi R, Malkawi WI, Al-Mahmoud Y, Tawalbeh J. Current trends on solid dispersions: past, present, and future. Adv Pharmacol Pharm Sci. 2022;2022:5916013.
14) Bhatane D., Chakraborty S., Bansal A.K. Applications of mesoporous silica particles in amorphous solid dispersion. J. Pharm. Investig. 2025;13(4):215-233.
15) Kumar R., Singh M., Sharma R. Advances in solid dispersion technology for improving oral bioavailability of poorly water-soluble drugs. Eur J Pharm Biopharm. 2024;194:112-130.
16) Serajuddin AT. Solid dispersion of poorly water-soluble drugs: early promises, subsequent problems, and recent breakthroughs. J Pharm Sci. 1999 Oct;88(10):1058-66.
17) 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):1068-75.

18)Repka MA, Battu SK, Upadhye SB, Thumma S, Crowley MM, Zhang F, et al. Pharmaceutical applications of hot-melt extrusion: part II. Drug Dev Ind Pharm. 2007;33(10):1043-57.
19)Khaled SA, Burley JC, Alexander MR, Yang J, Roberts CJ, Trenfield SJ. 3D printing of tablets: manufacturing techniques, research and regulatory considerations. J Pharm Sci. 2019;108(1):26-36.
20)Kostewicz ES, Abrahamsson B, Brewster M, Brouwers J, Butler J, Carlert S, et al. In vitro models for the prediction of in vivo performance of oral dosage forms. Eur J Pharm Sci. 2014;57:342-66.
21)Iyer R, Petrovska Jovanovska V, Berginc K, Jaklič M, Fabiani F, Harlacher C, et al. Amorphous solid dispersions (ASDs): the influence of material properties, manufacturing processes and analytical technologies in drug product development. Pharmaceutics. 2021;13(10):1682.
22)Démuth B, Nagy ZK, Balogh A, Vigh T, Marosi G, Verreck G, et al. Downstream processing of polymer-based amorphous solid dispersions to generate tablet formulations. Int J Pharm. 2015;486(1-2):268-86.
23)Raman V, Bansal AK. Characterization of polymorphs and amorphous forms. Int J Pharm. 2001;218(1-2):1-13.
24)Brittain HG. Polymorphism in pharmaceutical solids. 2nd ed. New York: Informa Healthcare; 2009.
25)Ma X, Williams RO. Characterization of amorphous solid dispersions: an update. J Drug Deliv Sci Technol. 2019;50.
26)Sitre D, Kamble R. Articulation of Quality By Design Elements for Product Development and its Unique Applications. J. Drug Delivery Ther. 2020;10(3):253-61.
27)Yu LX, Kopcha M, Portik-Dobos V, Hussain AS, Woodcock J. Pharmaceutical quality by design: a risk-based approach. J Pharm Innov. 2002;7(4):203-210.
28)Mack C. Implementing quality risk management in pharmaceutical manufacturing. Pharm Technol Eur. 2005;17(3):12-17.
29)U.S. Food and Drug Administration. Pharmaceutical cGMPs for the 21st century: a risk-based approach. Silver Spring (MD): U.S. Food and Drug Administration; 2004.
30)Guenard R, Thurau G. Implementation of process analytical technologies in the industrial setting. In: Bakeev KA, editor. Process analytical technology: spectroscopic tools and implementation strategies for the chemical and pharmaceutical industries. 2nd ed. Chichester (UK): Wiley; 2010.
31)Besseling R, Damen M, Wijgergangs JP, Hermes M, Wynia G, Gerich A. New unique PAT method and instrument for real-time inline size characterization of concentrated, flowing nanosuspensions. Eur J Pharm Sci. 2019;133:205-213.
32)Bondi RW, Drennen JK III. Quality by design and the importance of PAT in QbD. In: Ahuja S, Scypinski S, editors. Separation science and technology. Vol. 10. Amsterdam: Elsevier; 2011.
33)Yu LX. Pharmaceutical quality by design: product and process development, understanding, and control. Pharm Res. 2008;25(4):781-91.
