Thesis Portfolio

Growth Factor Release from Microporous Annealed Particle (MAP) Hydrogel to Improve Wound Healing

(Technical Report)

Scientific Discovery and the Diabetic Patient: How the Past Century Has Transformed Our Understanding of Diabetes

(STS Research Paper)

An Undergraduate Thesis

Presented to the Faculty of the School of Engineering and Applied Science
University of Virginia • Charlottesville, Virginia

In Fulfillment of the Requirements for the Degree
Bachelor of Science, School of Engineering

Regan Ellis
Fall 2019, Spring 2020

Department of Biomedical Engineering

Table of Contents

Sociotechnical Synthesis

Progress in the treatment of diabetes, a disease first documented in Ancient Egypt, remained stagnant for roughly 3,500 years (White, 2014). Until the 1920s, treatment consisted only of strict starvation diets. Millions of people today suffer from diabetes, a number that is only increasing (Margolis et al., 2011). Scientific breakthroughs, such as the discovery of insulin, in the physiology and treatment of diabetes that began in the 1920s transformed understanding of the disease and the lives of patients. These developments morphed diabetes into a chronic illness, unveiling a number of side effects and resulting conditions that had not previously characterized the acute disease (Cooper & Ainsberg, 2010). One such side effect is diabetic foot ulcers (DFUs). Up to 15% of the diabetic population suffers from DFUs, a wound with a complicated healing process and inadequate treatment options (Pop & Almquist, 2017). Over the past century, scientific breakthroughs in the diabetic research and pharmaceutical communities have provided critical understanding of the mechanisms of diabetes and consequently shaped the treatment and lives of diabetic patients. Investigating the societal impact of these developments coupled with scientific investigation into treatment options for one of the resulting conditions, DFUs, helps shine a light on the complex, modern meaning of being diabetic.

With an anticipated global diabetic population of 366 million by 2030, DFUs are a largely unmet clinical need as traditional treatments lack the biological cues that create a supportive wound healing environment (Pop & Almquist, 2017). Building upon Dr. Griffin's innovation, microporous annealed particle (MAP) gel, we are developing an optimized MAP gel formulation loaded with growth factor in order to provide a wound healing agent tailored to the chronic wound environment (Griffin & Weaver, n.d.). This optimized formulation was achieved in three parts. First, four potential formulations were developed with two weight percentages of

heparin and two concentrations of the growth factor, EGF. These four formulations were tested for efficacy in a cell migration study in order to elect the most efficient and efficacious candidate with which to move forward. The loading and release of the chosen formulation was then characterized and further understood using an ELISA. Finally, cell migration and loading and release studies were run with the formulation in non-freeze-dried MAP gel and lyophilized MAP gel to evaluate the effect of freeze-drying on product performance. The goal of these studies is to evaluate the potential for EGF-loaded MAP gel to enhance chronic wound healing over current treatment alternatives.

People have suffered from diabetes for centuries, with a diagnosis doubling as a death sentence until the mid-20th century (Cooper & Ainsberg, 2010). Delving into the discoveries and applications in diabetic research and the biopharmaceutical industry over the last century helps pinpoint the mechanisms that so dramatically changed patient outcomes and society's understanding of the disease. How did scientific breakthroughs in the understanding of diabetes affect treatment approaches and consequently shape the lives of diabetic patients over the course of the 20th century? To address this question, documentary research methods and historical case studies are implemented to investigate the development of animal-extracted insulin by Eli Lilly and recombinant human insulin by Genentech. Further, these methods help provide necessary context for the worlds of scientific research and the diabetic patient in the 20th century. Paradigm shift theory is applied to the evidence presented through these methods to evaluate how specific scientific discoveries and developments changed the perspective of the scientific, biopharmaceutical, and patient communities. From this investigation, the role of scientific breakthroughs in the shifts in biopharmaceutical approach, disease understanding, and patient quality of life is better understood. The discoveries and novel approaches used to tackle diabetes

transformed not only the immediately relevant population of diabetic patients and researchers, but the biopharmaceutical industry as a whole.

By evaluating the societal impact of treatments that arose from the discovery of insulin and developing a therapy for DFUs, a condition that emerged as diabetes became a chronic disease, simultaneously, I more fully grasped the experience of the diabetic patient and the multi-level paradigm shift sparked by the discovery of insulin. In the pre-insulin era, diabetes was accompanied by a mortality rate of 100 percent (Feudtner, 2004). As insulin treatments emerged in the 20th century, patients began to live decades beyond prior prognoses, unearthing new conditions that went along with chronic diabetes. Working firsthand to develop a treatment for one of these such chronic side effects, DFUs, broadened my perspective to the full range of effects that came with the transition of diabetes to a chronic illness, impacting patients, doctors, researchers, and manufacturers as well as the general public's understanding of the disease.

Works Cited

Cooper, T., & Ainsberg, A. (2010). *Breakthrough: Elizabeth Hughes, the Discovery of Insulin, and the Making of a Medical Miracle* (1 edition). St. Martin's Press.

Feudtner, C. (2004). *Bittersweet: Diabetes, Insulin, and the Transformation of Illness*. Univ of North Carolina Press.

Griffin, D., & Weaver, W. (n.d.). *Accelerated wound healing by injectable microporous gel scaffolds assembled from annealed building blocks | Nature Materials*. Retrieved April 5, 2019, from https://www.nature.com/articles/nmat4294

Margolis, D. J., Malay, D. S., Hoffstad, O. J., Leonard, C. E., MaCurdy, T., López de Nava, K., Tan, Y., Molina, T., & Siegel, K. L. (2011). Prevalence of diabetes, diabetic foot ulcer, and lower extremity amputation among Medicare beneficiaries, 2006 to 2008: Data Points #1. In *Data Points Publication Series*. Agency for Healthcare Research and Quality (US). http://www.ncbi.nlm.nih.gov/books/NBK63602/

Pop, M. A., & Almquist, B. D. (2017). Biomaterials: A potential pathway to healing chronic wounds? *Experimental Dermatology*, *26*(9), 760–763. https://doi.org/10.1111/exd.13290

White, J. R. (2014). A Brief History of the Development of Diabetes Medications. *Diabetes Spectrum : A Publication of the American Diabetes Association*, *27*(2), 82–86. https://doi.org/10.2337/diaspect.27.2.82