CAPSTONE EXPERIENCE 2012

β-Islet Cell Encapsulation

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Agricultural & Biological ENGINEERING

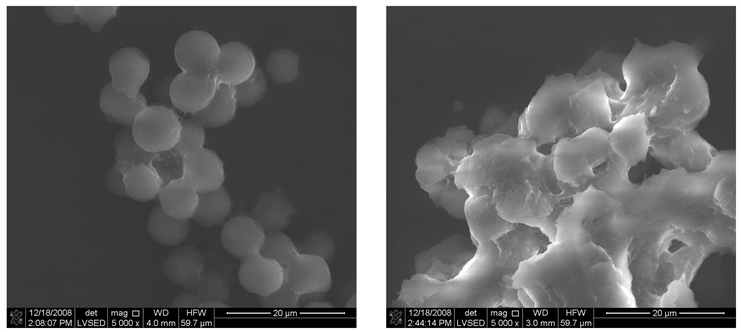
Objective: Design an automated process to encapsulate pancreatic β-islet cells in silica gel.

Background: There is currently no cure for Type I diabetes. The only treatment available is the administration of insulin injections. Xenotransplantation of encapsulated pancreatic β-islet cells provides the potential for a long-term cure for the illness; however, the process of encapsulating β-islet cells is only done as a manual, bench-scale process. There is a need for an automated process to increase the feasibility of β-islet cell transplantation as an alternative to insulin injections for Type I diabetic patients.

Benefits:
- ➢Long-term insulin independence
- ➢Simple injection procedure
- ➢Immuno-suppressants not required

Terminology:
- ➢Xenotransplantation: In this case, refers to cellular therapy via transplantation of β-islet cells from pig pancreas to humans
- ➢β-islet cells: Secrete insulin as a response to glucose levels
- ➢Encapsulation: Protect living cells in silica monomer gel (sol-gel) capsules in order to prevent destruction and immune rejection
- ➢TMOS: Tetramethylorthosilicate (silica monomer used for sol-gel)

Figure 1: *Encapsulated P19 Cells*



P19 cells are used for experimentation due to the high cost of islets

*(*Images courtesy of David Jaroch, Purdue University)*

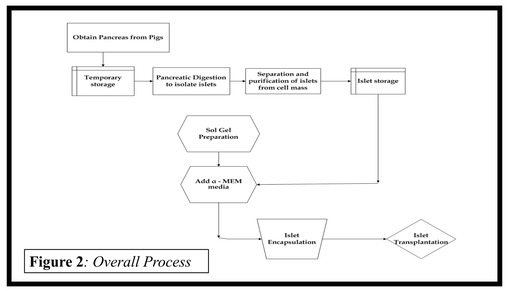


Figure 2: *Overall Process*

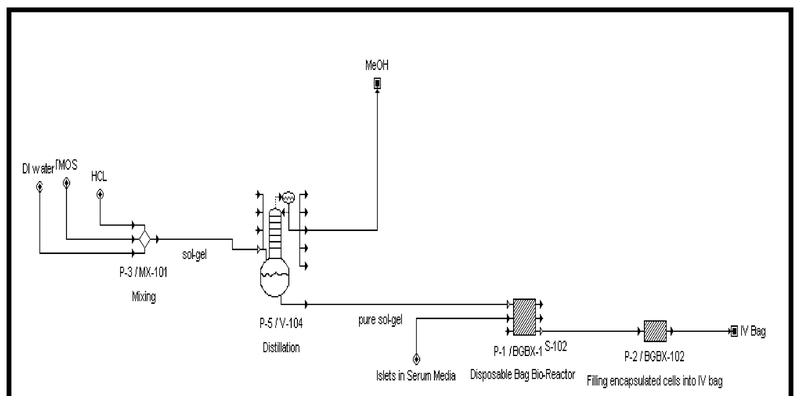


Figure 3: *Plant Layout*

Table 1:

Process Parameters
Distillation Temperature
Mixing Time
Pressure
Residence time in the Bio-Reactor