34)U.S. Food and Drug Administration. Guidance for industry: PAT — a framework for innovative pharmaceutical development, manufacturing, and quality assurance [Internet]. Silver Spring (MD): U.S. Food and Drug Administration; [cited 2026 Feb 25]. Available from: http://www.fda.gov/cvm/guidance/published.html
35)Rathore AS, Winkle H. Quality by design for biopharmaceuticals. Nat Biotechnol. 2009;27(1):26-34.
36)Patel RP, Patel MP, Suthar AM. Spray drying technology: an overview. Indian J Sci Technol. 2009;2:44-47.
37)Santos D, Maurício AC, Sencadas V, Santos JD, Fernandes MH, Gomes PS. Spray drying: an overview. In: Pignatello R, editor. Biomaterials – physics and chemistry – new edition. London (UK): IntechOpen; 2018.
38)Pikal MJ. The role of spray drying in pharmaceutical development. Dry Technol. 2001;19(2):333-350.
39)Al-Zoubi N, Gharaibeh S, Aljaberi A, Nikolakakis I. Spray drying for direct compression of pharmaceuticals. Processes. 2021;9:1-25.
40)Mandpe S, Kole E, Mujumdar A, Chatterjee A, Naik J. Design, development, and evaluation of spray dried flurbiprofen loaded sustained release polymeric nanoparticles using QBD approach to manage inflammation. Dry Technol. 2023;41.
41)Singh A, Van den Mooter G. Spray drying formulation of amorphous solid dispersions. Adv Drug Deliv Rev. 2016;100:27-50.
42)Ziaee A, Albadarin A, Padrela L, Faucher A, O'Reilly E, Walker G. Spray drying ternary amorphous solid dispersions of ibuprofen: an investigation into critical formulation and processing parameters. Eur J Pharm Biopharm. 2017;120.
43)Jaworek A, Sobczyk AT. Electrospray spraying: review of the fundamental physics. J Electrostat. 2008;66(3-4):197-219.
44)Gañán-Calvo A. On the general scaling theory for electrospraying. J Fluid Mech. 2004;507.
45)Gomaa E, Attia M, Ghazy FE, Hassan A, Hasan A. Pump-free electrospraying: a novel approach for fabricating Soluplus®-based solid dispersion nanoparticles. J Drug Deliv Sci Technol. 2021;67:103027.
46)Leuner C, Dressman J. Improving drug solubility for oral delivery using solid dispersion. Eur J Pharm Biopharm. 2000;50:47-60.
47)Patel VF, Liu F, Brown MB. Advances in oral drug delivery. Expert Opin Drug Deliv. 2012;9(1):1-19.
48)Jones D. Development, optimization, and scale-up of process parameters: Wurster coating. In: Qiu Y, Chen Y, Zhang GGZ, Liu L, Porter W, editors. Developing solid oral dosage forms: pharmaceutical theory and practice. 2nd ed. Amsterdam: Elsevier; 2017.
49)Beten DB, Amighi K, Moës AJ. Preparation of controlled-release coevaporates of dipyridamole by loading neutral pellets in a fluidized-bed coating system. Pharm Res. 1995;12(9):1269-72.

50) Dereymaker A, Scurr DJ, Steer ED, Roberts CJ, Van den Mooter G. Controlling the release of indomethacin from glass solutions layered with a rate controlling membrane using fluid-bed processing. Part 1: surface and cross-sectional chemical analysis. Mol Pharm. 2017;14(4):959-973.
51) Gajdziok J, Vetchý D, Vojtová L. Fluid bed granulation in pharmaceutical technology. Ceska Slov Farm. 2012;61(6):254-261.
52) Noyes R, Garvin J. Fluid bed technology: overview and parameters for process selection. Pharm Technol Eur. 2014;26(9):18-24.
53) Alekari PS, Patil VA, Satpute SA. A promising approach of solid dispersion for enhancement of solubility. Indian J Novel Drug Deliv. 2024;16:20-25
54) Reverchon E, De Marco I. Supercritical fluid extraction and fractionation of natural matter. J Supercrit Fluids. 2006;38:146-166.
