Development of Novel Stent Coating Process using Supercritical Fluid and Dry Powder Electrostatic Coating Methods to Deposit Crystalline Sirolimus

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Statement of Purpose: Many processes for spray coating stents require that drug and polymer be dissolved in solvent before spray coating can occur. Micell has developed new technology to spray coat stents with drug(s) and polymer(s) (trade name Criticoat™) in independent steps under conditions that do not require drug dissolution and separates drug and polymer spraying into discrete steps. Under the conditions employed either crystalline or amorphous drug can be spray deposited with high accuracy and precision at room temperature. Drug can be deposited at different depths within a polymer matrix. By not dissolving sirolimus, the drug stability can be maintained as it is in its native state because amorphous sirolimus is not created. Following spray coating, the coated stent is sintered in supercritical fluid to bind the drug and polymer coatings to the stent substrate at near room temperature conditions thereby minimizing sirolimus thermal degradation.

Methods: Sirolimus (98% purity) was purchased from LC Laboratories. Polyethylene-co-vinyl acetate (33% w/w vinyl acetate) and Polybutylmethacrylate were purchased from Sigma-Aldrich and used without further purification. All solvents unless otherwise noted were supplied by Sigma-Aldrich and were spectrophotometric grade and used without further purification. Four batches of three stents per batch manufactured to Micell's specifications (Burpee Materials Technology, L.L.C.) were coated simultaneously. Polymer was applied to stents using an electrostatic rapid expansion of a supercritical solution method[1] while sirolimus was applied to stents using a proprietary dry powder coating method. Drug and polymer coated proxy substrates were prepared using 316L stainless steel coupons for x-ray diffraction measurements (0 to 2θ scans) to confirm the crystalline morphology of the deposited drug. Coated stents were removed from the coating chamber and sintered at 30 °C and approximately 4 bar using Micell's Critiflo™ technology[1].

Results: Sirolimus was deposited in a crystalline morphology as determined by optical microscopy of a stent and powder x-ray diffraction of a sintered stainless steel coupon (figures 1 and 2).

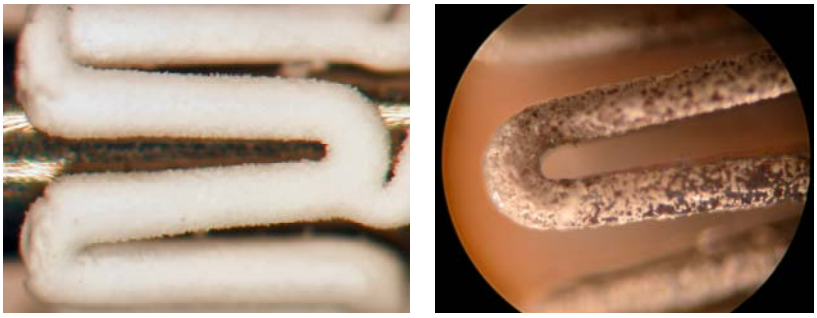

Figure 1. Pre-sintered (left) and sintered (right) stent images. Crystalline sirolimus is visible through the polymer film in the sintered image.

Conclusion: Using Micell's Citicoat™ technology to deposit crystalline sirolimus inhibits the degradation of sirolimus compared to deposition of amorphous sirolimus. The described technology demonstrates accurate and precise deposition of drug and polymeric materials enabling unique medical device properties.

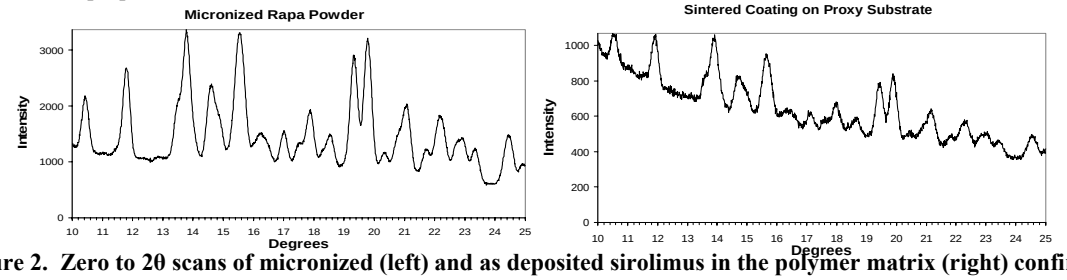

Figure 2. Zero to 2θ scans of micronized (left) and as deposited sirolimus in the polymer matrix (right) confirming the crystalline nature of the deposited sirolimus.

References:

1. Fulton, John L.and Deverman, George; Electrostatic deposition of particles generated from rapid expansion of supercritical fluid solutions, U.S. 6,756,084 (June 29, 2004). Fulton, John L and Deverman, George; Electrostatic deposition of particles generated from rapid expansion of supercritical fluid solutions U.S. 6,780,475 (August 24, 2004). Yonker, Clement R. and Fulton, John L.; Methods for producing films using supercritical fluids, U.S. 6,749,902 (June 15, 2004).