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

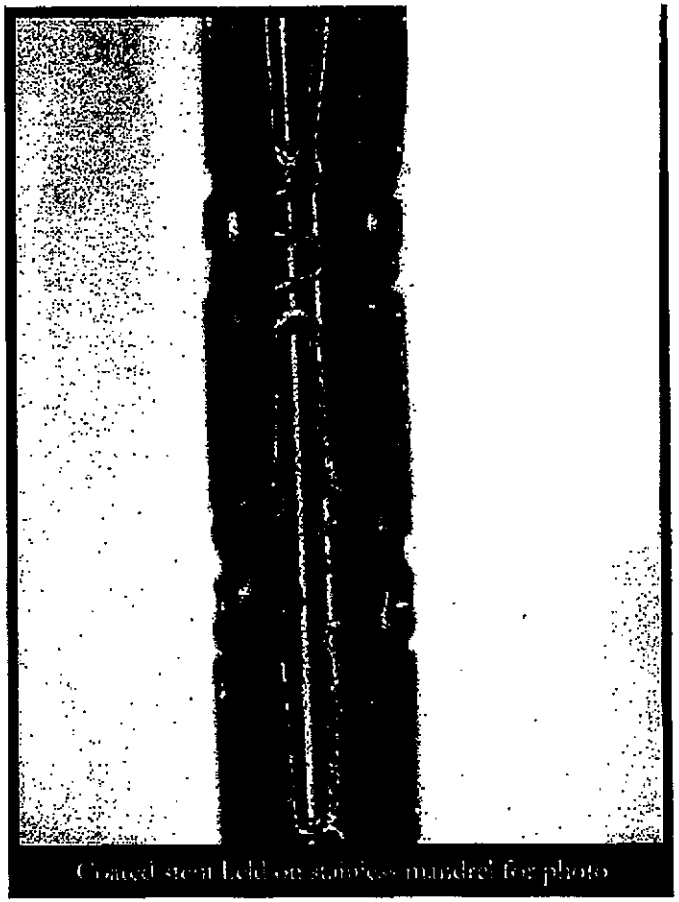


FIGURE 1

Process Technology

Step One

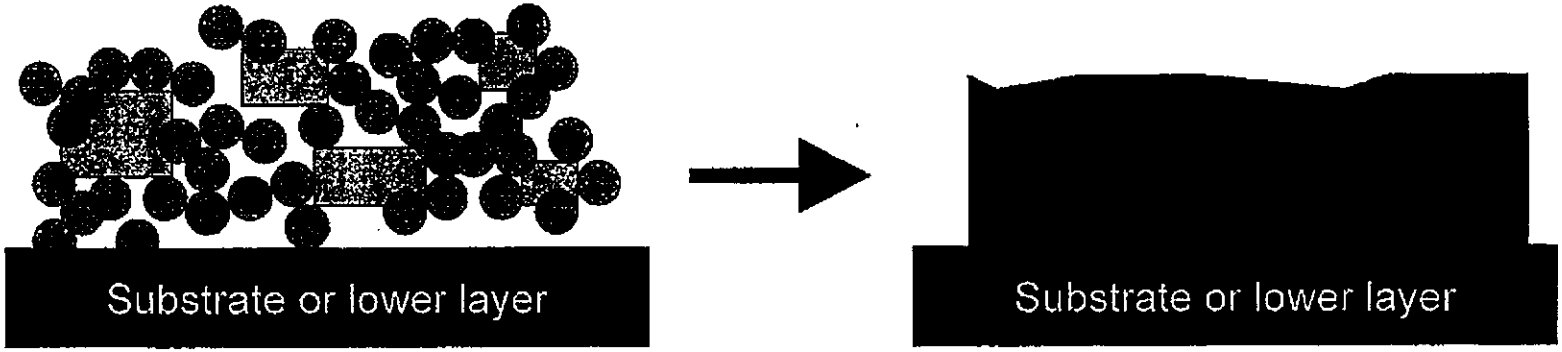
CritiCoat™: Electrostatic Coating

