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Review Article

Hot Melt Extrusion: A Viable Option for Implementing Continuous Manufacturing in the Pharmaceutical Industry

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Abstract

In recent years, hot melt extrusion (HME) has been most widely investigated for developing pharmaceutical medications. HME is a single-step manufacturing process and is suitable for the extrusion of drug-loaded filaments, films, or patches, and granules. The filaments can be processed as pellets or can be processed into tablets or capsules. The HME can be coupled with various downstream processing equipments and process analytical technology (PAT) tools for transforming into a continuous manufacturing line. Establishing a continuous manufacturing line will ensure product quality and will benefit both the industries and the patient population. In fact, the HME can also be paired with additive manufacturing platforms such as fused deposition modeling (FDM) for the fabrication of on-demand and patient-centric medications. Even complex medications can be easily manufactured using an additive manufacturing approach. Despite various advantages of HME, a few limitations, such as the availability of suitable materials and a more in-depth understanding of the process, is still warranted. However, compared with other manufacturing approaches, the HME-based continuous manufacturing is a viable option for the pharmaceutical industry.

Keywords: hot melt extrusion, solubility enhancement, continuous manufacturing, additive manufacturing, 3D printing

1. Introduction:

Hot melt extrusion (HME) technology is a well-established process in the pharmaceutical industry for developing various drug dosage forms. HME is a continuous and solvent-free manufacturing process in which drug compounds and excipients are melted and homogenized through an extruder to form a solid or semi-solid dosage form. HME technology provides several advantages over conventional manufacturing methods, including lower costs, reduced manufacturing steps, and improved drug bioavailability [1–4]. One of the key benefits of HME is its ability to enhance the solubility and bioavailability of poorly soluble drugs. HME can be used to prepare solid dispersions, which improve drug solubility and dissolution rates by dispersing the drug particles in a hydrophilic matrix. This approach has been successfully used for developing oral formulations of poorly soluble drugs, such as itraconazole, fenofibrate, and curcumin.

HME is also a well-suited process for developing sustained-release formulations, which release the drug gradually over an extended period. By controlling the extrusion conditions and selecting appropriate excipients, HME can be used to formulate dosage forms with varying release rates and profiles [5–8]. Sustained-release HME formulations have been developed for a variety of drugs, including metformin, diltiazem, and tramadol. Another advantage of HME is its ability to manufacture multi-layered dosage forms, which offer several benefits, including improved drug stability, reduced drug interactions, and sustained release. Multi-layered dosage forms can be designed with different drug release rates for combination therapies, or with separate compartments that are released at different times to provide a sequential drug release [9].

In addition to its benefits in drug formulation, HME has also been used for quality control and process optimization. Advanced analytical techniques, such as in-line monitoring and control systems, have been developed for HME, allowing for real-time process monitoring and control. These techniques enable manufacturers to optimize their manufacturing processes, reduce waste, and produce high-quality dosage forms consistently. HME is a valuable technology for developing pharmaceutical dosage forms [10–14]. Its ability to enhance drug solubility, produce sustained-release formulations, and manufacture multi-layered dosage forms makes it a versatile and cost-effective

process for drug development. As the pharmaceutical industry continues to explore new drug compounds and formulations, HME will undoubtedly remain an essential process for drug manufacturing and development [15,16]. Various applications of HME are shown in Figure 1.

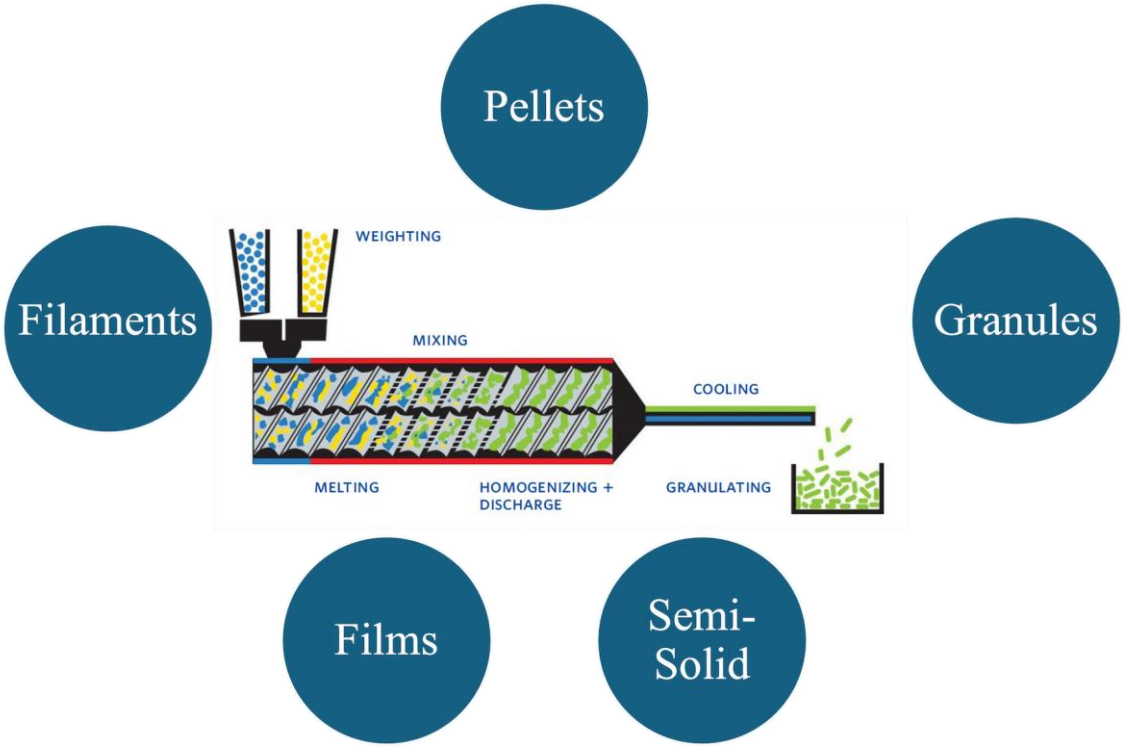

Figure 1: Various applications of hot melt extrusion technology

Advantages and limitations:

Hot melt extrusion (HME) technology has numerous advantages in pharmaceutical development, but also some limitations that must be considered. The key advantage of HME is its ability to enhance the solubility and bioavailability of poorly soluble drugs. This is achieved by dispersing drug particles in a hydrophilic matrix, resulting in improved solubility and dissolution rates. HME has been used successfully to develop oral formulations of poorly soluble drugs, including itraconazole, fenofibrate, and curcumin. Another significant advantage of HME is its ability to produce sustained-release formulations that release the drug gradually over an extended period [17–21]. This is achieved by controlling the extrusion conditions and selecting appropriate excipients to formulate dosage forms with varying release rates and profiles. Sustained-release HME formulations have been developed for a variety of drugs, including metformin, diltiazem, and tramadol. In addition, HME technology is cost-effective and allows for reduced manufacturing steps, resulting in lower production costs. Its continuous and solvent-free manufacturing process also reduces waste and improves efficiency. HME is also versatile, allowing the production of multi-layered dosage forms and the addition of various excipients, such as surfactants, plasticizers, and stabilizers, to modify the drug release properties.