55) Kalogiannis CG, Tsivintzelis I, Panayiotou C. Formation of pharmaceutical co-crystals with supercritical fluid technology. Eur J Pharm Biopharm. 2006;64(3):346-356.
56) Kaushik R, Budhwar V, Kaushik D. An overview on recent patents and technologies on solid dispersion. Recent Pat Drug Deliv Formul. 2020;14(1):63-74.
57) Khudaida S, Dai ZZ, Ciou JM, Su CS. Designing amorphous solid nanoparticle dispersion of sulfadiazine in polyvinylpyrrolidone using supercritical CO_2 as the antisolvent. Adv Powder Technol. 2024;35:104592.
58) Alavi F, Ciftci ON. Increasing the bioavailability of curcumin using a green supercritical fluid technology-assisted approach based on simultaneous starch aerogel formation-curcumin impregnation. Food Chem. 2024;455:139468.
59) Verreck G., Chun I., Rosenblatt J., Peeters J., Van Dijck A., Mensch J., Noppe M., Brewster M.E. Incorporation of drugs in an amorphous state into electrospun nanofibers composed of a water-soluble, semi-crystalline polymer, J Control Release., 2003,92(3),349-360.
60) Liao Y, Zhang L, Gao Y, Zhu Z, Fong H, Guo R. Electrospun nanofiber-based drug delivery systems. Curr Pharm Des. 2018;24(29):3457-3469.
61) Casian T, Borbás E, Ilyés K, Démuth B, Farkas A, Rapi Z, et al. Electrospun amorphous solid dispersions of meloxicam: influence of polymer type and downstream processing to orodispersible dosage forms. Int J Pharm. 2019;569:118593.
62) Zhou QT, Li T. Formulation and manufacturing of solid dosage forms. Pharm Res. 2018;36(1):16.
63) Patil H, Tiwari RV, Repka MA. Hot-melt extrusion: from theory to application in pharmaceutical formulation. AAPS PharmSciTech. 2016;17(1):20-42.
64) Crowley MM, Zhang F, Repka MA, Thumma S, Upadhye SB, Battu SK, et al. Pharmaceutical applications of hot-melt extrusion: part I. Drug Dev Ind Pharm. 2007;33(9):909-26.
65) Douroumis D. Practical approaches of taste masking technologies in oral solid forms. Expert Opin Drug Deliv. 2007;4(4):417-26.
66) Jara MO, Warnken ZN, Williams RO 3rd. Amorphous solid dispersions and the contribution of nanoparticles to in vitro dissolution and in vivo testing: niclosamide as a case study. Pharmaceutics. 2021;13(1):97.
67) de Assis JMC, Barbosa EJ, Bezzon VDN, Lourenço FR, Carvalho FMS, Matos JR, et al. Hot-melt extrudability of amorphous solid dispersions of flubendazole-copovidone: an exploratory study of the effect of drug loading and the balance of adjuvants on extrudability and dissolution. Int J Pharm. 2022;614:121456.
68) Maniruzzaman M, Boateng JS, Snowden MJ, Douroumis D. A review of hot-melt extrusion: process technology to pharmaceutical products. ISRN Pharm. 2012;2012:436763.
69) Zhang F, Aaltonen J, Tian F. Drug-polymer physicochemical interactions in hot-melt extrusion. Mol Pharm. 2018;15(9):4306-4321.
70) Miller DA, Keen JM. KinetiSol®-based amorphous solid dispersions. In: Amorphous solid dispersions. Advances in drug delivery science and technology. New York (NY): Springer; 2014.
71) DiNunzio JC, Brough C, Miller DA, Williams RO 3rd, McGinity JW. Applications of KinetiSol dispersing for the production of plasticizer free amorphous solid dispersions. Eur J Pharm Sci. 2010;40(3):179-87.
72) Parulski C, Gresse E, Jennotte O, Felten A, Ziemons E, Lechanteur A, et al. Fused deposition modeling 3D printing of solid oral dosage forms containing amorphous solid dispersions: how to elucidate drug dissolution mechanisms through surface spectral analysis techniques? Int J Pharm. 2022;626:122157.