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

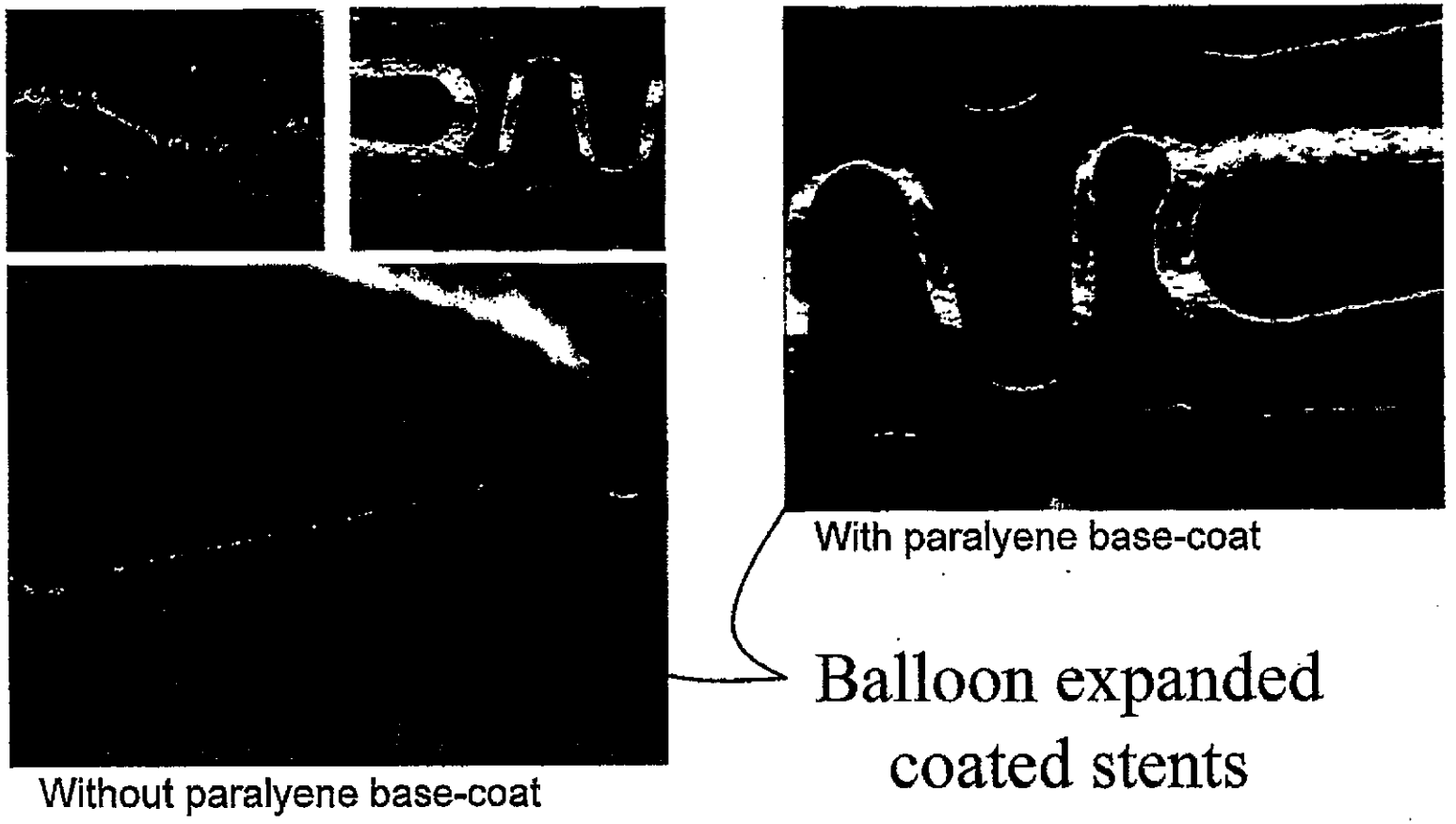


FIGURE 3

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

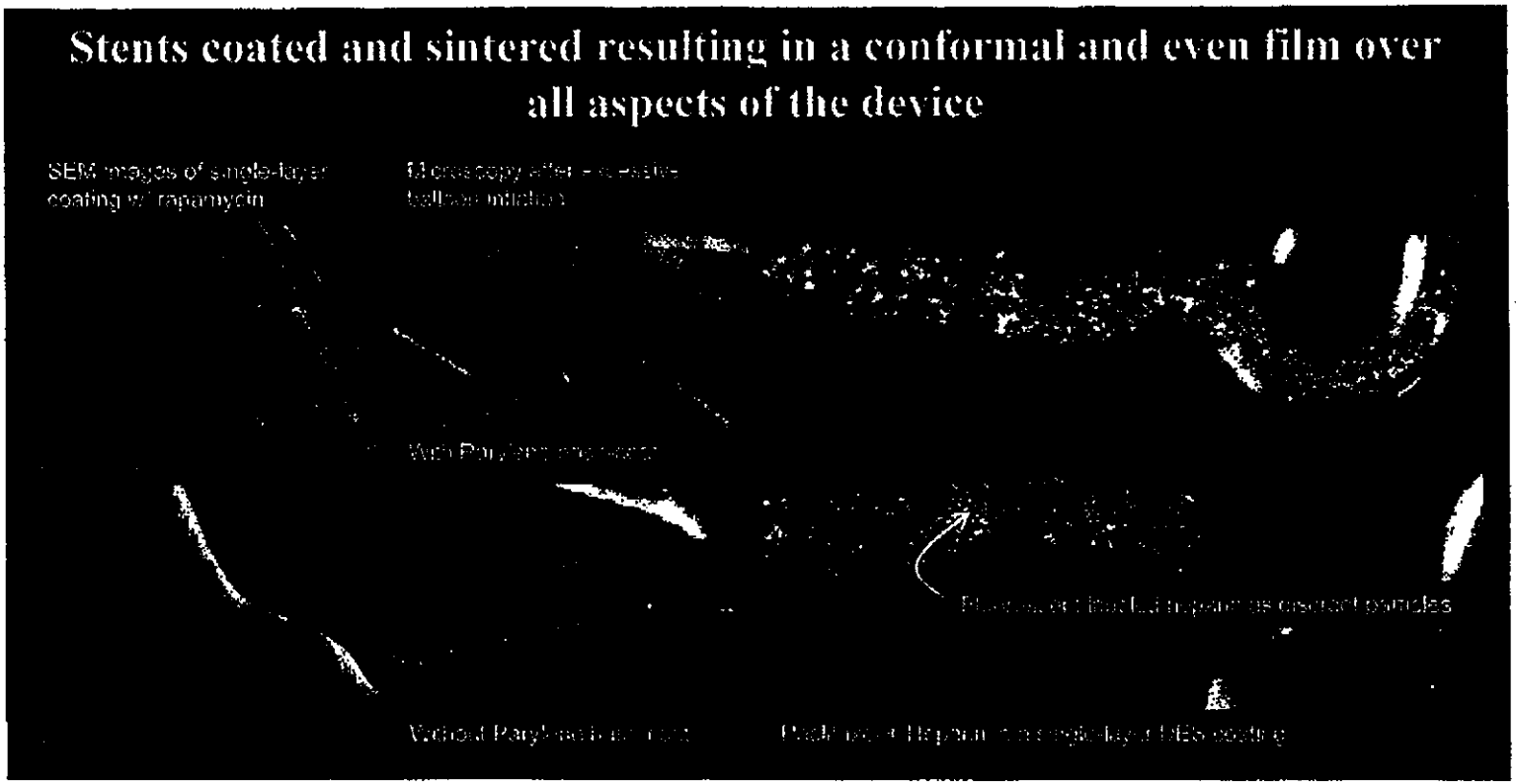


