

Technology

Utilizing supercritical fluids (E-RESS)

- Solvent-free
- Low temperature
- Multiple drugs
- "Dry": no bleeding of layers
- Excellent adhesion of layers and mechanical properties
- Excellent *precision of layers* and enables rapid batch processing

Capable of making novel devices

- Enables laminate structure
- Forming intricate, novel devices
- Unique laminate structure provides structural control without introducing new materials or new delivery system
- Demonstrated for drug-eluting coatings and coated membranes

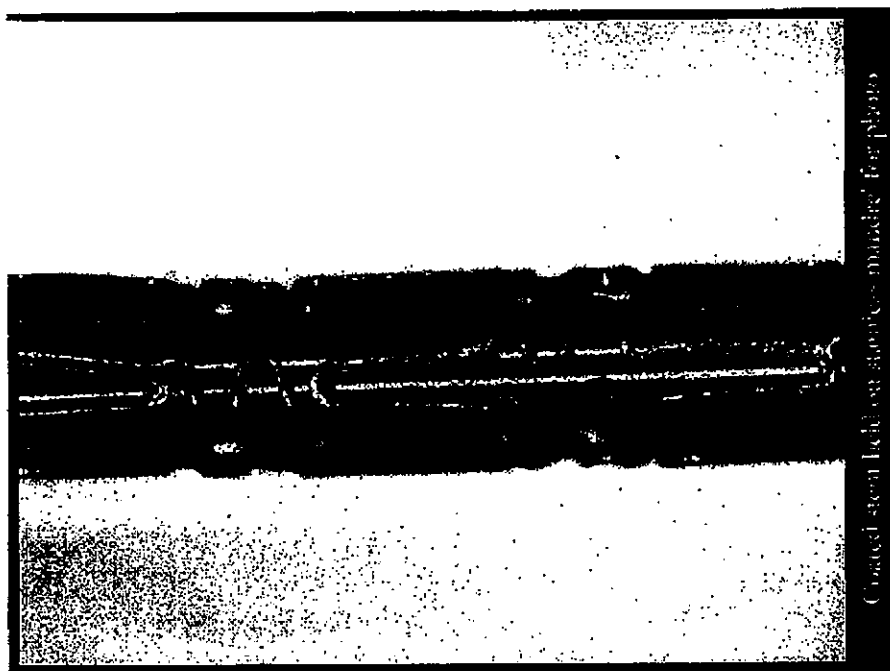


FIGURE 1

Process Technology

Step One

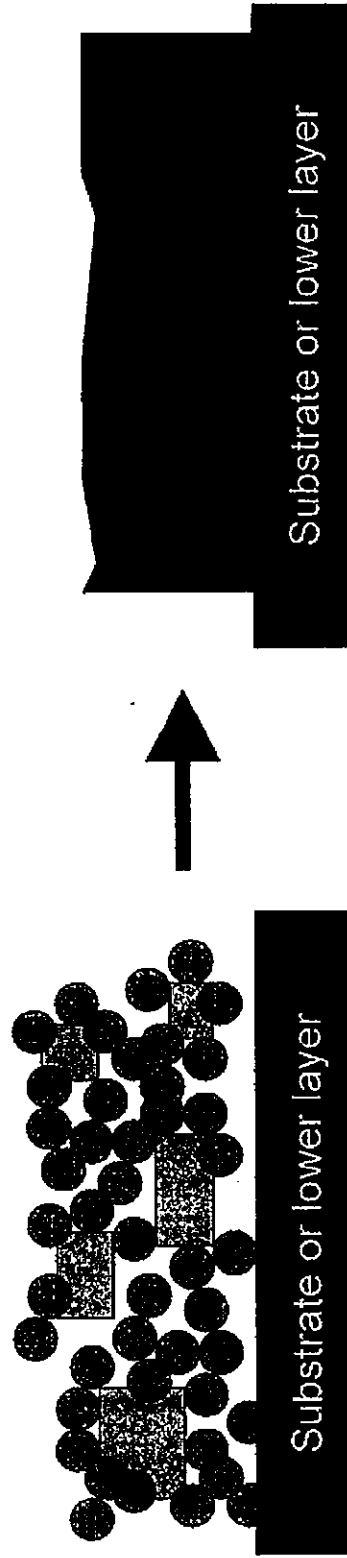
CritiCoat™: Electrostatic Coating

Nano and microparticles of polymer(s) and drug(s) are electrostatically captured, dry, upon a stent form

Step Two

CritiFlo™: Sintering

Polymer nanoparticles fused via SCF:
No solvents or high temperatures



The final material provides a smooth, adherently laminated layer with precise control over location of drug(s)