However, HME has some limitations that need to be acknowledged. The first limitation is the narrow processing window, which requires strict control over operating conditions, particularly the temperature, extruder speed, and screw design [22–26]. Any variations in these conditions can affect the drug's quality, crystallinity, and degradation, compromising the product quality and consistency. The second limitation is related to the complexity of HME technology, which requires significant expertise in material science, chemistry, and engineering. The development process entails selecting appropriate excipients, analyzing the physical and chemical properties of the drug and excipients, and optimizing the process parameters to achieve the desired drug release profile. This requires significant time and resources, which may not be feasible for all drug products. HME technology has several advantages in developing pharmaceuticals, including improved drug solubility, sustained-release formulations, and multi-layered dosage forms. However, the process's complexity and narrow processing window require close attention to optimize drug quality and consistency. These limitations should be considered when using HME technology and factored into the overall drug development strategy.

2. Various applications of HME:

Hot melt extrusion (HME) technology has numerous applications in developing pharmaceutical products. HME enables the production of a range of drug delivery systems, including tablets, capsules, and transdermal patches, thereby expanding the possibilities for drug formulation. Additionally, HME can be used to develop modified release formulations that can release

drugs over an extended period, thereby improving their therapeutic efficacy. One of the significant applications of HME is the production of solid dispersions. Solid dispersions are widely used to increase the solubility and bioavailability of poorly water-soluble drugs. HME technology can produce solid dispersions with improved homogeneity and uniformity of drug distribution, leading to improved drug efficacy [27–29].

Another area of application of HME is the production of mucoadhesive formulations. Mucoadhesive formulations are designed to adhere to mucosal surfaces and provide prolonged drug release. HME can produce mucoadhesive formulations that can adhere to the mucosal surfaces in the gastrointestinal tract, thereby improving drug absorption and efficacy. HME technology is also used to produce amorphous solid dispersions, which are useful in enhancing the bioavailability of poorly soluble drugs [30–32]. Amorphous solid dispersions produced using HME technology have shown better stability and solubility profiles compared to those produced using traditional methods.

In addition to the above applications, HME can also be used in the production of transdermal patches, which offer a convenient and comfortable way of drug administration. HME technology can produce transdermal patches that maintain a consistent drug release rate, thereby improving the therapeutic efficacy of drugs. Overall, the various applications of HME technology have revolutionized the pharmaceutical industry by enabling the development of novel drug delivery systems that offer improved solubility, bioavailability, and efficacy [33–37]. HME technology's versatility and flexibility have made it a valuable tool in the development of new drug delivery systems. As the technology continues to evolve, it is expected to open up new possibilities for drug formulation and delivery.

3. Continuous manufacturing of HME:

Continuous manufacturing is a crucial process for the pharmaceutical industry, as it allows for the rapid and efficient production of high-quality dosage forms consistently. Among the various technologies available for continuous manufacturing, hot melt extrusion (HME) stands out for its versatility, efficiency, and cost-effectiveness. In this essay, we will explore the key features and benefits of HME technology in pharmaceutical development, as well as its limitations and challenges. Hot melt extrusion is a process that involves melting a drug and one or more excipients together and then squeezing the molten mixture through a narrow orifice using a screw extruder. The mixture is then cooled and solidified to form a solid dosage form, such as a tablet or a capsule. This process offers several advantages over traditional manufacturing methods, such as wet granulation or compression [38,39].

One of the primary advantages of HME is its ability to enhance the solubility and bioavailability of poorly soluble drugs. Poorly soluble drugs are a significant challenge in pharmaceutical development, as they often exhibit poor absorption and low efficacy. HME technology enables the formulation of such drugs by dispersing drug particles in a hydrophilic matrix, resulting in improved solubility and dissolution rates. This leads to better absorption and efficacy of the drug, as well as reduced variability and increased patient compliance. Moreover, HME can produce sustained-release formulations that release the drug gradually over an extended period. Sustained release is a desirable feature for many drugs, as it allows for a prolonged therapeutic effect and a reduced dosing frequency. HME technology achieves sustained release by controlling the extrusion conditions and selecting appropriate excipients to formulate dosage forms with varying release rates and profiles. This enables the development of complex drug products that meet specific patient needs and preferences. Another advantage of HME is its cost-effectiveness and efficiency [40–44]. The continuous and solvent-free manufacturing process reduces waste and improves productivity, leading to lower production costs and faster time-to-market. HME is also versatile, allowing the production of multi-layered dosage forms and the addition of various excipients, such as surfactants, plasticizers, and stabilizers, to modify the drug release properties. This flexibility allows for the development of tailored drug products that meet diverse patient needs and preferences.

However, HME technology also has some limitations and challenges that need to be considered. The first limitation is the narrow processing window, which requires precise control over operating conditions, particularly the temperature, extruder speed, and screw design. Any variations in these conditions can affect the drug's quality, crystallinity, and degradation, compromising the product's quality and consistency. Establishing a robust and efficient process control strategy is therefore essential for optimizing the HME process and ensuring consistent product quality [45–49]. The second limitation is related to the complexity of HME technology, which requires significant expertise in material science, chemistry, and engineering. The development process entails selecting appropriate excipients, analyzing the physical and chemical properties of the drug and excipients, and optimizing the process parameters to achieve the desired drug release profile. This requires significant time and resources, which may not be feasible for all drug products[50].

In addition, regulatory authorities have raised concerns about the lack of clear guidelines and standards for implementing continuous manufacturing technologies such as HME. The current regulatory framework is generally designed for batch manufacturing, and the transition to continuous manufacturing requires new guidelines and standards to ensure the safety, quality, and efficacy of the drug products. This calls for collaboration between industry, academia, and regulatory agencies to develop a robust and harmonized regulatory framework for continuous manufacturing technologies [51–53]. HME technology is a valuable tool for developing pharmaceutical dosage forms that offer improved drug solubility, sustained release, and multi-layered dosage forms. The technology's cost-effectiveness, efficiency, and versatility make it an attractive option for pharmaceutical

companies looking to optimize their manufacturing processes and develop innovative drug products. However, the challenges and limitations of the technology require careful consideration and planning to ensure consistent product quality and regulatory compliance. Moving forward, the pharmaceutical industry needs to invest in developing robust and efficient continuous manufacturing strategies and collaborate with regulatory agencies to establish clear guidelines and standards for the safe and effective implementation of continuous manufacturing technologies such as HME [54–58].

4. PAT tools:

Hot melt extrusion (HME) is a continuous manufacturing technology that has been gaining traction in the pharmaceutical industry due to its cost-effectiveness, efficiency, and versatility. However, HME also comes with some challenges and limitations, such as the narrow processing window and complexity of the technology, which requires significant expertise in material science, chemistry, and engineering. In addition, there are currently no clear guidelines or standards for implementing this technology [59–62]. To ensure consistent product quality and regulatory compliance when using HME technology for pharmaceuticals production, it is important to invest in various compatible process analytical technology (PAT) tools. These PAT tools can be used to monitor critical process parameters such as temperature, pressure, flow rate, etc., providing real-time data on product quality throughout the entire manufacturing process. This helps identify any potential issues early on so they can be addressed quickly before they become major problems. Additionally, these PAT tools can help optimize process parameters to ensure consistent drug release profiles while minimizing waste and improving productivity, leading to lower production costs and faster time-to-market.

Hot melt extrusion (HME) technology has emerged as a cost-effective, efficient, and versatile process for producing pharmaceutical dosage forms. However, the complexity of the process poses some challenges in terms of ensuring consistent product quality and regulatory compliance. One solution to these challenges is the use of Process Analytical Technology (PAT) tools. In this article, we will explore various PAT tools that are suitable for use with HME technology [63–67]. PAT tools are designed to provide real-time monitoring of critical process parameters during manufacturing, enabling manufacturers to ensure consistent product quality, reduce cost, and improve the efficiency of their processes. Some of the common PAT tools used in the pharmaceutical industry include Near-Infrared (NIR) spectroscopy, Raman spectroscopy, and Mass Spectrometry.