FIGURE 4

Attributes

In a Single Layer For:

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

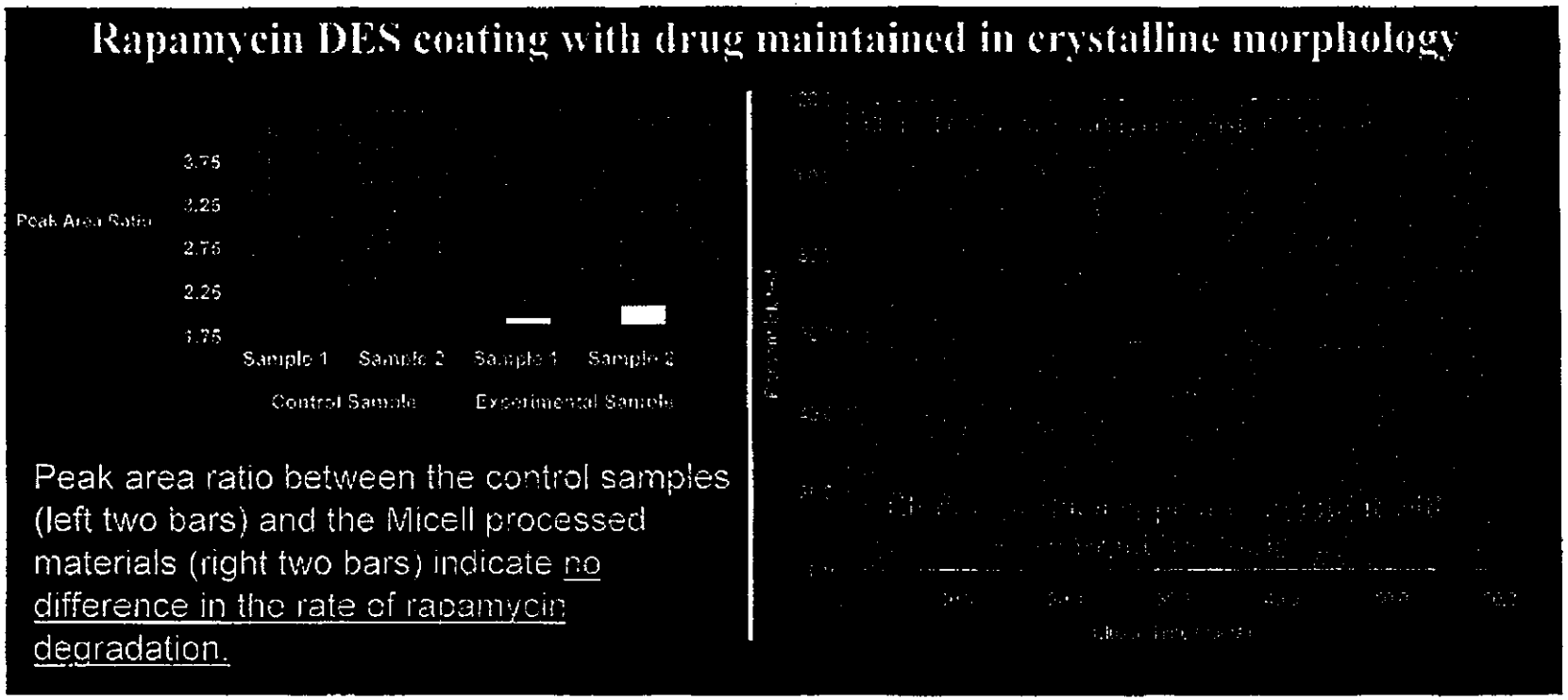
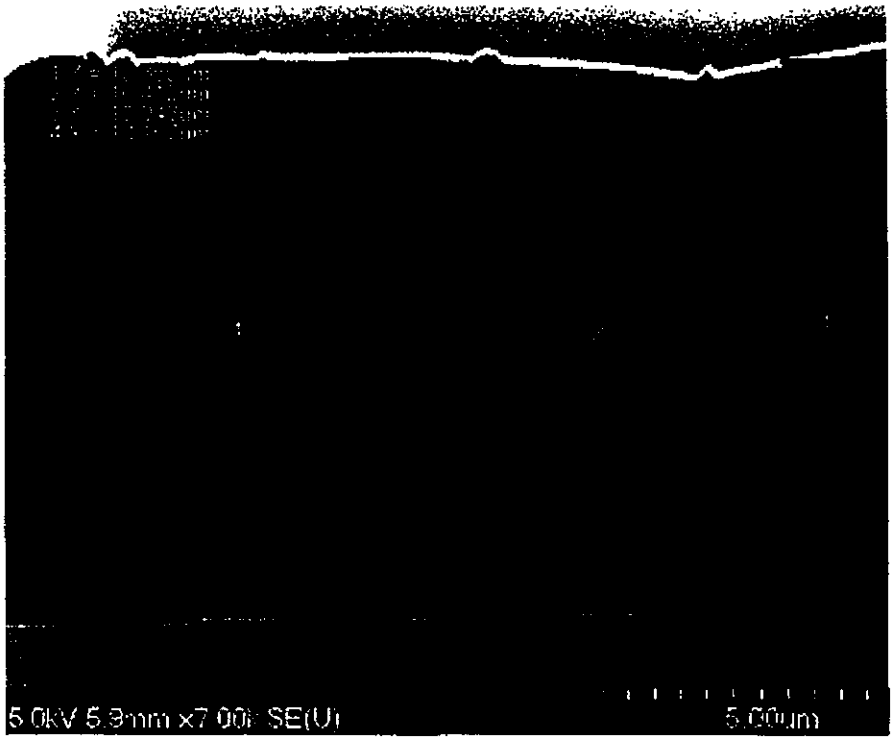