FIGURE 2

Mechanically Effective Coating With and Without Parylene Base-coat

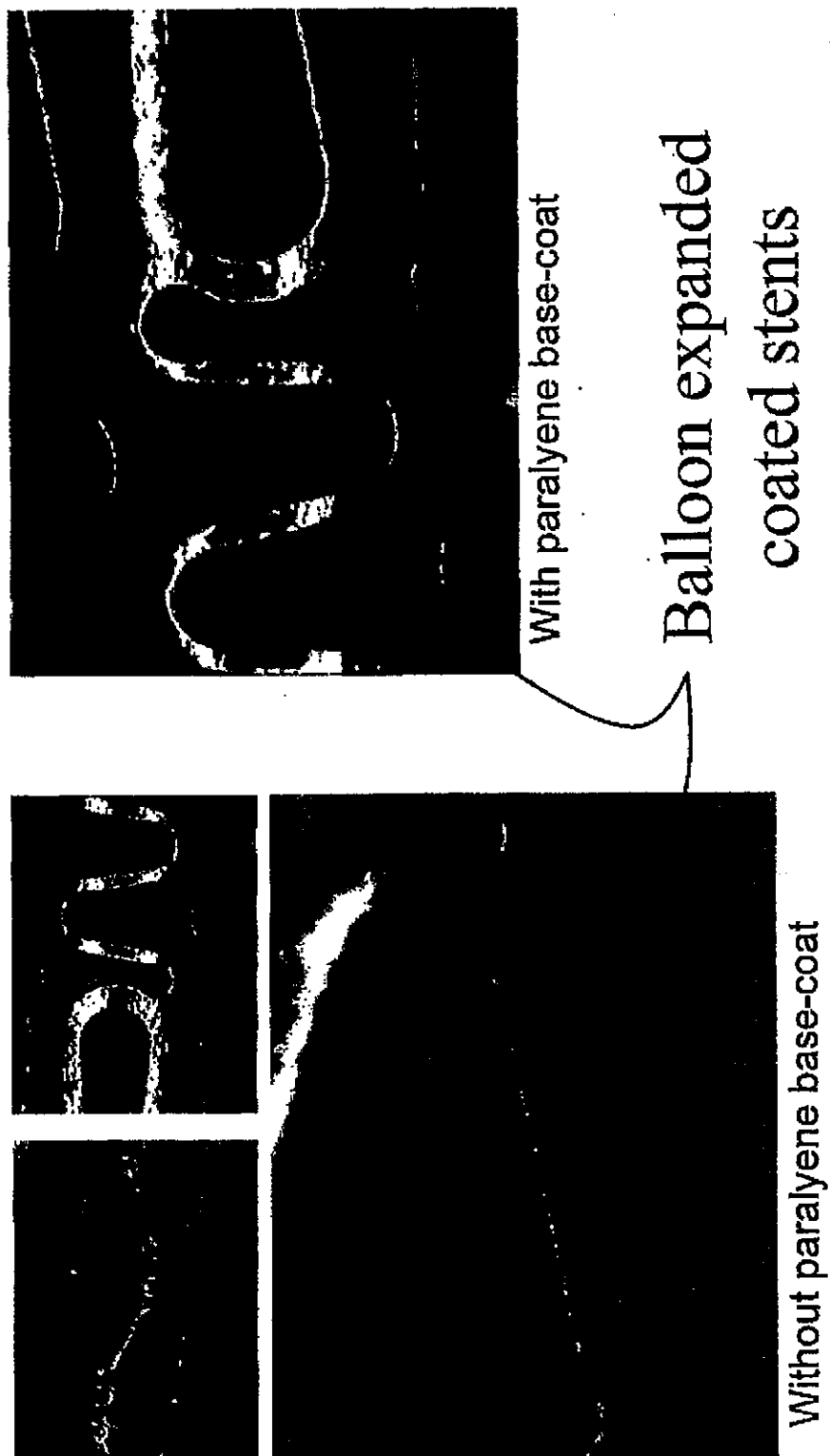


FIGURE 3

Attributes

In a Single Layer For:

- ✓ Smooth, conformal and mechanically adherent coating on different stent substrates
- ✓ Wide range of drugs (rapamycin, paclitaxel, heparin, small molecules, etc.)
- ✓ Multiple and dissimilar drugs (paclitaxel + heparin) in the same coating