73) Thakkar R, Jara MO, Swinnea S, Pillai AR, Maniruzzaman M. Impact of laser speed and drug particle size on selective laser sintering 3D printing of amorphous solid dispersions. Pharmaceutics. 2021;13(8):1149.
74) Kissi EO, Nilsson R, Nogueira LP, Larsson A, Tho I. Influence of drug load on the printability and solid-state properties of 3D-printed naproxen-based amorphous solid dispersion. Molecules. 2021;26(15):4492.
75) Davis DA, Thakkar R, Su Y, Williams RO, Maniruzzaman M. Selective laser sintering 3-dimensional printing as a single step process to prepare amorphous solid dispersion dosage forms for improved solubility and dissolution rate. J Pharm Sci. 2021;110(4):1432-43.
76) Buyukgoz GG, Soffer D, Defendre J, Pizzano GM, Davé RN. Exploring tablet design options for tailoring drug release and dose via fused deposition modeling (FDM) 3D printing. Int J Pharm. 2020;591:119987.
77) Thakkar R, Pillai AR, Zhang J, Zhang Y, Kulkarni V, Maniruzzaman M. Novel on-demand 3-dimensional (3-D) printed tablets using fill density as an effective release-controlling tool. Polymers. 2020;12:1872.

78) Gottschalk N, Bogdahn M, Quodbach J. 3D printing of amorphous solid dispersions: a comparison of fused deposition modeling and drop-on-powder printing. Int J Pharm X. 2023;5:100179.
79) Roche A, Sanchez-Ballester NM, Bataille B, Delannoy V, Soulairol I. Fused deposition modelling 3D printing and solubility improvement of BCS II and IV active ingredients: a narrative review. J Control Release. 2024;365:507-520.
80) Helmy AM, Lu A, Duggal I, Rodrigues KP, Maniruzzaman M. Electromagnetic drop-on-demand (DoD) technology as an innovative platform for amorphous solid dispersion production. Int J Pharm. 2024;658:124185.
81) Fina F, Goyanes A, Gaisford S, Basit AW. Selective laser sintering (SLS) 3D printing of medicines. Int J Pharm. 2017;529(1-2):285-293.
82) Charoo NA, Shamsher AA, Zidan AS, Rahman Z. Quality by design approach for formulation development: a case study of dispersible tablets. Int J Pharm. 2012;423(2):167-78.
83) Krummnow A, Danzer A, Voges K, Dohrn S, Kyerematen SO, Degenhardt M, et al. Explaining the release mechanism of ritonavir/PVPVA amorphous solid dispersions. Pharmaceutics. 2022;14(9):1904.
84) Chang SY, Li SW, Kowsari K, Shetty A, Sorrells L, Sen K, et al. Binder-jet 3D printing of indomethacin-laden pharmaceutical dosage forms. J Pharm Sci. 2020;109(10):3054-3063.
85) Holm TP, Knopp MM, Löbmann K, Berthelsen R. Microwave induced in situ amorphisation facilitated by crystalline hydrates. Eur J Pharm Sci. 2021;163:105858.
86) Sokač K, Miloloža M, Kučić Grgić D, Žižek K. Polymeric amorphous solid dispersions of dasatinib: formulation and ecotoxicological assessment. Pharmaceutics. 2024;16(4):551.
87) Laske S, Paudel A, Scheibelhofer O, Author Team. A review of PAT strategies in secondary solid oral dosage manufacturing of small molecules. J Pharm Sci. 2017;106(3):667-712.
88) Gerzon G, Sheng Y, Kirkitadze M. Process analytical technologies: advances in bioprocess integration and future perspectives. J Pharm Biomed Anal. 2022;207:114379.
89) Hinz DC. Process analytical technologies in the pharmaceutical industry: the FDA's PAT initiative. Anal Bioanal Chem. 2006;384(5):1036-42.
90) Chen ZP, Lovett D, Morris J. Process analytical technologies and real time process control: a review of some spectroscopic issues and challenges. J Process Control. 2011;21:1467-1482.
91) Yu LX, Lionberger RA, Raw AS, D'Costa R, Wu H, Hussain AS. Applications of process analytical technology to crystallization processes. Adv Drug Deliv Rev. 2004;56(3):349-69.