FIGURE 5

Attributes

Thin, conformal, defect-free coatings at target thickness



Mean Coating Thickness:
10.2 ± 0.2 µm

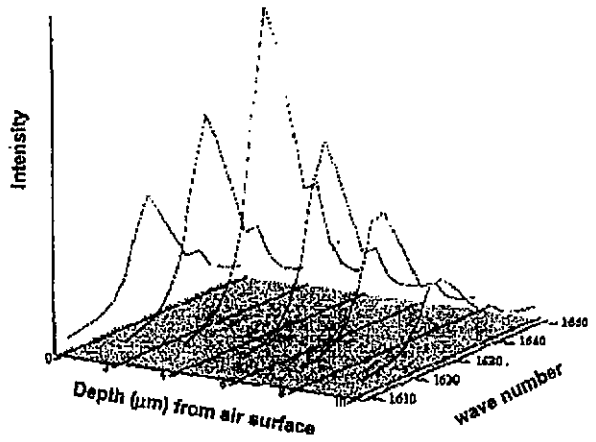
FIGURE 6

Attributes

Controlled Drug Placement

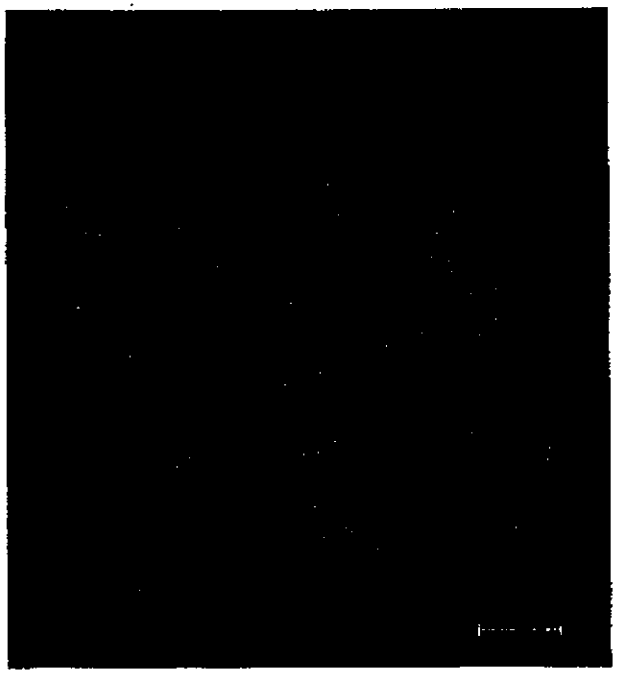
Drug loaded purposefully in the center of the 10µm DES coating