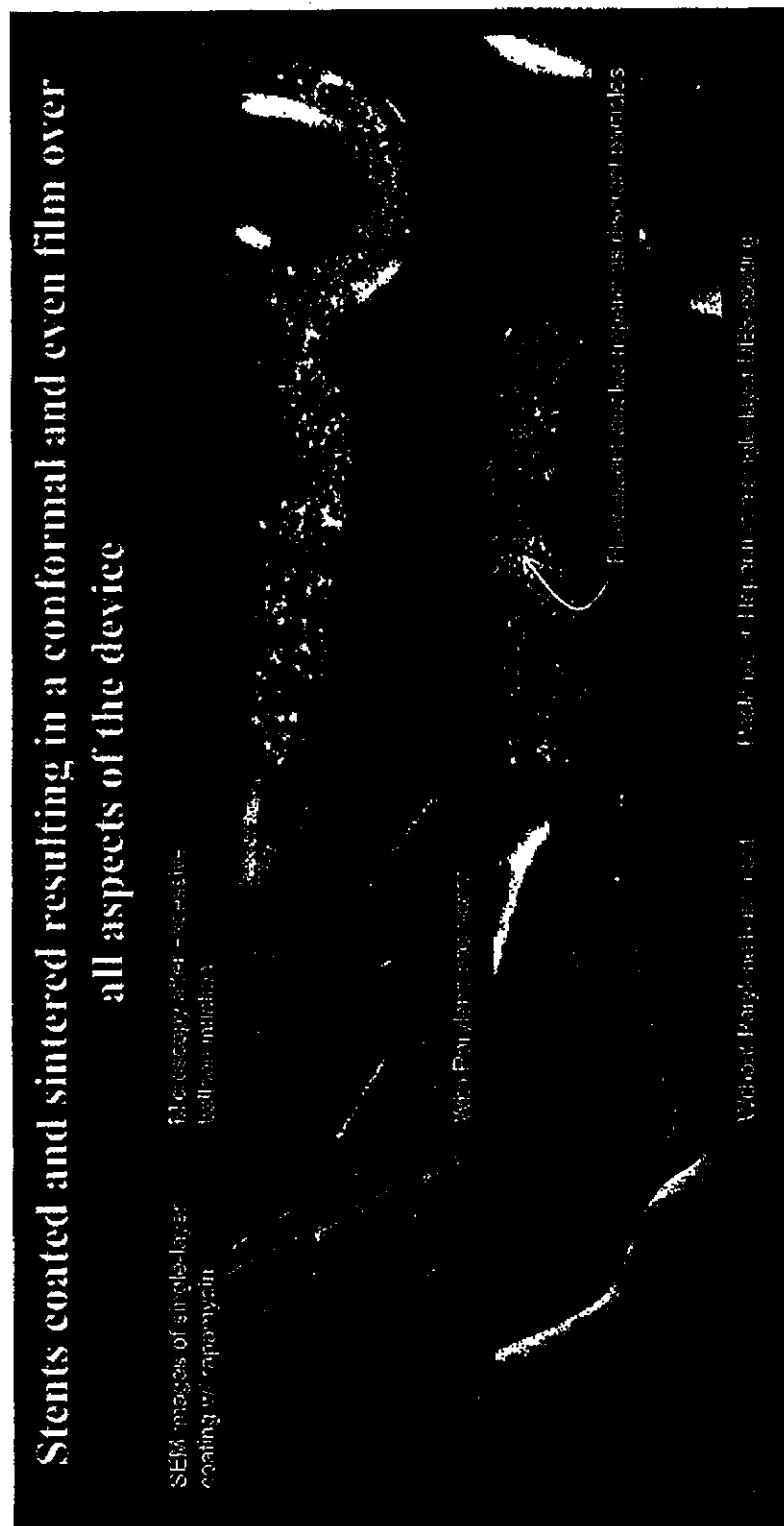


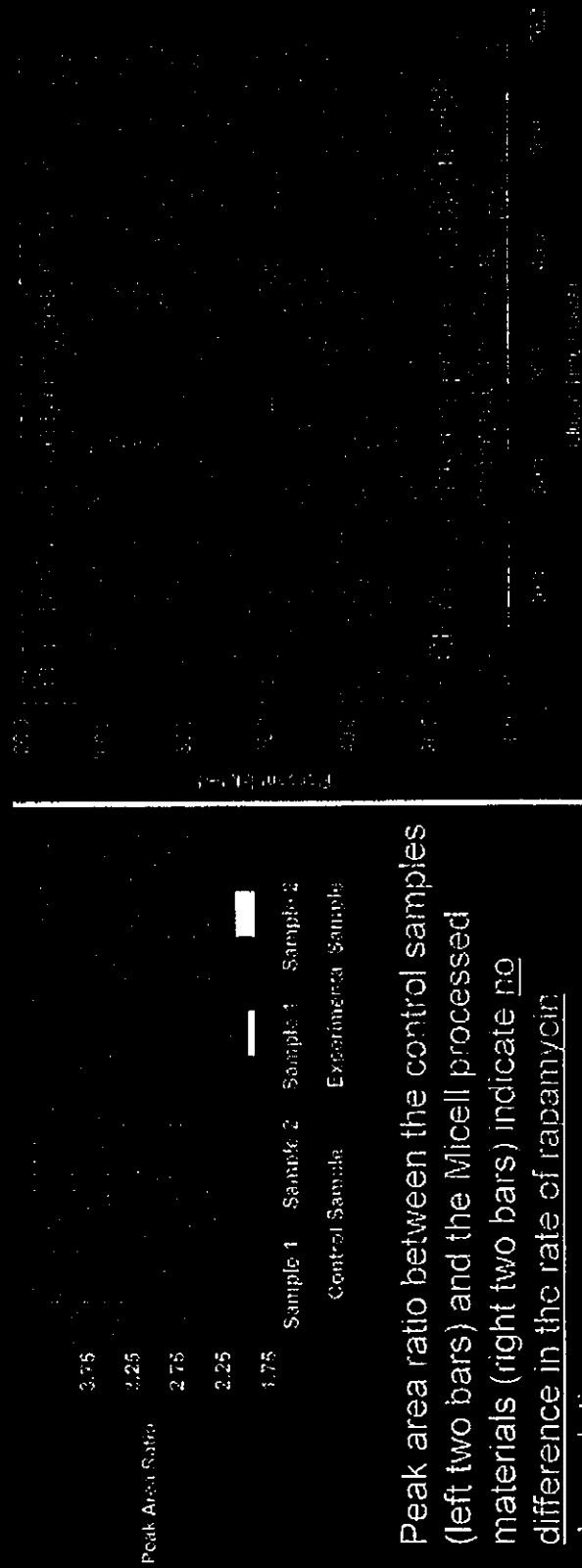
FIGURE 4

Attributes

In a Single Layer For:

- ✓ Control over drug morphology: crystalline or amorphous
- ✓ Maintain drug stability
- ✓ No effect on elution vs. commercial analogs

Rapamycin DES coating with drug maintained in crystalline morphology

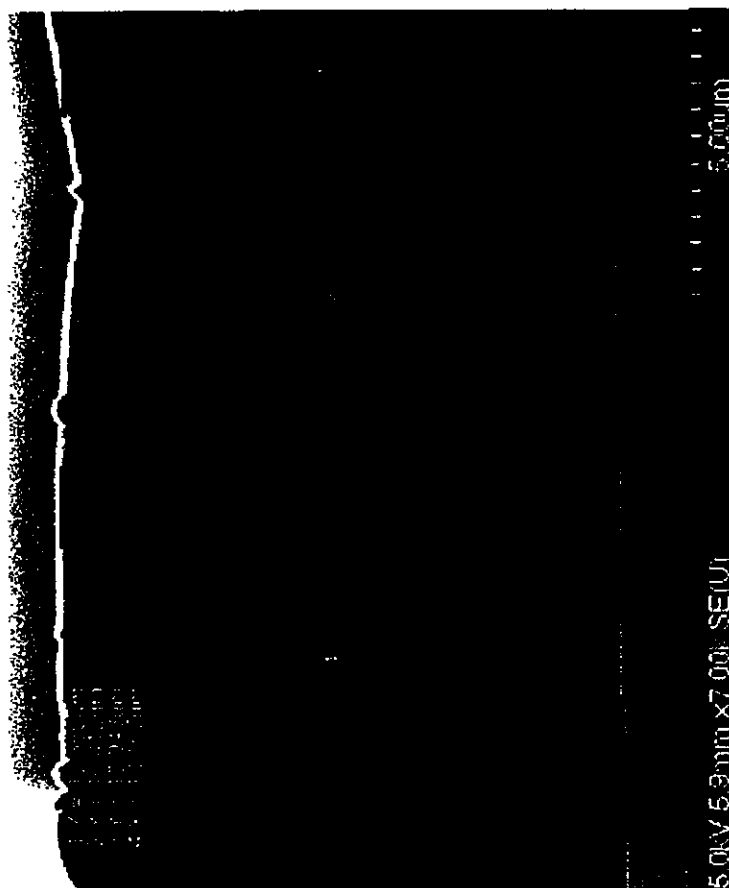


Peak area ratio between the control samples (left two bars) and the Micell processed materials (right two bars) indicate no difference in the rate of rapamycin degradation.

FIGURE 5

Attributes

Thin, conformal, defect-free coatings
at target thickness



Mean Coating Thickness:
 $10.2 \pm 0.2 \mu\text{m}$

FIGURE 6

Attributes

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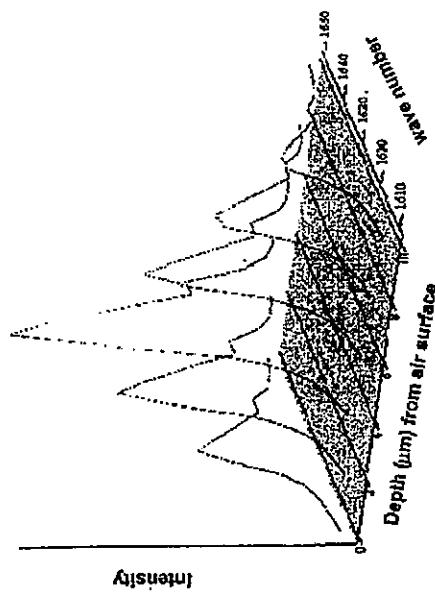
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Controlled Drug Placement

