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Solvent-Based Processing Techniques Provide Flexibility In Creating Drug Delivery Systems For Thermally Sensitive APIs

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By Matilde Putti, PhD., Scientist at DSM Biomedical

TheraPEA™ biodegradable polymer platform for use in coatings, thin films, and more.

Biodegradable long-acting drug delivery systems (DDS) have revolutionized the concept of medicine administration, whether as standalone implantable therapies or as combination devices. Sustained release formulations offer dose compliance at a target location for timeframes ranging from a few weeks up to several months, and the need for removal of the implant is eliminated thanks to biodegradation of the polymer.

Polymer-based DDS can be manufactured by thermal processes such as molding or extrusion to create standalone implants. The best-known examples are the non-resorbable Nuvaring® or Implanon® contraceptive devices. However, many active pharmaceutical ingredients (API) can be damaged by high processing temperatures typical of melt techniques. One way to overcome this challenge is to instead use solution processing techniques.

Solvent-based processing allows the DDS to work with thermally sensitive APIs, while at the same time offers great thickness flexibility and uniformity. Ultra-thin and homogeneous films or coatings are typically produced via techniques such as film casting, dip-coating, blade-coating and (ultrasonic) spray-coating. For specific applications, thin non-woven meshes can be prepared via advanced solution processing methods that yield nano- or microfibers, i.e. electrospinning.

Many solvent-based processing methods employ coating techniques that can be tailored to substrates with complex geometries, while controlling the thickness to micrometer precision. This is particularly appreciated in creating combination devices, such as drug eluting vascular stents (DES). In DES, an intricate geometry of the bare metal substrate is necessary for folding and unfolding, and a profile increase after addition of a drug eluting layer must be minimized since it can hamper insertion through a narrow opening or work in conjunction with deployment devices.

One of the most important parameters for solution process development are the viscoelastic properties of the solution. In the processing techniques mentioned above, the outcome is strongly influenced by solution viscosity, which ultimately depends on the polymer-solvent interaction. For this reason, process developers and formulators appreciate being able to choose from multiple solvent systems. At the same time, a common concern associated with solution processing is the residual level of organic solvents in the finished device, which restricts the ideal solvent selection panel to those with low boiling points, or solvents listed as least hazardous in relevant guidelines[1].

Previously, the benefits of the TheraPEA™ biodegradable polymer platform for DDS have been detailed, including their unique ability to control the release of a variety of APIs as well and do so without degrading into low-pH byproducts (see prior article). The TheraPEA™ platform is a family of fully amorphous polyester amide (PEA) polymers based on naturally occurring amino acids and contain a combination of ester and amide linkages. Due to their amorphous nature and balanced hydrophilicity, TheraPEA™ polymers exhibit solubility in a broad range of solvents. Like polyesters, TheraPEA™ polymers are soluble in common low boiling solvents such as tetrahydrofuran, chlorinated and fluorinated solvents. The solubility of TheraPEA™ polymers in low molecular weight hydrocarbon alcohols (methanol, ethanol, isopropanol, *tert*-butanol) differentiates the TheraPEA™ platform from polyesters and allows the formulator to homogenize the excipient with alcohol soluble APIs, while still allowing use of solvents with a favorable evaporation rate.

With a high flexibility in the choice of solvents and processing techniques, TheraPEA™ polymers have been processed into DDS with thicknesses as low as 6 µm on devices with intricate geometries using spray coating techniques[2]. Casting and blade coating are employed to create films, either free-standing or adhering to substrates. Microfibers with an average fiber diameter of 2 µm have been produced by electrospinning in ethanol solution. These microfibers can be formed into meshes with a wide range of three-dimensional geometries and thickness possibilities depending on the application requirements[3] (Figure 1).

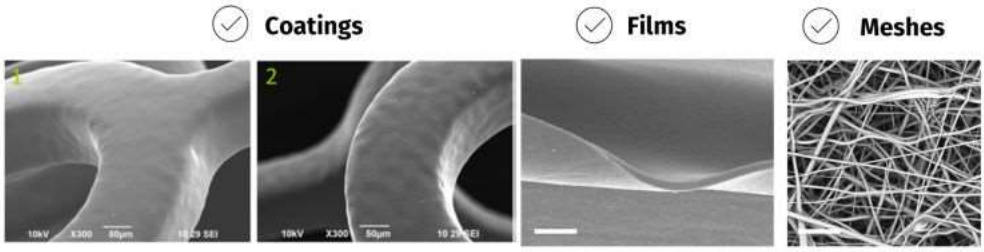

Figure 1. SEM micrographs of cardiovascular stent struts covered with drug-eluting coating based on TheraPEA polymer (left) [4]. The ultra-thin layer of DDS allows the low profile required for the application to be maintained. A thin film made by solvent casting (middle)[4]. A fibrous mesh produced via electrospinning TheraPEA™ polymer with 2 µm thick fibers and approximately 40 µm mat thickness (right)[5]. Scale bars are 5 µm.

DSM's TheraPEA™ biodegradable polymer platform is ultimately suitable for drug-eluting coatings thanks to its compatibility with many substrates. In particular, the outstanding adhesion to metals means it can be used as a reliable coating for, among other applications, cardiovascular stents which must withstand crimping procedures[6].

With a broad range of solution processing possibilities in terms of techniques, solvents, and substrates, TheraPEA™ biodegradable polymer platform can enable several applications as a drug eluting carrier with a wide variety of active pharmaceutical ingredients in both systemic and site-specific parenteral drug delivery. DSM Biomedical has the right expertise to provide guidance on drug loading potential and formulation approaches for your envisioned therapy. Want to learn more about the opportunities to partner with DSM to successfully bring your therapy to the market? Connect with us at DrugDelivery.Biomedical@dsm.com to start the discussion!

About DSM Biomedical

DSM Biomedical is the world's unrivalled biomaterials expert and committed partner driving sustainable innovation in healthcare. For 30+ years, their solutions have been recognized for their unmatched quality, consistency, and performance, ultimately supporting their company-wide vision of solving the world's healthcare needs through sustainable science.

To learn more, visit DSMBiomedical.com.

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