Poly(ethylene glycol) Hydrogel Microencapsulation of Islet Cells

Michael Hunckler

Department of Aerospace and Mechanical Engineering
University of Notre Dame, Notre Dame, IN 46556

Abstract

Due to the deleterious side effects of immunosuppression necessary for pancreatic islet transplants, encapsulation of islets has been pursued as an effective treatment for the lifelong autoimmune disorder, Type 1 Diabetes. Successful encapsulation of islets requires a membrane that can (1) selectively diffuse molecules based on their size, (2) mechanically support cells within, (3) remain biotolerant by interacting with the encapsulated cells while not eliciting an immune reaction, and (4) remain biostable and not degrade. Poly(ethylene glycol) (PEG) has demonstrated many desirable structural and chemical features that make it the ideal candidate for islet encapsulation. The hydrophilic and non-ionic structure, tunable molecular weight and crosslinking density, mechanical strength, and biotolerability all enhance cellular function and viability. However, because PEG is not biostable long-term, it must be combined with other encapsulation materials to slow down the rate of degradation.

1. Introduction

1.1. The Need for Immunoisolation of Islets of Langerhans

Type 1 Diabetes is a major worldwide health crisis with an estimated population of 10-20 million worldwide that continues to grow at 3-5% per year. The financial burden of diabetes in the United States is between $14-15 billion per year [1] with an estimated worldwide cost of treatment at $465 billion per year [2]. Diabetes is an autoimmune disease that causes progressive destruction and eventual elimination of the insulin-producing pancreatic β cells that are located in the islets of Langerhans.

Diabetes is characterized by its abnormal and deficient blood glucose regulation that results in prolonged hyperglycemia leading to many complications [3]. Such complications include retinopathy with potential blindness, nephropathy and renal failure, neuropathy, risk of foot ulcers and amputations, and cardiovascular disease [3,4]. The current treatment for diabetics includes daily injections of exogenous insulin to maintain some degree of control over blood glucose levels [5]. However, inadequate or imprecise dosing can lead to daily burdens of dehydration, excessive urination, dizziness, blurred vision, and tiredness. While the blood glucose monitoring and insulin therapy continue to improve, there are still many challenges, such as dangerous episodes of hypoglycemia, that prevent truly effective diabetes treatment [6].

In response to these issues, many have looked to more physiological solutions to regain glycemic control. Transplantation of the whole pancreas or the isolated insulin-producing islets of Langerhans has been pursued for many years with limited success; although recently, success rates have been reported to be as high as 90% [7]. However, pancreas and islet transplantations have several critical limitations. First, a severe shortage of donors in the United States (~7000 donors/year) limits the number of transplantations, especially because successful islet