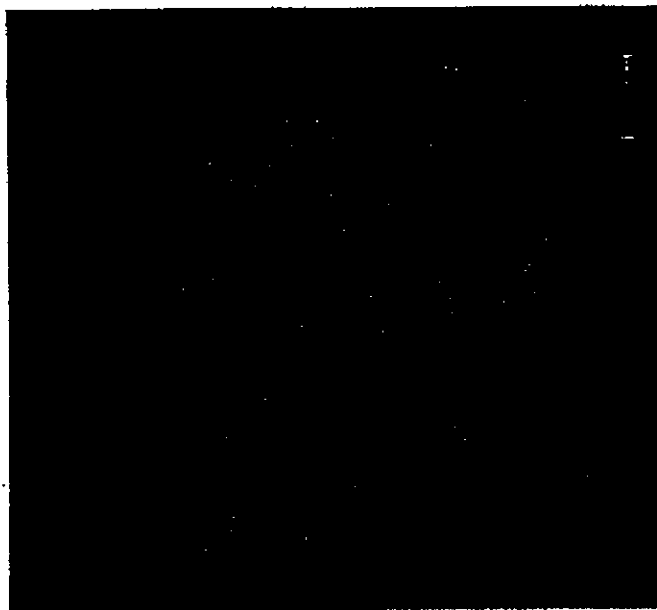
Drug loaded purposefully in the center of the 10 μ m DES coating

Drug loaded equally throughout the 10 μ m DES coating and evident in the surface

Drug peak ~1620



Confocal Raman spectra



SIMS of DES coating surface

FIGURE 7

Drug-Polymer coated coronary stent

(a) immediately after deposition,



(b) after annealing in a dense carbon dioxide environment at 40°C



FIGURE 8

Optical Microscopy of Rapamycin/PEVA/PBMA Coated Stents

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(a) Powder coated before sintering



Outside Surface



Edge Surface



Inside Surface

(b) Powder coated after sintering



Outside Surface



Edge Surface



Inside Surface

FIGURE 9

Optical Microscopy of Rapamycin/PEVA/PBMA Coated Stents

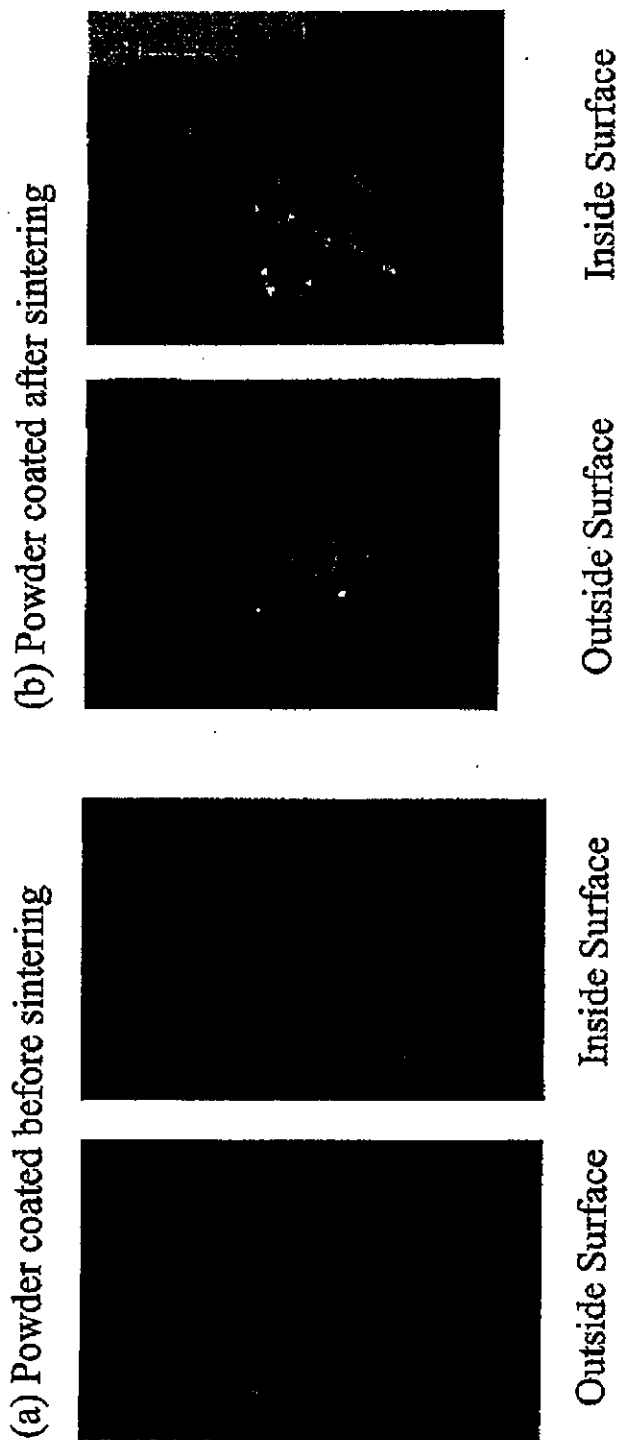


FIGURE 10

Optical Microscopy of Rapamycin/PEVA/PBMA Coated
Stents After Sintering at 100X magnification