92) Chavan RB, Bhargavi N, Lodagekar A, Shastri NR. Near infra red spectroscopy: a tool for solid state characterization. Drug Discov Today. 2017;22(12):1835-1843.
93) Guo JH, Skinner GW, Harcum WW, Malone JP, Weyer LG. Application of near-infrared spectroscopy in the pharmaceutical solid dosage form. Drug Dev Ind Pharm. 1999;25(12):1267-70.
94) Mansuri A, Münzner P, Heermant A, Patzina F, Feuerbach T, Winck J, et al. Molecular dynamics and diffusion in amorphous solid dispersions containing imidacloprid. Mol Pharm. 2023;20(4):2067-2079.
95) Wegiel LA, Mauer LJ, Edgar KJ, Taylor LS. Mid-infrared spectroscopy as a polymer selection tool for formulating amorphous solid dispersions. J Pharm Pharmacol. 2014;66(2):244-255.
96) Svetič S, Medved L, Korasa K, Vrečer F. Quantification of amlodipine maleate content in amorphous solid dispersions produced by fluidized bed granulation using process analytical technology tools. Pharmaceutics. 2024;16:1538.
97) Hitzer P, Bäuerle T, Drieschner T, Ostertag E, Paulsen K, van Lishaut H, et al. Process analytical techniques for hot-melt extrusion and their application to amorphous solid dispersions. Anal Bioanal Chem. 2017;409(18):4321-4333.
98) Netchacovitch L, Dumont E, Cailletaud J, Thiry J, De Bleye C, Sacré PY, et al. Development of an analytical method for crystalline content determination in amorphous solid dispersions produced by hot-melt extrusion using transmission Raman spectroscopy: a feasibility study. Int J Pharm. 2017;530.
99) Schlindwein W, Bezerra M, Almeida J, Berghaus A, Owen M, Muirhead G. In-line UV-Vis spectroscopy as a fast-working process analytical technology (PAT) during early phase product development using hot melt extrusion (HME). Pharmaceutics. 2018;10(4):166.
100) Liu X, Feng X, Williams RO, Zhang F. Characterization of amorphous solid dispersions. J Pharm Investig. 2017;48.
101) Chan LW, Tan LH, Heng PW. Process analytical technology: application to particle sizing in spray drying. AAPS PharmSciTech. 2008;9(1):259-66.
102) Munson J, Freeman Stanfield C, Gujral B. A review of process analytical technology (PAT) in the U.S. pharmaceutical industry. Curr Pharm Anal. 2006;2(4):405-414.
103) Wahl PR, Treffer D, Mohr S, Roblegg E, Koscher G, Khinast JG. Inline monitoring and a PAT strategy for pharmaceutical hot melt extrusion. Int J Pharm. 2013;455(1-2):159-68.
104) Kelly A, Halsey SA, Bottom RA, Korde S, Gough T, Paradkar A. A novel transflectance near infrared spectroscopy technique for monitoring hot melt extrusion. Int J Pharm. 2015;496(1):117-123.
105) Fischer D, Sahre K, Abdelrhim M, Voit B, Sadhu V, Pionteck J, et al. Process monitoring of polymers by in-line ATR-IR, NIR and Raman spectroscopy and ultrasonic measurements. C R Chim. 2006;9:1419-1424.

106) Barnes SE, Brown EC, Sibley MG, Edwards HG, Scowen IJ, Coates PD. Vibrational spectroscopic and ultrasound analysis for in-process characterization of high-density polyethylene/polypropylene blends during melt extrusion. Appl Spectrosc. 2005;59(5):611-619.
107) Saerens L, Vervaet C, Remon JP, De Beer T. Process monitoring and visualization solutions for hot-melt extrusion: a review. J Pharm Pharmacol. 2014;66(2):180-203.
108) Saerens L, Dierickx L, Quinten T, Adriaensens P, Carleer R, Vervaet C, et al. In-line NIR spectroscopy for the understanding of polymer-drug interaction during pharmaceutical hot-melt extrusion. Eur J Pharm Biopharm. 2012;81(1):230-237.

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