Exogenesis Corporation

Controlled Elution of Drugs and Other Therapeutic Compounds

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Introduction

Exogenesis Corporation is commercializing proprietary nanoscale surface modification and control technology which has application in improving the safety and performance of implantable medical devices. The Company's accelerated particle beam technology (Exogenesis Technology) is distinctly different from ion implantation, plasma and other surface treatments. The Exogenesis Technology has unique ability to produce important atomic level surface modification effects. While there are many ways to modify surfaces of materials, the Exogenesis Technology is fundamentally different and much superior for many applications.

Safe Controlled Elution of Drugs and Other Therapeutic Compounds

The Exogenesis Technology can be used for the controlled elution of drugs or therapeutic compounds such as bone morphogenic protein (BMP) from implantable medical devices. The controlled elution is achieved without i) requiring the use of a durable or biodegradable binding polymer or ii) using excessively high and potentially unsafe compound doses. Medical devices that will benefit from processing with this application of the Exogenesis Technology include drug eluting stents and numerous orthopedic implants including spinal implants.

Process Overview

The process for controlled elution includes the following:

- Drug or BMP is deposited onto the surface of the implant.
- The accelerated particle beam is applied to the outer surface of the deposited compound.
- Accelerated particle beam converts a few nanometers of the compound surface into a carbon matrix elution barrier which controls the rate of elution.
    - The accelerated particles are atoms of argon which is inert, non-toxic and non-additive.
    - The energy of the accelerated clusters of argon atoms converts the top 10 nanometers of the compound surface into a carbon matrix. Due to the unique design of the particle beam, below 10 nanometers there is no effect on the coated therapeutic compound.
    - Carbon is already in the compound being processed, it is not added by the process.
    - The process takes place in a vacuum chamber. Once the compound surface is bombarded by the accelerated particle beam, the gas atoms in the beam and the gas released from the bombarded surface are pumped away leaving a continuous carbon matrix elution barrier.
    - For longer elution, more layers of compound and particle beam can be added.

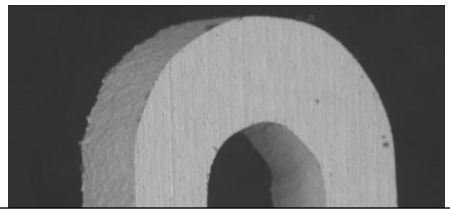
No Degradants

The Exogenesis Technology has been applied to a variety of compounds including both small molecules and proteins. There has been no observation of degradants being created by the Exogenesis Technology.

Demonstration of Elution Control

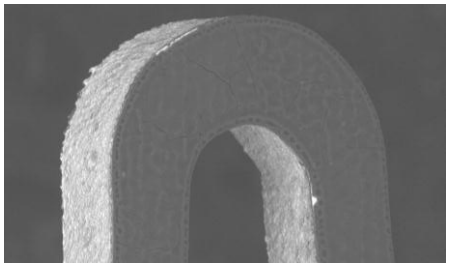
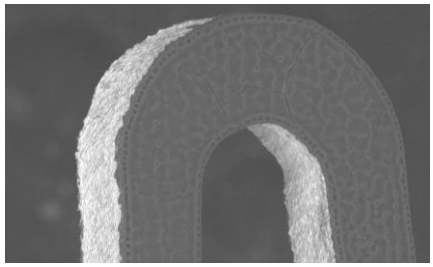
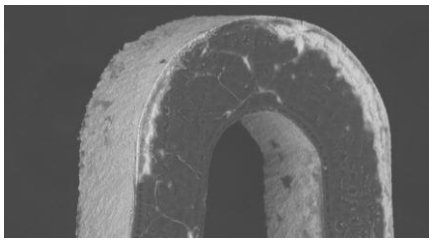
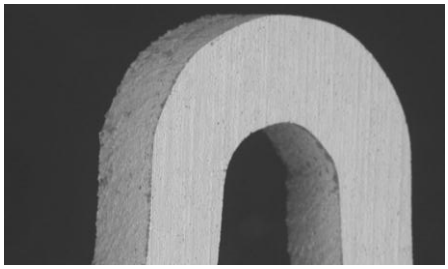
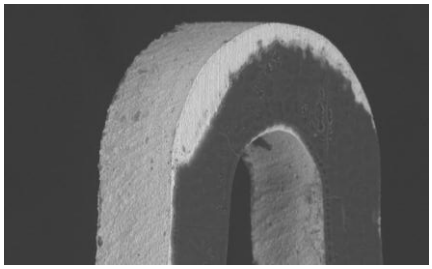
- Bare metal cobalt chrome stents were coated with approximately 50µg of Rapamycin. One half of the stents were processed with Exogenesis Technology and the others were left as controls.
- Stents were eluted in human plasma for up to 168 hours. Following removal from plasma, measurements of drug were determined by stent weight. The stents were also imaged by SEM.
- Stents that were coated with Rapamycin but not treated by the Exogenesis Technology resulted in drug being completely eluted off within 48 hours; however, stents that were treated with the Exogenesis Technology show a much slower and progressive decrease of drug over time of elution. See Figure 1 below showing SEM images of stents.
- The rate of elution was compared to historical data of commercially available Cypher drug eluting stents coated with a Rapamycin and polymer compound. Drug elution profile reveals the use of the Exogenesis Technology allows for a more controlled release of Rapamycin than without treatment and has a better release profile than Cypher for the first 7 days. See Figure 2.