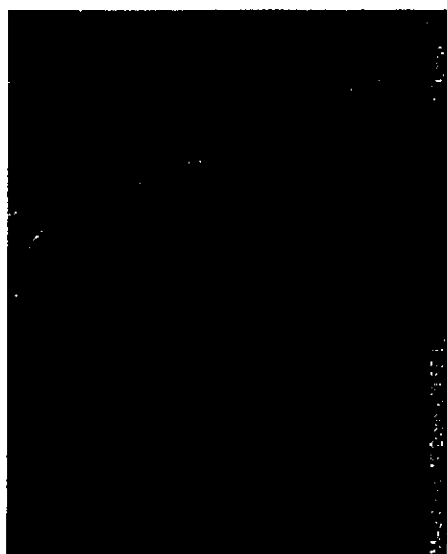
FIGURE 11

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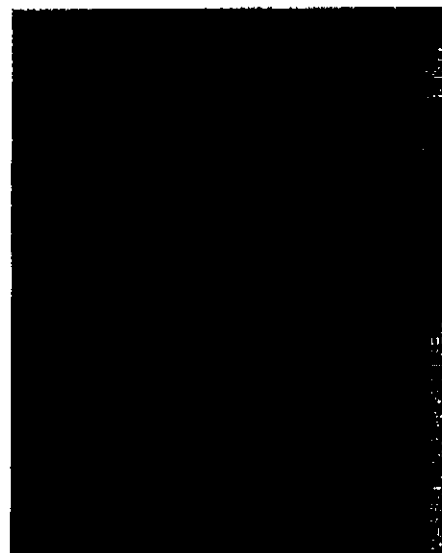
Scanning Electron Microscope Images of Rapamycin/PEVA/PBMA Coated Stents