Drug peak ~1620



Confocal Raman spectra

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



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

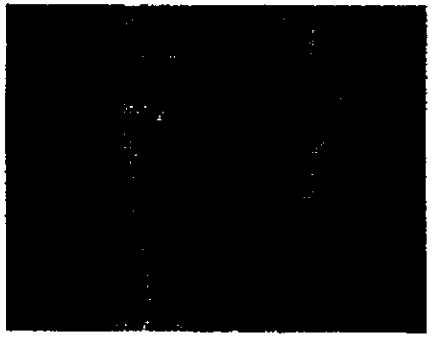
FIGURE 8

Optical Microscopy of Rapamycin/PEVA/PBMA Coated Stents

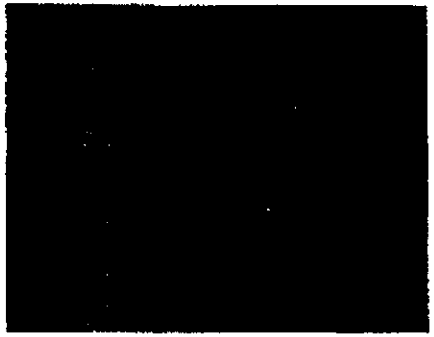
(a) Powder coated before sintering



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

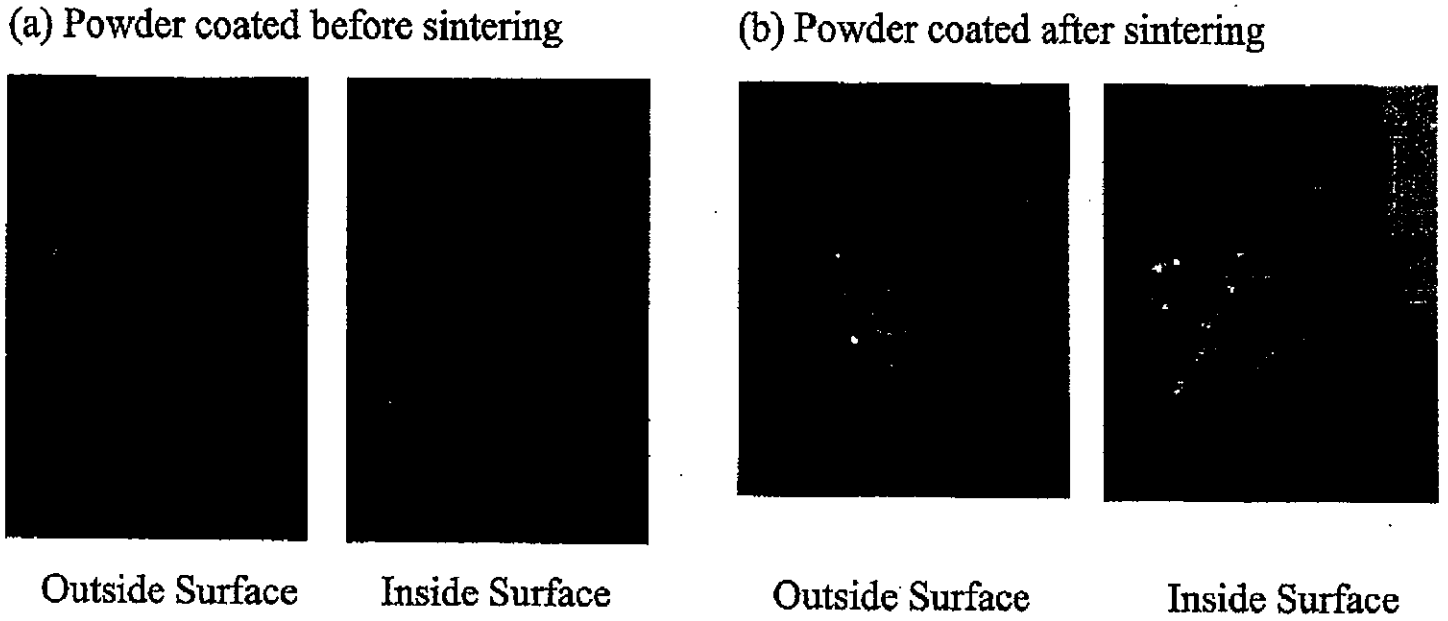


FIGURE 10

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

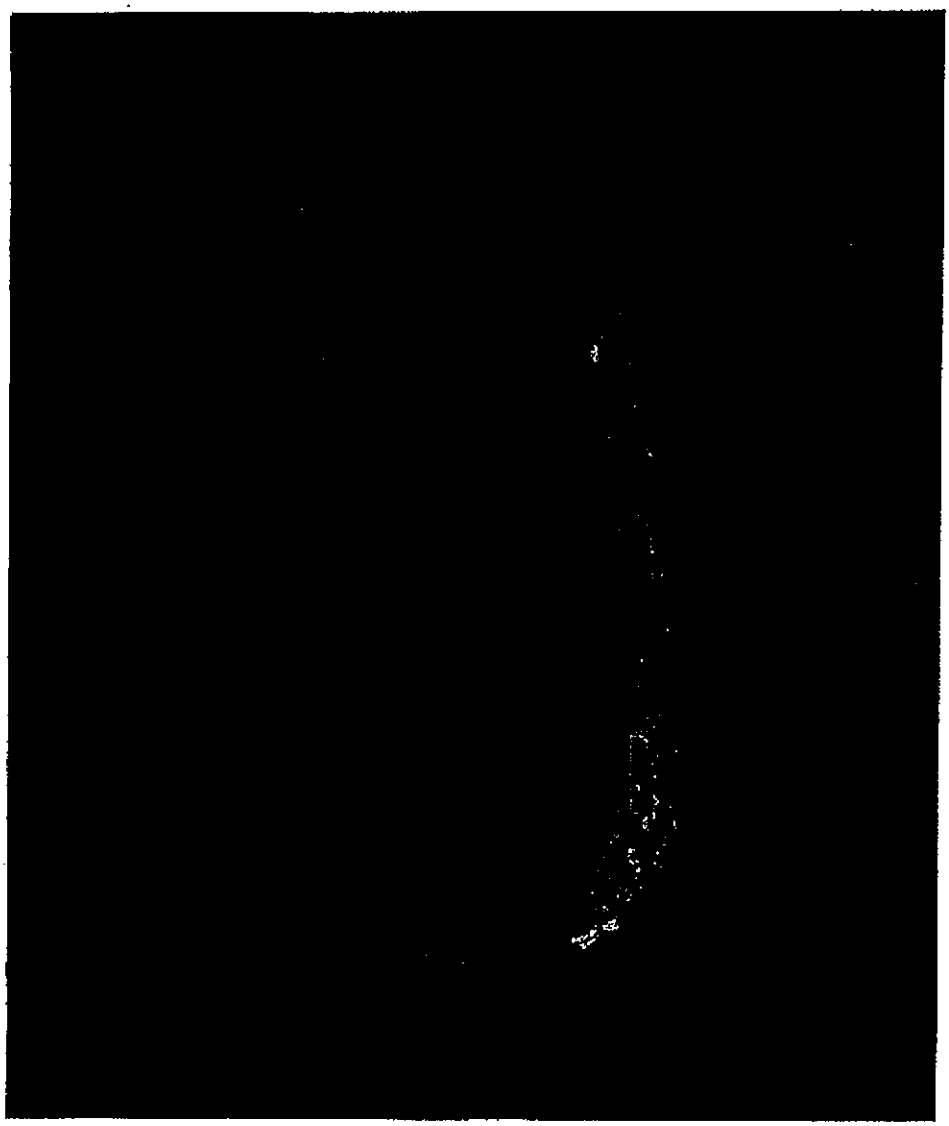
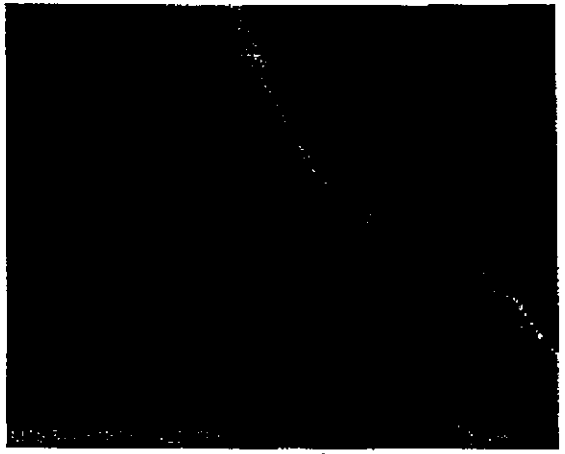