4.1. Near-Infrared (NIR) Spectroscopy

NIR spectroscopy is a widely used PAT tool for continuous process monitoring and control. This method involves the use of electromagnetic radiation in the NIR region of the spectrum to analyze the chemical composition of a sample. NIR spectroscopy can be used to analyze a wide range of materials, including powders, granules, tablets, and capsules.

NIR spectroscopy is particularly useful for HME technology because it allows for in situ analysis of the physical and chemical properties of the material during the manufacturing process. NIR spectroscopy can be used to monitor key process parameters such as temperature, pressure, and residence time [68–72]. This allows for real-time identification of process deviations that can impact product quality. NIR spectroscopy is also useful for identifying or quantifying the active pharmaceutical ingredient (API) in the formulation. This is especially important when the API is present at low concentrations, as is often the case in HME formulations.

4.2. Raman Spectroscopy

Raman spectroscopy is another PAT tool commonly used in the pharmaceutical industry for process monitoring and control. This technique is based on the interaction between light and matter. When a sample is illuminated with a laser, some of the light is scattered in different directions. The scattered light contains information about the composition and structure of the material.

Raman spectroscopy is particularly useful for monitoring the dispersion of particles in the melt during HME processing. The technique can be used to identify the location of drug particles within the melt and the extent to which they are dispersed [73–76]. This information can be used to optimize the process parameters to ensure consistent dispersion and minimize the risk of segregation.

4.3. Mass Spectrometry

Mass spectrometry is a third PAT tool that can be used for real-time monitoring of hot melt extrusion processes. This technique is based on the analysis of ionized molecules in a sample. The sample is ionized and then passed through a mass spectrometer, where the ions are separated based on their mass-to-charge ratio.

Mass spectrometry can be used to detect and quantify impurities in the formulation and verify the identity of the API [77–79]. The technique can also be used to monitor the degradation of the API and the stability of the formulation under different processing conditions. Mass spectrometry is a powerful tool that can provide valuable information about the chemical composition of the material. It can also be used to identify key product quality attributes and monitor changes in the physical and chemical properties of the material during the manufacturing process.

Process Analytical Technology (PAT) tools are essential for monitoring and controlling hot melt extrusion processes. Near-Infrared (NIR) spectroscopy, Raman spectroscopy, and Mass Spectrometry are the most commonly used PAT tools in the pharmaceutical industry. Each of these techniques provides valuable information about the physical and chemical properties of the material, enabling manufacturers to optimize process parameters, identify potential issues early, and ensure consistent product quality. By investing in these

tools, pharmaceutical manufacturers can improve the efficiency of their processes, reduce production costs, and bring innovative drug products to market faster. With continued advancements in PAT technology, the future of pharmaceutical manufacturing looks bright.

5. Coupling of HME with the additive manufacturing process:

Hot melt extrusion (HME) technology is a widely used industrial technique in the pharmaceutical industry that can be applied to various drug delivery systems such as tablets, capsules, transdermal patches, and more. However, the recent advances in additive manufacturing technology have provided a new pathway for designing complex geometries for medicine and devices. Three-dimensional (3D) printing is one of these methods that can be coupled with HME technology for the production of personalized drug delivery systems. By combining these two technologies, it is possible to develop pharmaceuticals by continuous manufacturing [80–82]. By implementing HME with 3D printing, it is possible to create a 3D model of the drug delivery system with precision and accuracy. The final product can be used for customized applications required by personalized medicine, eliminating any waste that may arise from conventional manufacturing methods. Three-dimensional printing allows for a wide range of materials to be used, including hydrogels that can be used in wound healing applications, biomaterials for tissue engineering, and polymer-based implants that can provide an extended release of drugs.

The coupling of HME and 3D printing has widespread applications that can be used in various medical fields. One practical example is the development of oral drug delivery systems that can offer controlled release and improved bioavailability by using hot melt extrusion to produce solid dispersions. These solid dispersions can be further incorporated with different polymers to create formulations that are suitable for 3D printing. The final product may include a complex geometry with specific porosity and shape to deliver the right dosage of the drug while minimizing any side effects [83–85]. Moreover, coupling the two technologies is also useful in creating customizable implants for tissue engineering. The implants can address specific medical issues that require personalized design by using 3D printing to fabricate the right size and shape with the correct function. The implant can be composed of biodegradable materials and the specific drug or protein that helps encourage tissue regeneration. By including the drug within the implant manufactured with the help of HME technology, the drug can be slowly released over time, creating a localized therapeutic effect. This can improve the efficacy of the drug and avoid any unwanted side effects from systemic administration.

The development of personalized drug delivery systems can also be applied to treating rare diseases. By using HME and 3D printing technologies, it is possible to create customized dosage forms with the exact drug concentration required for treatment. These personalized forms can be particularly useful for pediatric patients, who often require lower drug doses based on their body weight and age. By using these technologies, it is possible to reduce drug waste and create exact dosage forms that are needed. Furthermore, these technologies can be used to produce sustained-release formulations that ensure steady drug concentrations over a prolonged period. HME technology can be used to melt and mix different materials to form solid dispersions, which can then be used in 3D printing applications by creating homogenous materials necessary for printing complex geometries. In addition, coupling 3D printing with HME technology can provide more precision and accuracy in 3D printing, thus increasing the efficiency of the drug manufacturing process [86–89]. The ability to improve the drug manufacturing process has significant implications for the pharmaceutical industry. By adopting a Continuous Manufacturing process, which involves the integration of HME with 3D printing, the industry can produce drug products that are more efficient, cost-effective, and of high quality.

One of the challenges in coupling HME with 3D printing is the process of selecting the appropriate polymers for use in HME technology that can be subsequently printed via 3D printing. Researchers have been working on developing innovative polymeric systems that are compatible with both HME and 3D printing processes. One such example is the development of polymeric filaments that exhibit the necessary characteristics to be used in both the HME process and in 3D printing applications. The filaments are composed of different polymers that can be custom mixed to produce a material that meets the required compatibility and is suitable for drug development applications. Another challenge in coupling HME and 3D printing is the effect of shear forces on the drug delivery system. During HME, the materials are subjected to severe shear forces, which can modify the morphology and the chemical structure of the drug. A critical aspect of the development process is to use simulation software that can efficiently predict the physical and chemical changes that may happen during the HME process. This will help optimize the composition and control the process parameters to ultimately predict the outcome of 3D printing.

In conclusion, coupling 3D printing technologies with hot melt extrusion can revolutionize the pharmaceutical industry [90–93]. The technology can produce personalized drug delivery systems, implants, and other medical devices with a higher degree of accuracy and precision. It can offer a range of applications that can be used in various medical fields, including controlled release, improved bioavailability, and providing localized therapies. The combination of HME with

6. Regulatory Requirements for Continuous Manufacturing:

The regulatory requirements for the continuous manufacturing of HME technology fall under the current Good Manufacturing Practice (cGMP) regulations, which are enforced by regulatory agencies worldwide. These regulations require pharmaceutical companies to establish robust quality systems that ensure the

consistent production of safe and effective drug products. The guidelines are designed to minimize the risk of contamination, errors, and deviations from the established procedures and specifications. In 2018, the US Food and Drug Administration (FDA) released its "Quality Considerations for Continuous Manufacturing" guidance document, which provides recommendations for pharmaceutical companies using continuous manufacturing technologies, such as HME. The guidance document outlines the key elements that should be considered when implementing a continuous manufacturing process, including process monitoring, control, validation, and data integrity.