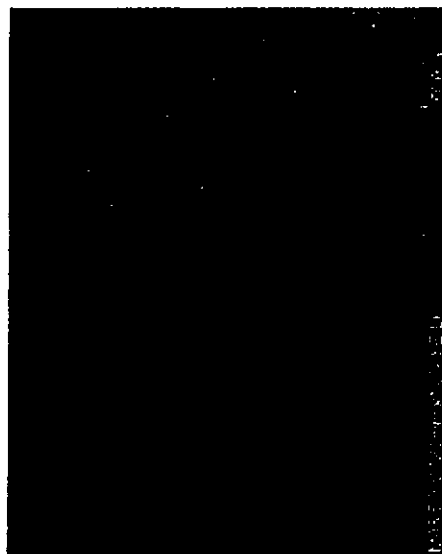
(a) x30 magnification



(b) x250 magnification



(c) x1000 magnification



(d) x3000 magnification

FIGURE 12

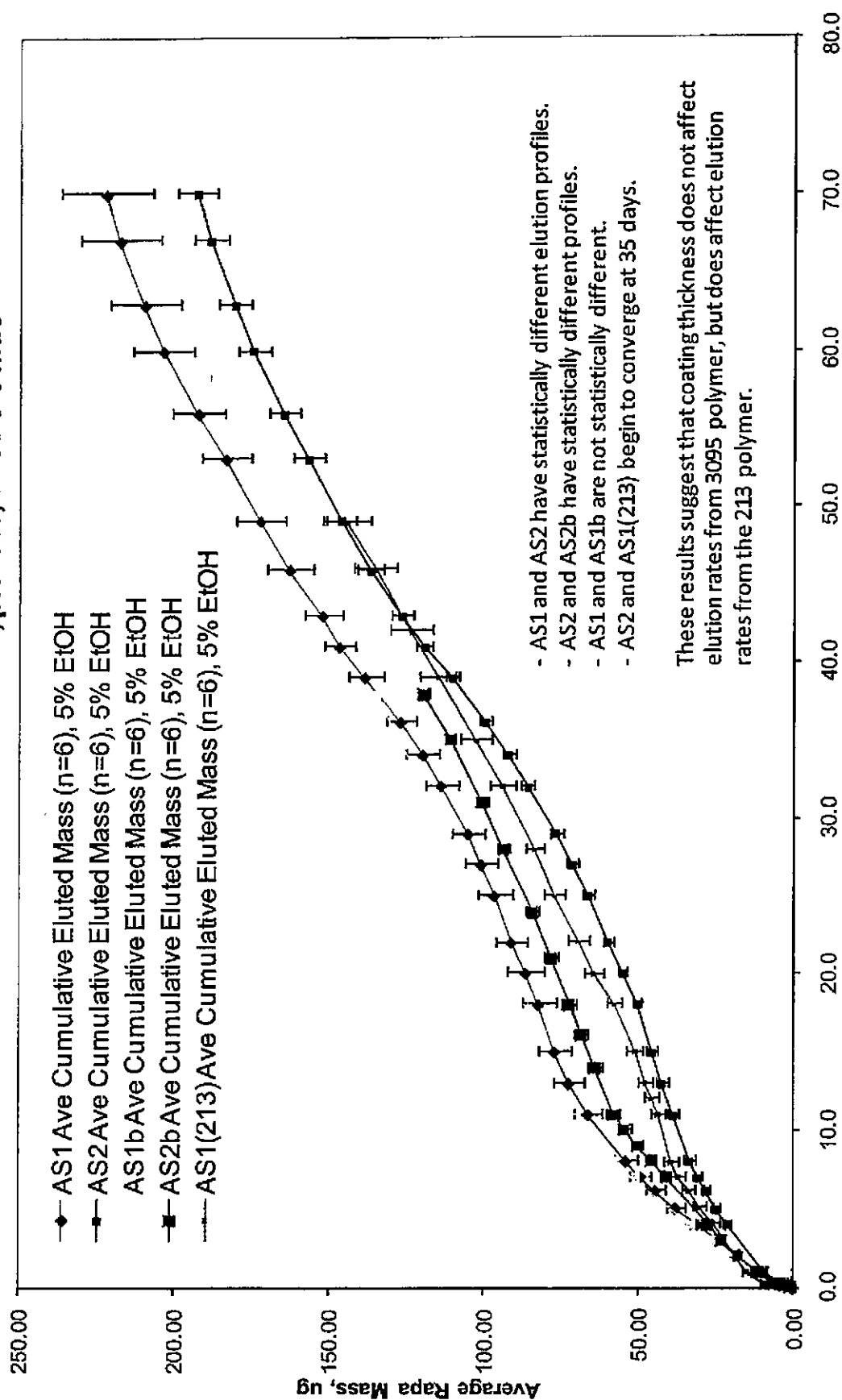
Average Coating Masses

Stent Coating	Ave. Rapamycin, ug	Ave. Polymer, ug	Ave. Total Mass, ug
AS1	175		
AS2	153	717	870
AS1(B)	224	737	961
AS1b	171	322	493
AS2b	167	380	547

FIGURE 13

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Comparison of Stent Polymer Coatings **Elution Media 5% Ethanol/Water, pH=7.4, T=37C Static**



