**Development of Novel Drug Eluting Coating for a Dual Drug Eluting Stent**

Jim McClain[1], John Fulton[2], Clint Smoke[1], Doug Taylor[1], George Deverman[2], and Yongsheng Chen[2]
[1]Micell Technologies, Inc., 7516 Precision Dr., Raleigh, NC 2761 and [2]Pacific Northwest National Laboratories, Richland, WA 99352

**Statement of Purpose:** Many processes for spray coating stents require that drug and polymer be dissolved in solvent or mutual solvent before spray coating can occur. Micell has developed new technology to spray coat stents with drug(s) and polymer(s) in independent steps under conditions that do not require dissolved drug and separates drug and polymer spraying into individual steps. This capability allows discrete placement of drug within a polymer matrix and makes possible placing more than one drug on a single medical device with or without an intervening polymer layer. We report the discrete deposition and elution of a dual drug coated drug eluting stent using Micell's proprietary technology.

**Methods:** Taxol (98% purity) was purchased from Toronto Research Chemicals. Heparin was purchased from Polysciences, Inc. 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. Three stents 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 Heparin and Taxol were applied to stents using a proprietary dry powder coating method. Heparin was deposited prior to depositing Taxol with an intervening polymer layer. Heparin was analyzed by UV-Vis spectrophotometry (Ocean Optics) and quantified using the Beer-Lambert relationship using an Azure A assay while Taxol was determined directly from the elution medium at 227 nm. Coated stents were removed from the coating chamber and sintered at 30 °C and approximately 4 bar using Micell's Critiflo™ technology[1]. Taxol drug elution from the polymer matrix was completed by eluting stents in phosphate buffered saline at pH 7.4 with added tween 20 (0.05 % w/w) in a thermostatically controlled temperature bath held at 37 °C. An aqueous media was used to elute heparin from the polymer matrix. Because of surfactant interference with the azure A assay, heparin elution was quantitatively determined separately from Taxol.

**Results:** Heparin was loaded on the stent at 70 micrograms and Taxol was loaded on the stent at 78 micrograms. The total polymer mass deposited on the stent was 2.1 milligrams (figure 1). Heparin and Taxol elution was monitored for 15 days. Figure 2 shows the cumulative mass of heparin eluted as well as the elution rate. The ability of azure A to continue to bind to heparin suggests that no chemical reaction between heparin and Taxol occurs. Further work is under way to confirm this hypothesis. Additional work is under way to decrease the elution rate of heparin and to demonstrate various control strategies to alter the elution rate of Taxol.

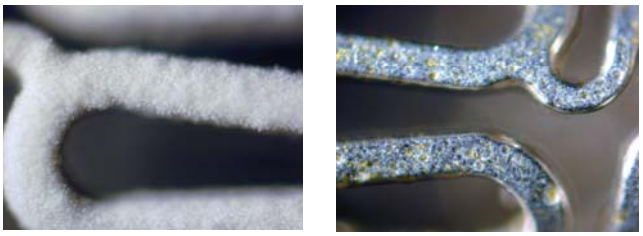

**Figure 1. Pre-sintered (left) and sintered (right) stent images. Fluorescently tagged heparin (yellow) and Taxol can be seen through the clear polymer.**

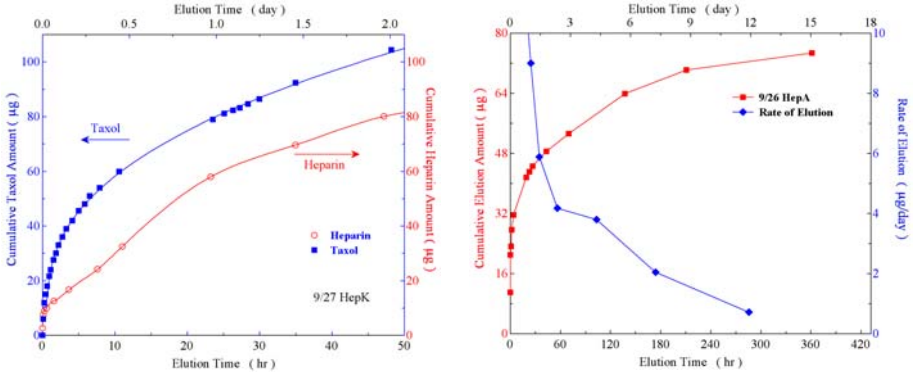


**Figure 2. Elution of Taxol and heparin from dual drug coated stent. Heparin continues to elute after 15 days.**

**Conclusion:** Two drug can be independently deposited on a single stent, and both heparin and Taxol can be eluted from the same stent. Elution of heparin was maintained for at least 15 days although elution rate decreased with increasing time.

**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).