One critical aspect of the FDA's guidance is the requirement for process understanding, which involves a thorough characterization of the product and process parameters that affect product quality. This includes the use of process analytical technology (PAT) tools such as NIR spectroscopy, Raman spectroscopy, and mass spectrometry, which can provide real-time monitoring of the production process and identify any deviations before they impact product quality. The European Medicines Agency (EMA) has also published guidance related to continuous manufacturing, including its "Guideline on Process Validation for Finished Products - Information and Data to be Provided in Regulatory Submissions." This guidance document emphasizes the importance of process validation and the need to provide extensive data to regulatory agencies to demonstrate the robustness of the manufacturing process. The EMA also recommends the use of Continuous Process Verification (CPV), which involves the ongoing monitoring of the manufacturing process to ensure that the product consistently meets its required quality attributes [94–98].

7. Benefits of Continuous Manufacturing:

Continuous manufacturing using HME technology provides several benefits to pharmaceutical companies, including cost savings, reduced production time, and improved product quality. The use of HME enables the production of solid dispersions, mucoadhesive drug delivery systems, and amorphous solid dispersions, which can improve the solubility, dissolution rate, and bioavailability of poorly soluble drugs.

Continuous manufacturing also reduces the risk of batch failures and product recalls, as the process provides real-time monitoring and control of critical process parameters. The use of PAT tools enables pharmaceutical companies to identify any deviations from the established process before they impact product quality, reducing the risk of manufacturing errors and avoiding the costly consequences of product recalls [99,100].

8. Challenges of Continuous Manufacturing:

Although the use of continuous manufacturing using HME technology provides several benefits, it also presents some challenges that must be addressed to ensure product quality and patient safety. One major challenge is the need for process understanding, which involves extensive characterization of the product and process parameters. Process understanding is critical for the successful implementation of continuous manufacturing, as it enables pharmaceutical companies to optimize the process, ensure consistent product quality, and avoid issues that could impact patient safety.

Another significant challenge is the need for regulatory approval. The regulatory requirements for the continuous manufacturing of pharmaceuticals are still evolving, and pharmaceutical companies must work closely with regulatory agencies to ensure that they comply with the latest regulations and guidelines. In addition to regulatory approval, pharmaceutical companies must also consider the potential impact of continuous manufacturing on their supply chains. Continuous manufacturing requires different equipment, skills, and processes than traditional batch manufacturing, and companies must invest in training, equipment, and facilities to support this change. The continuous manufacturing of HME technology enables pharmaceutical companies to produce various dosage forms with improved drug properties and consistent quality while reducing the risk of batch failures and product recalls. However, this technology also presents challenges that must be addressed to ensure patient safety and product quality. Pharmaceutical companies must work closely with regulatory agencies to ensure compliance with the latest regulations and guidelines, invest in training and equipment, and establish robust quality systems that ensure the consistent production of safe and effective drug products [101,102]. With the continued advancement of PAT tools and regulatory guidance, the future looks promising for the widespread implementation of continuous manufacturing using HME technology in the pharmaceutical industry.

9. Future Perspectives of Continuous Manufacturing:

Continuous manufacturing using hot melt extrusion (HME) technology has been gaining traction in the pharmaceutical industry due to its numerous benefits. As the industry continues to evolve, HME-based continuous manufacturing is expected to become more widespread. In the future, it is anticipated that there will be advancements in several areas that will further enable the adoption of this technology [9,103]. One area of advancement is process control and optimization. As the industry moves toward Industry 4.0, there will be increased use of process analytical technology (PAT) and automation, which will provide real-time monitoring and control of critical process parameters. This will further improve the consistency and efficiency of the manufacturing process, ultimately resulting in higher-quality drug products [17,18].

Another area of research and development is the use of novel materials in continuous manufacturing. HME technology can be used to produce a variety of drug delivery systems, including solid dispersions, mucoadhesive formulations, and amorphous solid dispersions. With the exploration of new materials and formulations, it is anticipated that HME continuous manufacturing could produce even more innovative and effective drug products. The regulatory landscape for continuous manufacturing is also expected to become

clearer in the future. As more pharmaceutical companies adopt this technology, regulatory bodies are likely to establish clearer guidelines and regulations for its use. This will provide more certainty for pharmaceutical companies and encourage further adoption of HME continuous manufacturing.

Additionally, the integration of continuous manufacturing with other emerging technologies, such as artificial intelligence and machine learning, could lead to further improvements in process efficiency and optimization. These technologies could help predict deviations and optimize process parameters, thus reducing waste and improving product quality. The future of HME continuous manufacturing is bright and holds great promise for the pharmaceutical industry [23,29]. Through advancements in process control and optimization, the use of novel materials, clearer regulatory guidelines, and integration with emerging technologies, continuous manufacturing using HME technology is expected to become more efficient, cost-effective, and capable of producing high-quality drug products.

10. Conclusion

With the increasing demand for pharmaceutical medications, meeting the demands of supply chain implementation of continuous manufacturing will benefit both the industries and the patient population. Among various manufacturing platforms, HME is capable of being transformed into a continuous manufacturing line. The concept of screw design and mixing efficiency makes the HME platform a viable equipment for continuous manufacturing. Along with amorphous solid dispersions, the HME is also capable of a continuous granulation process, which can be coupled with various downstream equipments for the fabrication of the final desired dosage form. The HME can also be paired with an additive manufacturing platform for developing on-demand and patient-centric medications. By mounting suitable PAT tools, the quality of the product can be continuously monitored and controlled, ensuring enhanced assurance for patient safety. Overall, the HME-based continuous manufacturing platform has various advantages and is a viable opportunity for the industrial sector.

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References:

1. Mamidi H. Establishment of Design Space for Direct Compression of PEG (400) Loaded Neusilin® US2 by Modified SeDeM Expert System. St. John's University; 2017. https://scholar.google.com/scholar?hl=en&as_sdt=0%2C22&q=Establishment+of+Design+Space+for+Direct+Compression+of+PEG+%28400%29+Loaded+Neusilin%C2%AE+US2+by+Modified+SeDeM+Expert+System&btnG=

2. Siddharatha Dhoppalapudi, Prashanth Parupathi. Hot melt extrusion: A single-step continuous manufacturing process for developing amorphous solid dispersions of poorly soluble drug substances. GSC Advanced Research and Reviews. 2022;13(2):126-135. https://doi.org/10.30574/gscarr.2022.13.2.0311

3. Konda K, Dhoppalapudi S. A Review of Various Manufacturing Approaches for Developing Amorphous Solid Dispersions. Journal of Drug Delivery and Therapeutics. 2022;12(6):189-200. https://doi.org/10.22270/jddt.v12i6.5787

4. Indulkar AS, Lou X, Zhang GGZ, Taylor LS. Role of Surfactants on Release Performance of Amorphous Solid Dispersions of Ritonavir and Copovidone. Pharm Res. 2022;39(2):381-397. https://doi.org/10.1007/s11095-022-03183-4 PMid:35169959

5. Schittny A, Philipp-Bauer S, Detampel P, Huwyler J, Punchkov M. Mechanistic insights into effect of surfactants on oral bioavailability of amorphous solid dispersions. Journal of Controlled Release. 2020;320:214-225. https://doi.org/10.1016/j.jconrel.2020.01.031 PMid:31978445

6. Deshpande TM, Shi H, Pietryka J, Hoag SW, Medek A. Investigation of Polymer/Surfactant Interactions and Their Impact on Itraconazole Solubility and Precipitation Kinetics for Developing Spray-Dried Amorphous Solid Dispersions. Mol Pharm. 2018;15(3):962-974. https://doi.org/10.1021/acs.molpharmaceut.7b00902 PMid:29345955