FIGURE 11

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

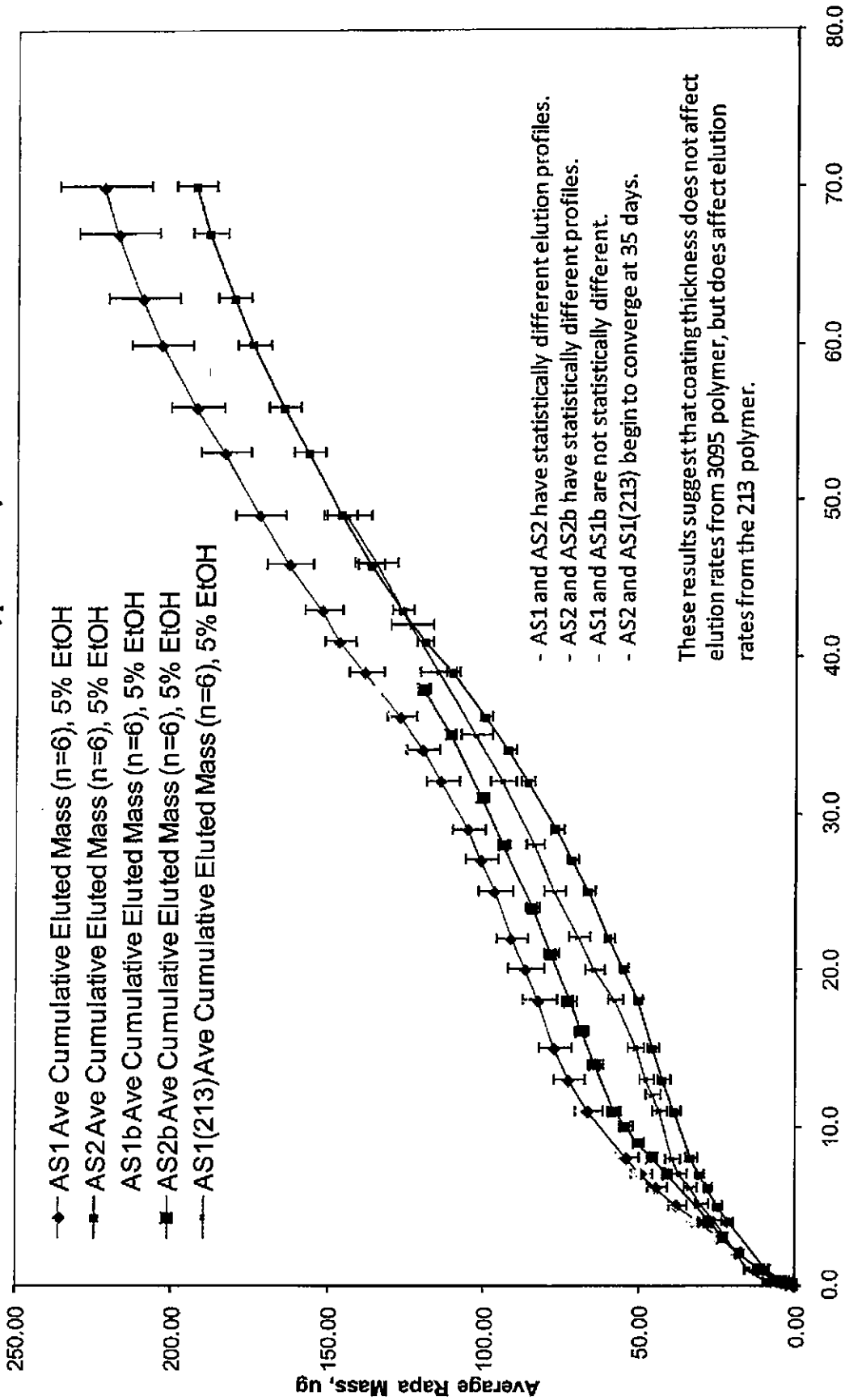

Comparison of Stent Polymer Coatings
Elution Media 5% Ethanol/Water, pH=7.4, T=37C Static
AS1 Ave Cumulative Eluted Mass (n=6), 5% EtOH
AS2 Ave Cumulative Eluted Mass (n=6), 5% EtOH
AS1b Ave Cumulative Eluted Mass (n=6), 5% EtOH
AS2b Ave Cumulative Eluted Mass (n=6), 5% EtOH
AS1(213) Ave Cumulative Eluted Mass (n=6), 5% EtOH
- AS1 and AS2 have statistically different elution profiles.
- AS2 and AS2b have statistically different profiles.
- AS1 and AS1b are not statistically different.
- AS2 and AS1(213) begin to converge at 35 days.
These results suggest that coating thickness does not affect elution rates from 3095 polymer, but does affect elution rates from the 213 polymer.
