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Overcoming Melt Processing Challenges For Polymer-Based Drug Delivery Systems

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TheraPEA™ Biodegradable Polymer Platform: Enabling Flexibility In Formulation

Drug delivery solutions come in many forms, from implants and injectables to coatings and films. The preferred form of a therapy is dependent upon many variables, including the required release profile, the intended delivery site and the nature of the active pharmaceutical ingredient (API) being delivered. Despite great advances, processing of such therapies remains far from trivial.

Implantables are one solution for long-acting drug delivery, with fibers and rods typically produced via melt processing. Several challenges exist when melt processing is applied, which need to be overcome to produce reliable therapies. Temperature is one key consideration. When processing conventional drug delivery excipients such as semi-crystalline biodegradable polyesters, temperatures in excess of 160°C typically need to be applied to the polymer-API combination in order for it to reach its melted state. For many APIs, exposure to such elevated temperatures during melt processing can cause a loss of potency.

DSM has developed the TheraPEA™ biodegradable polymer platform which can be easily applied with hot melt processing for drug loaded therapies. The TheraPEA™ platform consists of polyester amides (PEAs) based on naturally occurring amino acids and containing a combination of both ester and amide bonds. This combination of ester and amide linkages provides a unique balance between hydrolytic stability and hydrophilicity. This balance ensures TheraPEA™ polymers can tolerate residual water, up to 500 ppm, during high temperature processing, with no molecular weight drop observed.[1] TheraPEA™ polymers are fully amorphous, as such they can be processed at a relatively low temperature with required melt properties achieved between 120-160°C without the addition of processing aids. As such, they are well suited for melt processing in combination with temperature sensitive APIs.

One additional challenge with melt processing can be the large amount of material that is consumed. This often limits the ability to evaluate novel APIs in formulation development studies due to a limited quantity of the pharmaceutical being available. Common processing methods include piston or twin-screw extrusion and compression molding to achieve the desired shape. These methods typically require tens to hundreds of grams of the drug-polymer formulation. To overcome this challenge, DSM has designed custom compression molding equipment to enable execution of processing feasibilities with minimal amounts of formulation, starting from only 200 mg. It is possible to prepare highly loaded implant forms (up to 50% API by weight), ranging in diameter from 200 µm to 2 mm, see Figure 1. Several thousand test articles prepared via this method exhibited excellent batch-to-batch consistency in terms of dimensions with coefficient of variation of less than 15% for an implant diameter of 250 µm, including some created for use in preclinical in-vivo trials.[2]

Figure 1: Injection molded PEA rods with diametsd of 2000, 850, and 200 µm (L to R).

From the initially-produced implant, DSM has the capability to implement post-processing refinements to achieve a specific drug release profile. Using a series of such post-processing treatments, the release profile can be further tuned and initial burst release can be minimised. This can be noted in the example for a formulation with a TheraPEA™ polymer loaded with a glucagon-like peptide receptor agonist (GLP-1 RA), shown in Figure 2.

Figure 2: TheraPEA™ PEA III X polymer formulated with GLP-1 RA (~4KDa). Blue line is the original melt processed implant at 50% weight loading, red line is the same implant with post-processing technique applied, green line is an optimized melt processed implant at 40% weight loading with post-processing for burst reduction.[3]

In the next article, the TheraPEA™ biodegradable polymer's unique solubility properties will be discussed and how they can enable flexibility in formulating therapies through solution-based processing. Want to learn more? Connect with DSM at DrugDelivery.Biomedical@dsm.com or visit www.DSMBiomedical.com.

About DSM Biomedical

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1. Data on file at DSM (Report time-temperature window.docx)
2. Data on file at DSM (TD-00997 – customer specs)
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