7. Correa Soto CE, Gao Y, Indulkar AS, Ueda K, Zhang GGZ, Taylor LS. Impact of Surfactants on the Performance of Clopidogrel-Copovidone Amorphous Solid Dispersions: Increased Drug Loading and Stabilization of Nanodroplets. Pharm Res. 2022;39(1):167-188. https://doi.org/10.1007/s11095-021-03159-w PMid:35013849

8. Baghel S, Cathcart H, O'Reilly NJ. Investigation into the Solid-State Properties and Dissolution Profile of Spray-Dried Ternary Amorphous Solid Dispersions: A Rational Step toward the Design and Development of a Multicomponent Amorphous System. Mol Pharm. 2018;15(9):3796-3812. https://doi.org/10.1021/acs.molpharmaceut.8b00306 PMid:30020788

9. Vidiyala N, Parupathi P, Sunkishala P, et al. Artificial intelligence: a new era in prostate cancer diagnosis and treatment. Int J Pharm. 2025;683:126024. https://doi.org/10.1016/j.ijpharm.2025.126024 PMid:40769449

10. Szabo E, Za P, Brecska niel, et al. Comparison of amorphous solid dispersions of spironolactone prepared by spray drying and electrospinning: The influence of the preparation method on the. Mol Pharm. 2021;18(1):317-327. https://doi.org/10.1021/acs.molpharmaceut.0c00965 PMid:33301326 PMCid:PMC7788570

11. Dã B, Farkas A, Szabó B, et al. Development and tableting of directly compressible powder from electrospun nanofibrous amorphous solid dispersion. Elsevier. Published online 2017. https://doi.org/10.1016/j.apt.2017.03.026

12. Li J, Li C, Zhang H, et al. Preparation of Azithromycin Amorphous Solid Dispersion by Hot-Melt Extrusion: An Advantageous Technology with Taste Masking and Solubilization Effects. Polymers 2022, Vol 14, Page 495. 2022;14(3):495. https://doi.org/10.3390/polym14030495 PMid:35160485 PMCid:PMC8840525

13. Janssens S, Van den Mooter G. Review: Physical chemistry of solid dispersions. Journal of Pharmacy and Pharmacology. 2009;61(12):1571-1586. https://doi.org/10.1211/jpp/61.12.0001 PMid:19958579

14. Kennedy M, Hu J, Gao P, et al. Enhanced bioavailability of a poorly soluble VR1 antagonist using an amorphous solid dispersion approach: A case study. Mol Pharm. 2008;5(6):981-993. https://doi.org/10.1021/mp800061r PMid:19434920

15. Nyavanandi D, Mandati P, Narala S, et al. Twin Screw Melt Granulation: A Single Step Approach for Developing Self-

Emulsifying Drug Delivery System for Lipophilic Drugs. Pharmaceutics. 2023;15(9):2267. https://doi.org/10.3390/pharmaceutics15092267 PMid:37765237 PMCid:PMC10534719

16. Nyavanandi D, Mandati P, Vidiyala N, Parupathi P, Kolimi P, Mamidi HK. Enhancing Patient-Centric Drug Development: Coupling Hot Melt Extrusion with Fused Deposition Modeling and Pressure-Assisted Microsyringe Additive Manufacturing Platforms with Quality by Design. Pharmaceutics. 2024;17(1):14. https://doi.org/10.3390/pharmaceutics17010014 PMid:39861666 PMCid:PMC11769097

17. Andrews G, AbuDiak O, Jones D. Physicochemical characterization of hot melt extruded bicalutamide-polyvinylpyrrolidone solid dispersions. J Pharm Sci. 2010;99(3):1322-1335. https://doi.org/10.1002/jps.21914 PMid:19798757

18. Cid A, Simonazzi A, Palma S, Bermudez J. Solid dispersion technology as a strategy to improve the bioavailability of poorly soluble drugs. Ther Deliv. 2019;10(6). https://doi.org/10.4155/tde-2019-0007 PMid:31094298

19. Alonzo DE, Gao YI, Zhou D, Mo H, Zhang GGZ, Taylor LS. Dissolution and precipitation behavior of amorphous solid dispersions. J Pharm Sci. 2011;100(8):3316-3331. https://doi.org/10.1002/jps.22579 PMid:21607951

20. Konno H, Handa T, Alonzo D, Taylor L. Effect of polymer type on the dissolution profile of amorphous solid dispersions containing felodipine. European Journal of Pharmaceutics and Biopharmaceutics. 2008;70(2):493-499. https://doi.org/10.1016/j.ejpb.2008.05.023 PMid:18577451

21. Marsac PJ, Li T, Taylor LS. Estimation of drug-polymer miscibility and solubility in amorphous solid dispersions using experimentally determined interaction parameters. Pharm Res. 2009;26(1):139-151. https://doi.org/10.1007/s11095-008-9721-1 PMid:18779927

22. Rumondor ACF, Stanford LA, Taylor LS. Effects of polymer type and storage relative humidity on the kinetics of felodipine crystallization from amorphous solid dispersions. Pharm Res. 2009;26(12):2599-2606. https://doi.org/10.1007/s11095-009-9974-3 PMid:19806435

23. Mooter G Van den, Wuyts M, Blaton N, et al. Physical stabilisation of amorphous ketoconazole in solid dispersions with polyvinylpyrrolidone K25. European Journal of Pharmaceutical Sciences. 2001;12(3):261-269. https://doi.org/10.1016/S0928-0987(00)00173-1 PMid:11113645

24. Ambike A, Mahadik K, Paradkar A. Spray-dried amorphous solid dispersions of simvastatin, a low Tg drug: in vitro and in vivo evaluations. Pharm Res. 2005;22(6):990-998. https://doi.org/10.1007/s11095-005-4594-z PMid:15948043

25. Qian F, Huang J, Hussain M. Drug-polymer solubility and miscibility: stability consideration and practical challenges in amorphous solid dispersion development. J Pharm Sci. 2010;99(7):2941-2947. https://doi.org/10.1002/jps.22074 PMid:20127825

26. Teja SB, Patil SP, Shete G, Patel S, Kumar Bansal A. Drug-excipient behavior in polymeric amorphous solid dispersions. Journal of Excipients and Food Chemicals4. 2013;4(3):70-94. Accessed October 18, 2022. https://jefc.scholasticahq.com/article/1048.pdf

27. Baghel S, Cathcart H, O'Reilly N. Polymeric amorphous solid dispersions: a review of amorphization, crystallization, stabilization, solid-state characterization, and aqueous solubilization of. J Pharm Sci. 2016;105(9):2527-2544. https://doi.org/10.1016/j.xphs.2015.10.008 PMid:26886314

28. Azs D Emuth B, Farkas A, Balogh A, et al. Lubricant-induced crystallization of itraconazole from tablets made of electrospun amorphous solid dispersion. J Pharm Sci. 2016;105(9):2982-2988. https://doi.org/10.1016/j.xphs.2016.04.032 PMid:27290626

29. Balogh A, Farkas B, Farkas A, et al. Homogenization of amorphous solid dispersions prepared by electrospinning in low-dose tablet formulation. Pharmaceutics. 2018;10(3):114. https://doi.org/10.3390/pharmaceutics10030114 PMid:30072667 PMCid:PMC6161125

30. Casian T, Borbás E, Ilyés K, 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. https://doi.org/10.1016/j.ijpharm.2019.118593 PMid:31398371