Average Rapa Mass, ug
Time, days
0.00
50.00
100.00
150.00
200.00
250.00
0.0
10.0
20.0
30.0
40.0
50.0
60.0
70.0
80.0

FIGURE 14

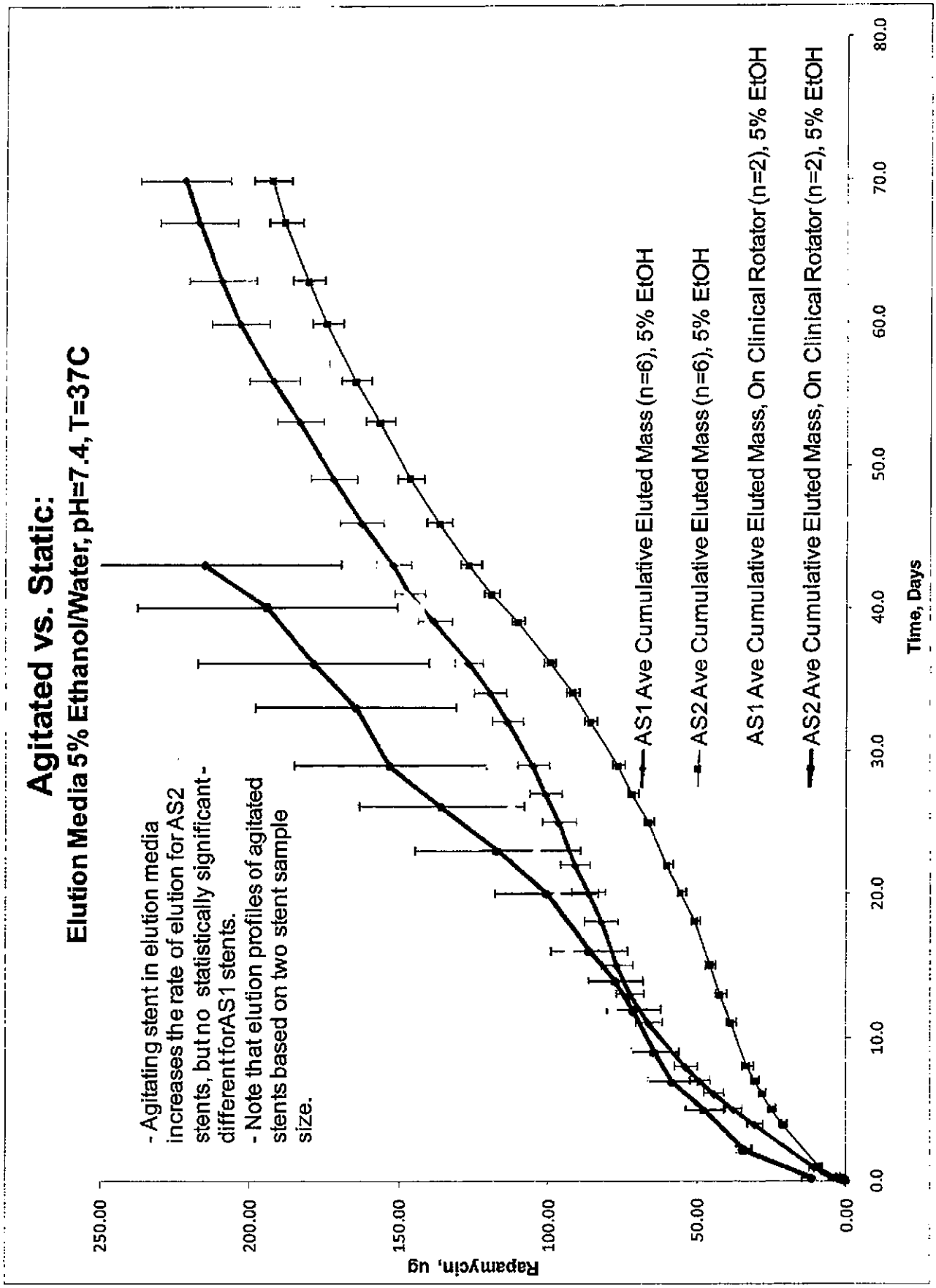

Agitated vs. Static:
Elution Media 5% Ethanol/Water, pH=7.4, T=37C
- Agitating stent in elution media increases the rate of elution for AS2 stents, but no statistically significant - different for AS1 stents.
- Note that elution profiles of agitated stents based on two stent sample size.
Rapamycin, ug
Time, Days
AS1 Ave Cumulative Eluted Mass (n=6), 5% EtOH
AS2 Ave Cumulative Eluted Mass (n=6), 5% EtOH
AS1 Ave Cumulative Eluted Mass, On Clinical Rotator (n=2), 5% EtOH
AS2 Ave Cumulative Eluted Mass, On Clinical Rotator (n=2), 5% EtOH

