AAPS PharmSciTech, Vol. 17, No. 1, February 2016 (© 2016)
DOI: 10.1208/s12249-016-0486-2

Editorial

Theme: Pharmaceutical Thermal Processing
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Pharmaceutical Thermal Processing

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published online 9 February 2016

Thermal processing has flourished as a novel technology to prepare a wide range of drug delivery systems over the past decade. Thermal processing is built on the principle of efficient conversion of the mechanical energy into the thermal energy of the formulation matrix. Single and twin screw extruders are the most commonly employed thermal processing equipment. Kinetisol® Dispersing technology, an innovative thermal process, was invented recently. This theme issue of AAPS PharmSciTech provides a broad overview of (a) the history and recent advancement of thermal processing, (b) scientific approaches to develop drug delivery systems using thermal processing, and (c) examples of a wide range of drug delivery systems prepared using thermal processing.

This issue of AAPS PharmSciTech offers three review articles. Martin provided a historical and technical review of a twin screw extruder as a continuous mixer for thermal processing in both the plastic and pharmaceutical industry from an equipment engineer's perspective (1). From his personal experience, Martin believed that the evolution of twin screw extrusion-based thermal processing in the pharmaceutical industry resembles what occurred for the plastics industry in 1980s. Patil et al. reviewed the application of melt extrusion in the production of diverse pharmaceutical delivery systems (2). The authors emphasized the critical role of the quality-by-design approach and process analytical technology in pharmaceutical melt extrusion monitoring and control. LaFountaine et al. discussed a number of formulation and process-driven strategies to enable thermal processing of challenging compositions (3). These included the use of traditional plasticizers and surfactants, temporary plasticizers utilizing sub- or supercritical carbon dioxide, designer polymers, and KinetiSol® Dispersing technology.

This theme issue also contains 15 original research articles. Bhagurkar et al. proposes the use of melt extrusion processing for the preparation of a polyethylene glycol base ointment (4). A modified screw design was used and parameters such as feeding rate, barrel temperature, and screw speed were optimized to obtain a uniform product. Zhang successfully applied a melt extrusion process to prepare Eudragit FS-based granules for colon-targeting drug delivery (5). Maniruzzaman et al. investigated the effect of novel melt-extruded polymer and lipid formulations on the dissolution rates of indomethacin (6). A synergy between the polymer and lipid in enhancing the drug release was reported. Ye et al. demonstrated the feasibility of producing nanocrystal solid dispersions by conjugating high-pressure homogenization and melt extrusion processes (7). Jedinger et al. developed cornstarch-based flexible deformable multiple-unit pellets with abuse deterrence properties using a twin screw extruder (8). Lamm and his colleagues characterized the phase behavior and morphology of melt-extruded amorphous solid dispersions comprised of copovidone and TPGS 1000 using atomic force microscopy and differential scanning calorimetry (9). Both the processing parameters including screw speed and cooling method as well as the compositional effects on the resulting melt extrudate were studied. Agrawal et al. presented a case study of systematic development and scale up of an amorphous solid dispersion dosage to the clinical scale using less than 500 g drug (10). The melt extrusion process was scaled up from lab scale to clinical scale using a volumetric scale up approach and scale independent-specific energy parameter. In a separate study, Agrawal et al. evaluated the influence of extra-granular components on dissolution of tablets containing melt-extruded amorphous solid dispersion granules (11). To achieve rapid disintegration and acceptable tensile strength, the authors found that the extra-granular composition was also dependent on both the type of polymer the drug-polymer interaction. LaFountaine et al. demonstrated that Kinetisol® Dispersing technology produced amorphous dispersions at higher drug loads than could be prepared by melt extrusion, as well as with higher molecular weight polymers that were not processable by melt extrusion (12). Li et al. applied Flory–Huggins and temperature–composition phase diagrams to not only understand drug–polymer miscibility behavior but also rationalize the selection of important processing parameters for melt extrusion to ensure miscibility of drug and polymer (13). Five research articles are focused on the application of novel excipients in melt extrusion process. Brough et al. enabled polyvinyl alcohol as the polymeric carrier for amorphous solid

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dispersions using Kinetisol® Dispersing technology (14,15). Juluri et al. investigated the potential of Kleptose Linecaps in masking the bitter taste of therapeutic agents by melt extrusion (16). Thermal and viscoelastic properties of AFFINISOL™ hypromellose relevant to melt extrusion were fully characterized by Gupta et al. (17). Their study demonstrated that AFFINISOl™ hypromellose could be processed at larger windows of processing temperature as compared to that of copovidone. AFFINISOL™ hypromellose with a significantly lower glass transition temperature and melt viscosity than Methocel® hypromellose was demonstrated to be a desirable polymer carrier for the preparation of amorphous solid dispersion using melt extrusion processing by Huang et al. (18).

With all the progress achieved over the last decade, thermal processing is anticipated to become even more broadly applied to manufacture a wide range of drug delivery systems in near future. Concerted efforts among scientists in various research areas including excipient design, formulation development, process engineering, and material characterization are required to further advance thermal processing.

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