Time, days

FIGURE 14

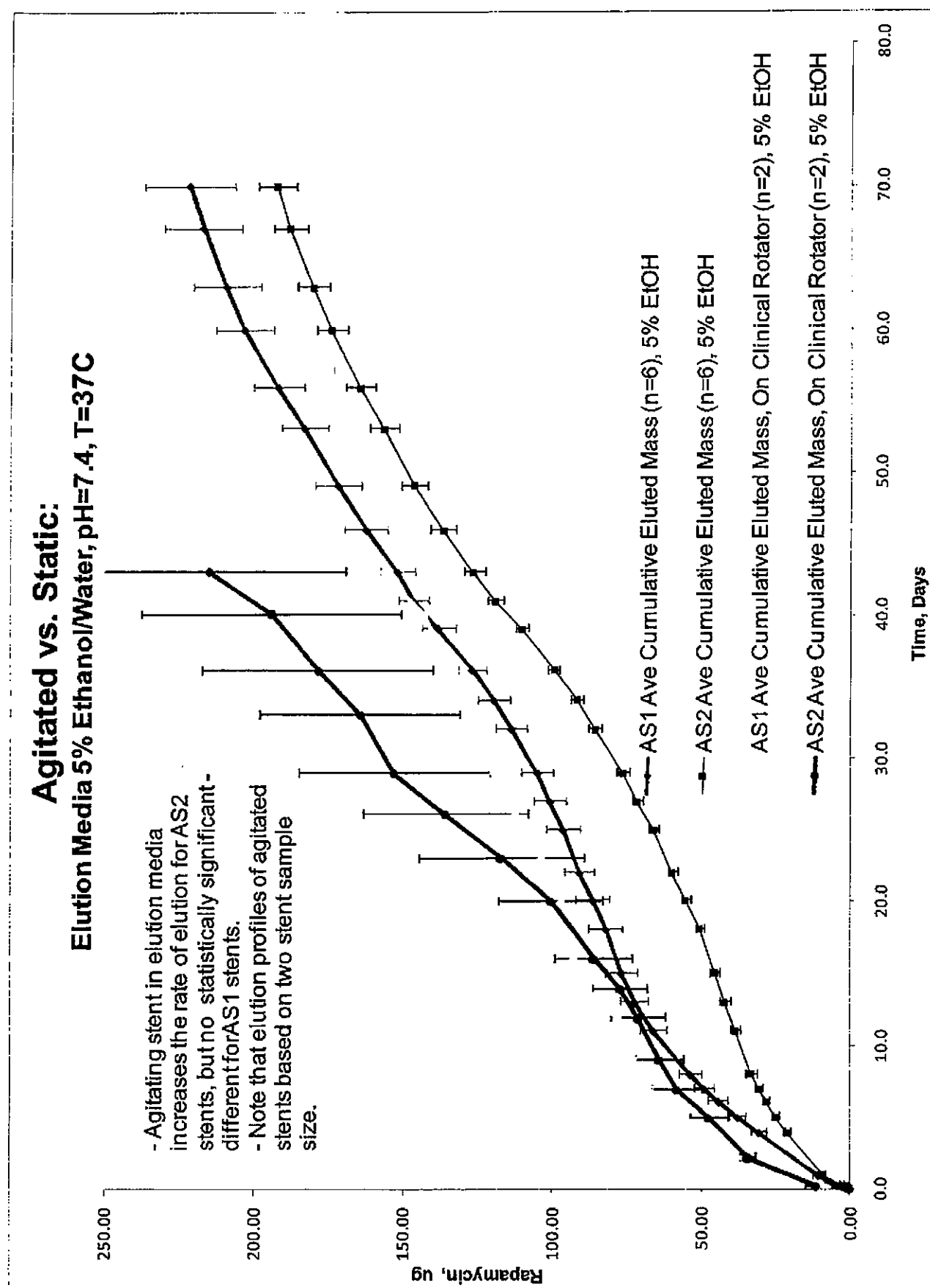


FIGURE 15

Comparison of Elution Media at pH=7.4, T=37C: 5% Ethanol/Water vs. Phosphate Buffered Saline

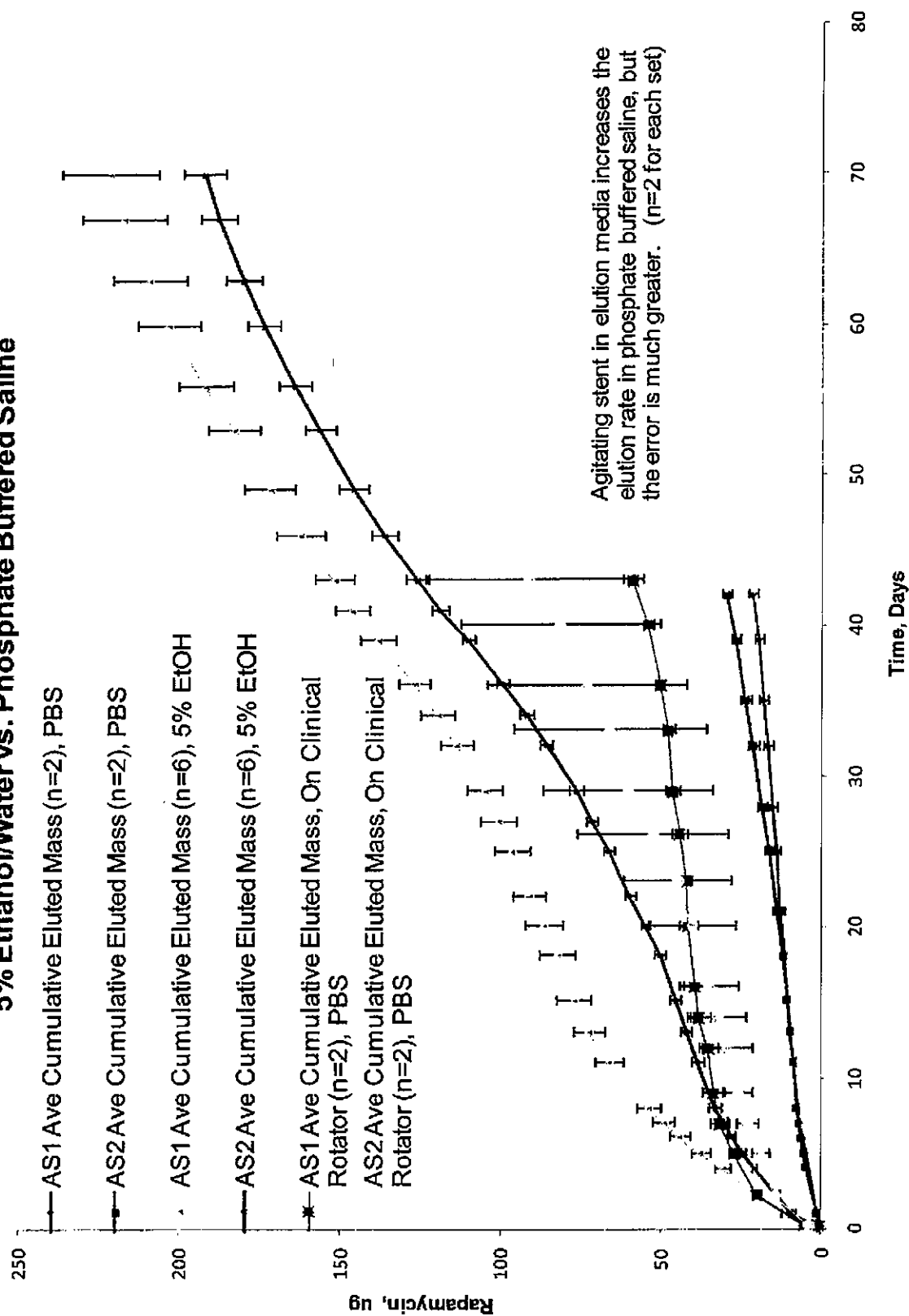


FIGURE 16