FIGURE 15

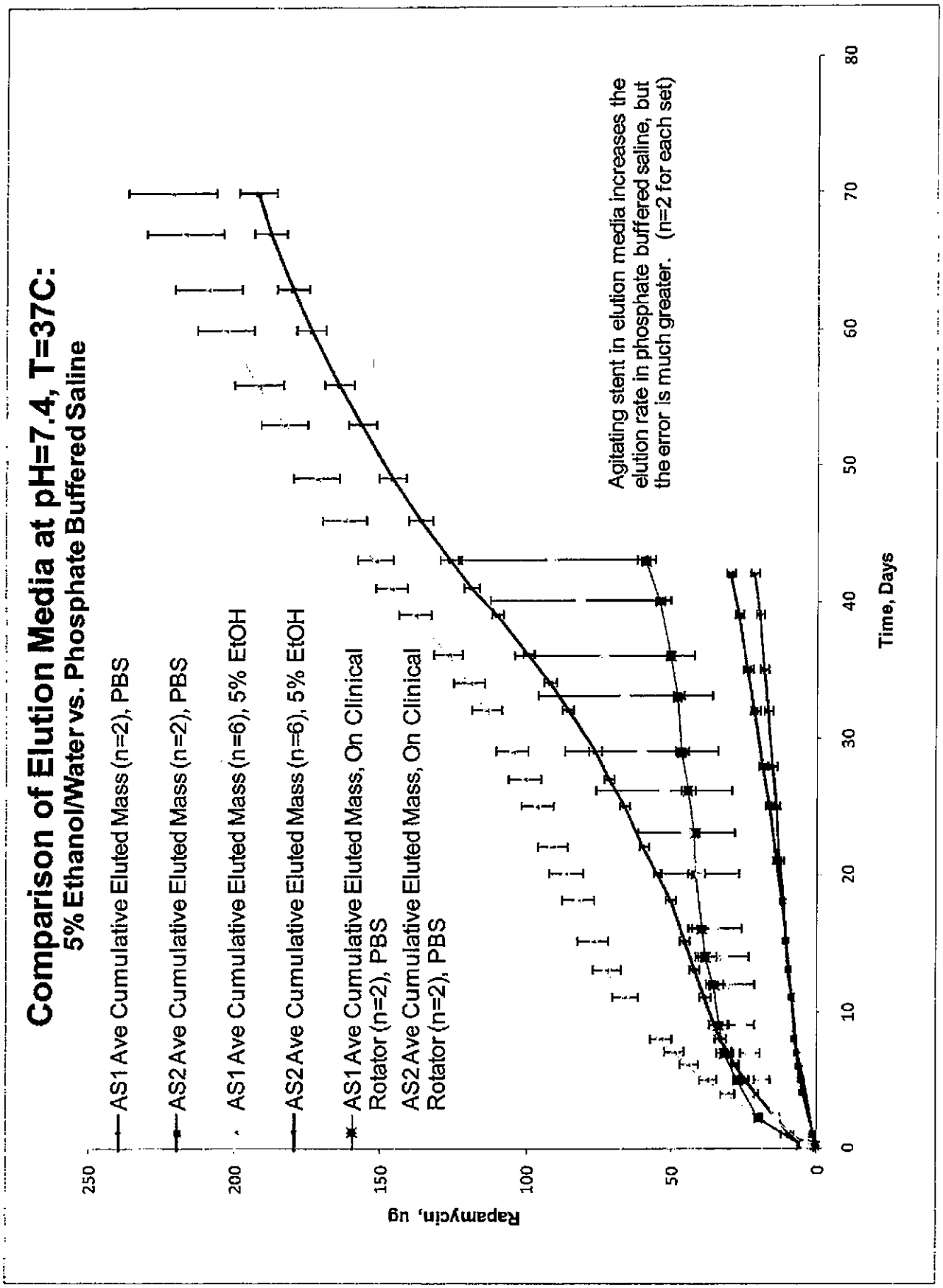

Comparison of Elution Media at pH=7.4, T=37C:
5% Ethanol/Water vs. Phosphate Buffered Saline
AS1 Ave Cumulative Eluted Mass (n=2), PBS
AS2 Ave Cumulative Eluted Mass (n=2), PBS
AS1 Ave Cumulative Eluted Mass (n=6), 5% EtOH
AS2 Ave Cumulative Eluted Mass (n=6), 5% EtOH
AS1 Ave Cumulative Eluted Mass, On Clinical Rotator (n=2), PBS
AS2 Ave Cumulative Eluted Mass, On Clinical Rotator (n=2), PBS
Agitating stent in elution media increases the elution rate in phosphate buffered saline, but the error is much greater. (n=2 for each set)
Rapamycin, ug
Time, Days
0
50
100
150
200
250
0
10
20
30
40
50
60
70
80

FIGURE 16