31. Becelaere J, Van E, Broeck D, et al. Stable amorphous solid dispersion of flubendazole with high loading via electrospinning. Journal of Controlled Release. 2022;351:123-136. https://doi.org/10.1016/j.jconrel.2022.09.028 PMid:36122898

32. Démuth B, Farkas A, Pataki H, et al. Detailed stability investigation of amorphous solid dispersions prepared by single-needle and high speed electrospinning. Int J Pharm. 2017;498(1-2):234-244. https://doi.org/10.1016/j.ijpharm.2015.12.029 PMid:26705153

33. Dã B, Farkas A, Szabó B, et al. Development and tableting of directly compressible powder from electrospun nanofibrous amorphous solid dispersion. Advanced Powder Technology. 2017;28(6):1554-1563. https://doi.org/10.1016/j.apt.2017.03.026

34. Nagy Z, Balogh A, Démuth B, et al. High speed electrospinning for scaled-up production of amorphous solid dispersion of itraconazole. Int J Pharm. 2015;480(1-2):137-142. https://doi.org/10.1016/j.ijpharm.2015.01.025 PMid:25596415

35. Yu D, Yang J, Branford-White C, Lu P, Zhang L, Zhu L. Third generation solid dispersions of ferulic acid in electrospun composite nanofibers. Int J Pharm. 2010;400(1-2):158-164. https://doi.org/10.1016/j.ijpharm.2010.08.010 PMid:20713138

36. Karanth H, Shenoy VS, Murthy RR. Industrially feasible alternative approaches in the manufacture of solid dispersions: A technical report. AAPS PharmSciTech. 2006;7(4). https://doi.org/10.1208/pt070487 PMid:17233539 PMCid:PMC2750324

37. Paudel A, Geppi M, Van den Mooter G. Structural and dynamic properties of amorphous solid dispersions: the role of solid-state nuclear magnetic resonance spectroscopy and relaxometry. J Pharm Sci. 2014;103(9):2635-2662. https://doi.org/10.1002/jps.23966 PMid:24715618

38. 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;586:119560. https://doi.org/10.1016/j.ijpharm.2020.119560 PMid:32565285 PMCid:PMC8691091

39. Marano S, Barker S, Raimi-Abraham B, Missaghi S, Rajabi-Siahboomi A, Craig D. Development of micro-fibrous solid dispersions of poorly water-soluble drugs in sucrose using temperature-controlled centrifugal spinning. European Journal of Pharmaceutics and Biopharmaceutics. 2016;103:84-94. https://doi.org/10.1016/j.ejpb.2016.03.021 PMid:27012901 PMCid:PMC4866555

40. Keen JM, LaFountaine JS, Hughey JR, Miller DA, McGinity JW. Development of Itraconazole Tablets Containing Viscous KinetiSol Solid Dispersions: In Vitro and In Vivo Analysis in Dogs. AAPS PharmSciTech. 2018;19(5):1998-2008. https://doi.org/10.1208/s12249-017-0903-1 PMid:29192405

41. Gala U, Miller D, Su Y, Spangenberg A, Williams III R. The effect of drug loading on the properties of abiraterone-hydroxypropyl beta cyclodextrin solid dispersions processed by solvent free KinetiSol® technology. European Journal of Pharmaceutics and Biopharmaceutics. 2021;165:52-65. https://doi.org/10.1016/j.ejpb.2021.05.001 PMid:33979662

42. Ellenberger DJ, Miller DA, Kucera SU, Williams RO. Improved Vemurafenib Dissolution and Pharmacokinetics as an Amorphous Solid Dispersion Produced by KinetiSol® Processing. AAPS PharmSciTech. 2018;19(5):1957-1970. https://doi.org/10.1208/s12249-018-0988-1 PMid:29541940

43. LaFountaine J, Jermain S, Prasad L, et al. Enabling thermal processing of ritonavir-polyvinyl alcohol amorphous solid dispersions by KinetiSol® dispersing. European Journal of Pharmaceutics and Biopharmaceutics. 2016;101:72-81. https://doi.org/10.1016/j.ejpb.2016.01.018 PMid:26861929

44. Jermain S V., Miller D, Spangenberg A, et al. Homogeneity of amorphous solid dispersions-an example with KinetiSol®. Drug Dev Ind Pharm. 2019;45(5):724-735. https://doi.org/10.1080/03639045.2019.1569037 PMid:30653376

45. Hughey J, Keen J, Brough C, Saeger S, McGinity J. Thermal processing of a poorly water-soluble drug substance exhibiting a high melting point: the utility of KinetiSol® dispersing. Int J Pharm. 2011;419(1-2):222-230. https://doi.org/10.1016/j.ijpharm.2011.08.007 PMid:21864663

46. DiNunzio J, Brough C, Miller D, Williams R, McGinity J. Applications of KinetiSol® Dispersing for the production of plasticizer free amorphous solid dispersions. European Journal of Pharmaceutical Sciences. 2010;40(3):179-187. https://doi.org/10.1016/j.ejps.2010.03.002 PMid:20230894

47. DiNunzio J, Brough C, Hughey J, Miller D, Williams R, McGinity J. Fusion production of solid dispersions containing a heat-sensitive active ingredient by hot melt extrusion and Kinetisol® dispersing. European Journal of Pharmaceutics and Biopharmaceutics. 2010;74(2):340-351. https://doi.org/10.1016/j.ejpb.2009.09.007 PMid:19818402

48. Brough C, RO Williams R. Amorphous solid dispersions and nano-crystal technologies for poorly water-soluble drug delivery. Int J Pharm. 2013;453(1):157-166. https://doi.org/10.1016/j.ijpharm.2013.05.061 PMid:23751341

49. He Y, Ho C. Amorphous solid dispersions: utilization and challenges in drug discovery and development. J Pharm Sci. 2015;104(10):3237-3258. https://doi.org/10.1002/jps.24541 PMid:26175316

50. Vidiyala N, Sunkishala P, Parupathi P, et al. High Drug Loading of Amorphous Solid Dispersion by Hot Melt Extrusion: The Role of Magnesium Aluminometasilicate (Neusilin® US2). Sci Pharm. 2025;93(3):30. https://doi.org/10.3390/scipharm93030030

51. Tan DK, Davis DA, Miller DA, Williams RO, Nokhodchi A. Innovations in Thermal Processing: Hot-Melt Extrusion and KinetiSol® Dispersing. AAPS PharmSciTech. 2020;21(8). https://doi.org/10.1208/s12249-020-01854-2 PMid:33161479 PMCid:PMC7649167

52. Ellenberger DJ, Miller DA, Kucera SU, Williams RO. Generation of a Weakly Acidic Amorphous Solid Dispersion of the Weak Base Ritonavir with Equivalent In Vitro and In Vivo Performance to Norvir Tablet. AAPS PharmSciTech. 2018;19(5):1985-1997. https://doi.org/10.1208/s12249-018-1060-x PMid:29869311

53. Jr DD, Miller D, Santitewagun S, Zeitler J, Su Y, Williams R. Formulating a heat-and shear-labile drug in an amorphous solid dispersion: Balancing drug degradation and crystallinity. Int J Pharm X. 2021;3:100092. https://doi.org/10.1016/j.ijpx.2021.100092 PMid:34977559 PMCid:PMC8683684

54. Dinunzio JC, Hughey JR, Brough C, Miller DA, Williams RO, McGinity JW. Production of advanced solid dispersions for enhanced bioavailability of itraconazole using KinetiSol® Dispersing. Drug Dev Ind Pharm. 2010;36(9):1064-1078. https://doi.org/10.3109/03639041003652973 PMid:20334539