Figure 4: *Disposable Bioreactor and Shaker*

GE Wave Bioreactor

Process Flow:
- ➢Water, Hydrochloric Acid and TMOS (silicate) mixed rigorously in a vessel until solution is homogeneous
- ➢Solution transferred to distillation column for complete removal of methanol
- ➢Remaining silica solution sent to disposable bioreactor
- ➢Isolated β-islet cells in ***α***-MEM solution are filtered into reactor
- ➢Encapsulation of islets inside the bioreactor occurs
- ➢Encapsulated islets are filtered and packaged in IV bags

**All material transfer between unit operations done using pharmaceutical-grade piping systems.*

Table 2: *Economics*

Total Capital Investment	$149,069,000.00
Capital Investment	$149,069,000.00
Operating cost	$128,606,000.00
Net Operating cost	$128,606,179.00
Revenues	$157,500,000.00
Cost Basis Annual Rate	$35,000.00
Unit Production Cost	$3,674.46
Unit Production Revenue	$4,500.00
Gross Margin	18.35%
Return On Investment	19.75%
Payback Time	5.06 years
IRR (After Taxes)	10.70%
NPV (at 7.0% Interest)	$39,583,000.00

Table 3: *HACCP*

Step	Classification	Hazard	Possible Control Measure
Obtaining Pancreas From Pigs	CCP	Microbial Contamination, Damage of Organs	Maintenance of Sterile Conditions
Storage of Pancreas	CCP	Optimal Conditions for Storage	Temperature and Preservation Solution
Pancreatic Digestion, Separation and Purification	GMP	Contamination of Islet Cells, Presence of Extra-Cellular Mass	Effective Removal of Excess Tissues Sterile Conditions
Islet Storage	CCP	Viability	Strict Temperature Control
Material Handling (TMOS)	GMP	Toxic, Flammable	Keep Away from High Heat, Avoid Inhalation, and Skin & Eye Contact
Material Handling (De-Ionized water)	GMP	Purity/Sterility Level of De-Ionized Water	Heat Sterilization
Material Handling (HCl)	GMP	Caustic	Keep Away from Metals, Provide Exhaust Ventilation, Avoid Inhalation, Ingestion and Skin & Eye Contacts
Material Transfer between Unit Operations	GMP	Sterility, Fouling (material accumulation)	Use Pharmaceutical Grade Piping systems
Distillation	CCP	Optimal Pressure	Control systems, Close Monitoring
Encapsulation	GMP & CCP	Sterility and Excess Encapsulation	Control of Residence Time in Bioreactor
Plant Conditions	GMP	Sterility	Strict Adherence to Pharmaceutical GMP
Waste Disposal	GMP	Chemical Waste Flammability, Bio-Hazard	Follow Federal and State Regulations

Future Work:

Short Term (Optimize Processing Conditions)
- ➢Encapsulation with porcine islet cells
- ➢Determine optimum conditions for robustness of capsules

Long Term (Product Packaging Method)
- ➢Do-it-yourself encapsulation kit for hospitals
- ➢Intravenous Therapy Bag

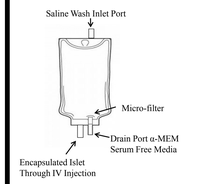


Figure 3: *Package design for transportation and use of encapsulated cells for treatment in hospitals*

As the saline wash port is opened, the drain port is opened to remove the serum free media. A micro-filter is placed at the drain port to ensure the islet cells are not lost. Once the bag is full with the encapsulated cells in saline solution, the IV injection port is connected to the patient.

Acknowledgements:
Dr. Martin Okos, Professor in Agricultural and Biological Engineering, Mentor and Technical Guidance
Dr. Jenna Rickus, Professor in Agricultural and Biological Engineering, Project Advisor
Dr. Nathan Mosier, Professor in Agricultural and Biological Engineering, Advice on Scale-Up Equipment
David Jaroch, Ph.D, Immense Guidance with Experimentation and Laboratory Procedures
Guy Telesnicki, Laboratory Technician at Birck Nanotechnology Center
Rajtarun Madangopal, Graduate Student, Biomedical Engineering, Procurement of Mimic Cells for Experimentation
Mike Green, Senior Research Scientist, VitaCyte LLC, Detailed Explanation and Insight on the Isolation of Porcine Islet Cells

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