FIGURE 1
SEM Images



Bare Metal Stent

Rapamycin Coating

	Control	**Processed with Beam**
0 hours		
24 hours		
48 hours		

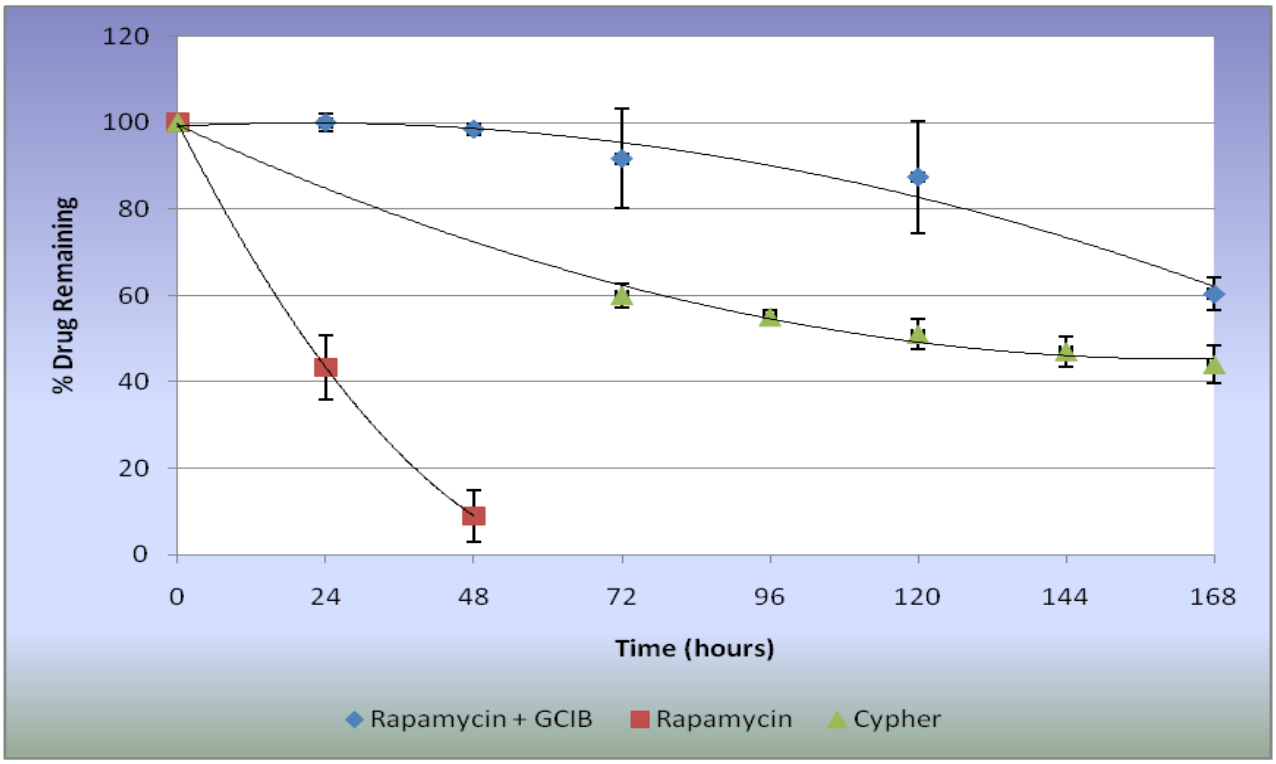


Figure 2
Elution Control with Exogenesis GCIB Technology

Efficacy with Enhanced Safety with Reduced Doses of BMP

BMP is known for its ability to stimulate bone formation, however there have been some concerns that excessive amounts of BMP can potentially lead to unintended negative side effects.

The Exogenesis Technology offers the potential to create implants containing predetermined precise doses of BMP. For example, BMP would be adhered to a spinal implant with the Exogenesis Technology. Elution of the BMP would be at a controlled release rate. Following elution, no residual would be left behind.

Any concerns would be mitigated by the use of lower doses of BMP than presently used by surgeons.

Based on Exogenesis initial research including review of the scientific literature and discussions with scientific experts who have worked extensively in the fields of BMP research indicate that nanogram to microgram doses should be sufficient to stimulate proper bone formation. In addition, in previously conducted in-vitro studies, members of the Exogenesis team have used 200ng of BMP-2 to stimulate MSCs to differentiate into osteoblasts in a scaffold system. In contrast, it is our understanding that surgeons often use anywhere from 4.2 to 12 milligrams of BMP-2 per spinal cage. Exogenesis Technology offers the ability to provide controlled, safe and efficacious elution of BMP at dramatically reduced BMP doses (i.e., a potentially 100 fold reduction in dose).