55. Ekdahl A, Mudie D, Malewski D, Amidon G, Goodwin A. Effect of spray-dried particle morphology on mechanical and flow properties of felodipine in PVP VA amorphous solid dispersions. J Pharm Sci. 2019;108(11):3657-3666. https://doi.org/10.1016/j.xphs.2019.08.008 PMid:31446144

56. Poudel S, Kim D. Developing pH-modulated spray dried amorphous solid dispersion of candesartan cilexetil with enhanced in vitro and in vivo performance. Pharmaceutics. 2021;13(4):497. https://doi.org/10.3390/pharmaceutics13040497 PMid:33917403 PMCid:PMC8067465

57. Sawicki E, Beijnen J, Schellens J, Nuijen B. Pharmaceutical development of an oral tablet formulation containing a spray dried amorphous solid dispersion of docetaxel or paclitaxel. Int J Pharm. 2016;511(2):765-773. https://doi.org/10.1016/j.ijpharm.2016.07.068 PMid:27480397

58. Zaitone A, Al-Zahrani B;, Ahmed O, Saeed U, Taimoor AA. Spray Drying of PEG6000 Suspension: Reaction Engineering Approach (REA) Modeling of Single Droplet Drying Kinetics. Process. 2022;10(7):1365. https://doi.org/10.3390/pr10071365

59. Li J, Zordan C, Ponce S, Lu X. Impact of Swelling of Spray Dried Dispersions in Dissolution Media on their Dissolution: An Investigation Based on UV Imaging. J Pharm Sci. 2022;111(6):1761-1769. https://doi.org/10.1016/j.xphs.2021.12.007 PMid:34896344

60. Patel K, Shah S, Patel J. Solid dispersion technology as a formulation strategy for the fabrication of modified release dosage forms: A comprehensive review. DARU, Journal of Pharmaceutical Sciences. 2022;30(1):165-189. https://doi.org/10.1007/s40199-022-00440-0 PMid:35437630 PMCid:PMC9114203

61. Ding Z, Wang X, Wang L, et al. Characterisation of spray dried microencapsules with amorphous lutein nanoparticles: Enhancement of processability, dissolution rate, and storage stability. Food Chem. 2022;383:132200. https://doi.org/10.1016/j.foodchem.2022.132200 PMid:35168049

62. Ikeda C, Zhou G, Lee Y, et al. Application of Online NIR Spectroscopy to Enhance Process Understanding and Enable In-process Control Testing of Secondary Drying Process for a Spray-dried. J Pharm Sci. 2022;111(9):2540-2551. https://doi.org/10.1016/j.xphs.2022.04.009 PMid:35439470

63. Boel E, Reniers F, Dehaen W, Van den Mooter G. The Value of Bead Coating in the Manufacturing of Amorphous Solid Dispersions: A Comparative Evaluation with Spray Drying. Pharmaceutics. 2022;14(3):613. https://doi.org/10.3390/pharmaceutics14030613 PMid:35335989 PMCid:PMC8955898

64. Newman A, Zografi G. Considerations in the Development of Physically Stable High Drug Load API-Polymer Amorphous Solid Dispersions in the Glassy State. J Pharm Sci. 2022;In Press. https://doi.org/10.1016/j.xphs.2022.08.007 PMid:35948156

65. Duarte Í, Santos JL, Pinto JF, Temtem M. Screening methodologies for the development of spray-dried amorphous solid dispersions. Pharm Res. 2015;32(1):222-237. https://doi.org/10.1007/s11095-014-1457-5 PMid:25135702

66. Lang B, Liu S, McGinity JW, Williams RO. Effect of hydrophilic additives on the dissolution and pharmacokinetic properties of itraconazole-enteric polymer hot-melt extruded amorphous solid dispersions. Drug Dev Ind Pharm. 2016;42(3):429-445. https://doi.org/10.3109/03639045.2015.1075031 PMid:26355819

67. Kowalczuk M, Li J, Li C, et al. Preparation of Azithromycin Amorphous Solid Dispersion by Hot-Melt Extrusion: An Advantageous Technology with Taste Masking and Solubilization Effects. Polymers (Basel). 2022;14(3):495. https://doi.org/10.3390/polym14030495 PMid:35160485 PMCid:PMC8840525

68. Liu X, Lu M, Guo Z, Huang L, Feng X, Wu C. Improving the chemical stability of amorphous solid dispersion with cocrystal technique by hot melt extrusion. Pharm Res. 2012;29(3):806-817. https://doi.org/10.1007/s11095-011-0605-4 PMid:22009589

69. Sarode A, Sandhu H, Shah N, Malick W, Zia H. Hot melt extrusion (HME) for amorphous solid dispersions: predictive tools for processing and impact of drug-polymer interactions on supersaturation. European Journal of Pharmaceutical Sciences. 2013;48(3):371-384. https://doi.org/10.1016/j.ejps.2012.12.012 PMid:23267847

70. Tian Y, Jacobs E, Jones D, McCoy C, Wu H, Andrews G. The design and development of high drug loading amorphous solid dispersion for hot-melt extrusion platform. Int J Pharm. 2020;586:119545. https://doi.org/10.1016/j.ijpharm.2020.119545 PMid:32553496

71. Giri BR, Kwon J, Vo AQ, Bhagurkar AM, Bandari S, Kim DW. Hot-melt extruded amorphous solid dispersion for solubility, stability, and bioavailability enhancement of telmisartan. Pharmaceutics. 2021;14(1):73. https://doi.org/10.3390/ph14010073 PMid:33477557 PMCid:PMC7831136

72. Fan W, Zhu W, Zhang X, Xu Y, Di L. Application of the combination of ball-milling and hot-melt extrusion in the development of an amorphous solid dispersion of a poorly water-soluble drug with. RSC Adv. 2019;9:22263-22273. https://doi.org/10.1039/C9RA00810A PMid:35519487 PMCid:PMC9066646

73. Mishra S, Richter M, Mejia L, Sauer A. Downstream Processing of Itraconazole: HPMCAS Amorphous Solid Dispersion: From Hot-Melt Extrudate to Tablet Using a Quality by Design Approach. Pharmaceutics. 2022;14(7):1429. https://doi.org/10.3390/pharmaceutics14071429 PMid:35890324 PMCid:PMC9323274

74. Pawar J, Narkhede R, Amin P, Tawde V. Design and Evaluation of Topical Diclofenac Sodium Gel Using Hot Melt Extrusion Technology as a Continuous Manufacturing Process with Kolliphor® P407. AAPS PharmSciTech. 2017;18(6):2303-2315. https://doi.org/10.1208/s12249-017-0713-5 PMid:28108974

75. Genina N, Hadi B, Löbmann K. Hot melt extrusion as solvent-free technique for a continuous manufacturing of drug-loaded mesoporous silica. J Pharm Sci. 2018;107(1):149-155. https://doi.org/10.1016/j.xphs.2017.05.039 PMid:28603020

76. Patil H, Kulkarni V, Majumdar S, Repka M. Continuous manufacturing of solid lipid nanoparticles by hot melt extrusion. Int J Pharm. 2014;471(1-2):153-156. https://doi.org/10.1016/j.ijpharm.2014.05.024 PMid:24853459

77. Maniruzzaman M, Nokhodchi A. Continuous manufacturing via hot-melt extrusion and scale up: regulatory matters. Drug Discov Today. 2016;22(2):340-351. https://doi.org/10.1016/j.drudis.2016.11.007 PMid:27866007

78. Seem T, Rowson N, Ingram A, et al. Twin screw granulation-A literature review. Elsevier Powder Technology. 2015;276:89-102. https://doi.org/10.1016/j.powtec.2015.01.075

79. Mamidi H, Mishra S, Rohera B. Application of modified SeDeM expert diagram system for selection of direct compression excipient for liquisolid formulation of Neusilin® US2. J Drug Deliv Sci Technol. 2021;64:102506. https://doi.org/10.1016/j.jddst.2021.102506

80. Melocchi A, Parietti F, Maroni A, Foppoli A, Gazzaniga A, Zema L. Hot-melt extruded filaments based on pharmaceutical grade polymers for 3D printing by fused deposition modeling. Int J Pharm. 2016;509(1-2):255-263. https://doi.org/10.1016/j.ijpharm.2016.05.036 PMid:27215535

81. Santos J Dos, Silveira Da Silva G, Velho MC, Carlos R, Beck R. Eudragit®: A Versatile Family of Polymers for Hot Melt Extrusion and 3D Printing Processes in Pharmaceutics. Pharmaceutics. 2021;13(9):1424. https://doi.org/10.3390/pharmaceutics13091424 PMid:34575500 PMCid:PMC8471576

82. Cunha-Filho M, Araújo MR, Gelfuso GM, Gratieri T. FDM 3D printing of modified drug-delivery systems using hot melt extrusion: A new approach for individualized therapy. Ther Deliv. 2017;8(11):957-966. https://doi.org/10.4155/tde-2017-0067 PMid:29061104

83. Madan S, Madan S. Hot melt extrusion and its pharmaceutical applications. Asian J Pharm Sci. 2012;7(1):123-133. Accessed October 18, 2022. https://search.ebscohost.com/login.aspx?direct=true&profile=ehost&scope=site&authtype=crawler&jrnl=18180876&AN=76385092&h=E%2BnVOb8JShE%2Fb6%2Bg80lQW%2BBTmz%2BnljjuMYmY%2FvaKoGIsN47xWWlcY76lISjNTYsgoAT8kIdiEdvkiONgQRBsuw%3D%3D&crl=c

84. Simões M, Pinto R, Simões S. Hot-melt extrusion in the pharmaceutical industry: toward filing a new drug application. Drug Discov Today. 2019;24(9):1749-1768. https://doi.org/10.1016/j.drudis.2019.05.013 PMid:31132415

85. Lang B, McGinity JW, Williams RO. Hot-melt extrusion-basic principles and pharmaceutical applications. Drug Dev Ind Pharm. 2014;40(9):1133-1155. https://doi.org/10.3109/03639045.2013.838577 PMid:24520867

86. Maniruzzaman M, Boateng JS, Snowden MJ, et al. A review of hot-melt extrusion: process technology to pharmaceutical products. ISRN Pharm. 2012;2012. https://doi.org/10.5402/2012/436763 PMid:23326686 PMCid:PMC3543799

87. Newman A, Knipp G, Zografi G. Assessing the performance of amorphous solid dispersions. J Pharm Sci. 2012;101(4):1355-1377. https://doi.org/10.1002/jps.23031 PMid:22213468

88. Thompson S, Williams III R. Specific mechanical energy-An essential parameter in the processing of amorphous solid dispersions. Adv Drug Deliv Rev. 2021;173:374-393. https://doi.org/10.1016/j.addr.2021.03.006 PMid:33781785

89. Vasconcelos T, Marques S, Neves J, Sarmento B. Amorphous solid dispersions: Rational selection of a manufacturing process. Adv Drug Deliv Rev. 2016;100:85-101. https://doi.org/10.1016/j.addr.2016.01.012 PMid:26826438

90. Ma X, Williams III R. Characterization of amorphous solid dispersions: An update. J Drug Deliv Sci Technol. 2019;50:113-124. https://doi.org/10.1016/j.jddst.2019.01.017

91. Van der Mooter G. The use of amorphous solid dispersions: A formulation strategy to overcome poor solubility and dissolution rate. Drug Discov Today Technol. 2012;9(2):79-85. https://doi.org/10.1016/j.ddtec.2011.10.002 PMid:24064267

92. LaFountaine JS, McGinity JW, Williams RO. Challenges and Strategies in Thermal Processing of Amorphous Solid Dispersions: A Review. AAPS PharmSciTech. 2016;17(1):43-55. https://doi.org/10.1208/s12249-015-0393-y PMid:26307759 PMCid:PMC4766121

93. Park S, Rajesh P, Sim Y, et al. Addressing scale-up challenges and enhancement in performance of hydrogen-producing microbial electrolysis cell through electrode modifications. Energy Reports. 2022;8:2726-2746. https://doi.org/10.1016/j.egyr.2022.01.198

94. Ghadge R, Nagwani N, Saxena N, Dasgupta S, Sapre A. Design and scale-up challenges in hydrothermal liquefaction process for biocrude production and its upgradation. Energy Conversion and Management: X. 2022;14:100223. https://doi.org/10.1016/j.ecmx.2022.100223

95. Tonkovich A, Kuhlmann D, Rogers A, et al. Microchannel technology scale-up to commercial capacity. Chemical Engineering Research and Design. 2005;83(6):634-639. https://doi.org/10.1205/cherd.04354

96. Khairnar S V, Pagare P, Thakre A, et al. Review on the Scale-Up Methods for the Preparation of Solid Lipid Nanoparticles. Pharmaceutics. 2022;14(9):1886. https://doi.org/10.3390/pharmaceutics14091886 PMid:36145632 PMCid:PMC9503303

97. Tran P, Pyo Y, Kim D, Lee S, Kim J, Park J. Overview of the manufacturing methods of solid dispersion technology for improving the solubility of poorly water-soluble drugs and application to anticancer drugs. Pharmaceutics. 2019;11(3):132. https://doi.org/10.3390/pharmaceutics11030132 PMid:30893899 PMCid:PMC6470797

98. Sharma A, Jain C. Solid dispersion: A promising technique to enhance solubility of poorly water soluble drug. International Journal of Drug Delivery. Published online 2011. https://citeseerx.ist.psu.edu/viewdoc/download?doi=10.1.1.856.1002&rep=rep1&type=pdf

99. Lima ÁAN, Sobrinho JLS, Corrêa RAC, Neto PJR. Alternative technologies to improve solubility of poorly water soluble drugs. Latin American Journal of Pharmacy. 2008;27(5):789-797. http://www.latamjpharm.org/trabajos/27/5/LAJOP_27_5_4_2_7QVYB4J43B.pdf

100. Chaudhari S, Dugar R. Application of surfactants in solid dispersion technology for improving solubility of poorly water soluble drugs. J Drug Deliv Sci Technol. 2017;41:68-77. https://doi.org/10.1016/j.jddst.2017.06.010

101. Singh D, Bedi N, Tiwary AK. Enhancing solubility of poorly aqueous soluble drugs: critical appraisal of techniques. Journal of Pharmaceutical Investigation 2017 48:5. 2017;48(5):509-526. https://doi.org/10.1007/s40005-017-0357-1

102. Singh A, Worku ZA, Van Den Mooter G. Oral formulation strategies to improve solubility of poorly water-soluble drugs. Expert Opin Drug Deliv. 2011;8(10):1361-1378. dohttps://doi.org/10.1517/17425247.2011.606808 PMid:21810062

103. Vidiyala N, Sunkishala P, Parupathi P, Nyavanandi D. The Role of Artificial Intelligence in Drug Discovery and Pharmaceutical Development: A Paradigm Shift in the History of Pharmaceutical Industries. AAPS PharmSciTech. 2025;26(5):1-21. https://doi.org/10.1208/s12249-025-03134-3 PMid:40360908