Amperometric Detection of Ultrasound-Induced Secretory Events in Potential Treatment of Type 2 Diabetes

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TYPE 2 DIABETES MELLITUS

Type 2 diabetes mellitus is a complex metabolic disease that has now reached epidemic proportions in the United States. Current pharmacological treatments are very complex and include many side effects which can result in further complications. The objective of this study is to explore a potential new treatment method that utilizes the non-invasive application of ultrasound energy to induce exocytosis of insulin from pancreatic β-cells.

METHODS

SECRETION DETECTION

- Exocytotic secretion from β-cells was detected using carbon fiber amperometry.
- Commercially available electrodes were obtained from Kation Scientific.
- AgAgCl reference electrode was held at 650 V to produce sufficient potential difference such that a current was generated when dopamine was oxidized.

EXPERIMENTAL SETUP

- Pancreatic β-cells were loaded with dopamine and plated on polyethylene wells in a modified Krebs Bicarbonate Solution (KBS).
- Planar ultrasound transducer was used to stimulate pancreatic β-cells.
  - Center frequency: 800 kHz and 1 MHz
  - Intensity: 1 W/cm2
- Transducer was positioned at the point between the transducer’s near and far field distance (dFF distance).
- Ultrasound was applied to the well at three minute intervals for up to 12 minutes either in 100 cycle bursts or short pulses of continuous ultrasound.

RESULTS

Preliminary results indicate that application of ultrasound to pancreatic β-cells leads to exocytosis. Continuous US pulses of varying durations produced sustained responses proportional to the duration of the pulse.

SIMULATIONS OF ACOUSTIC FIELDS

- Pressure measurements conducted with a lipstick hydrophone. These measurements were used to verify simulations of the acoustic fields experienced by the cells that were preformed in the modeling software, PZFLEX. The maximum pressures cells were exposed to was 5.95 x 10⁵ Pa for 800 kHz and 1 MHz respectively.

CONCLUSION AND FUTURE STUDIES

Low intensity ultrasound remains a potential treatment that directly targets one of the underlying causes of insulin deficiency in Type 2 diabetes. If proven successful, the non invasive nature of ultrasound treatment could present an alternative to current medications in the treatment of Type 2 diabetes mellitus. Future studies will look at how different parameters (intensity, pulse length) would affect the amount of insulin released. Consequently, in vivo studies will be done to further explore how the changes of certain parameters affect the pancreas wholly (in terms of potentially stimulating other endocrine cells).

POTENTIAL PRODUCT

Our potential product consists of a planar US transducer that can be strapped to the back of a patient. The parameters of US delivery are controlled by a wireless remote which also functions as a glucose monitor to allow the patient to optimize insulin release.

SPECIFIC AIDS

- Determine effectiveness of ultrasound stimulation of insulin release from pancreatic β-cells.
- Detection of exocytotic secretion from beta cells.
- Explore two different experimental parameters.
- Explore the pressure and thermal conditions cells are subjected to under experimental conditions.

ELECTRODE MANUFACTURING

1. A 7 µm carbon fiber thread was inserted into a 0.60 mm diameter capillary tube via vacuum suction.
2. Using a Sutton electrode puller, the threaded capillary tubes were pulled in half to create the taper around the carbon fiber.
3. The tapered end of the electrode was sealed with epoxy to prevent electron leakage and reduce noise during experimentation.
4. The open end of the capillary tube was filled with 3 M KCl, which acted as an electrical connection between the carbon fiber and wire.
5. AgAgCl wire attached to a connector pin was then inserted into the open end. Epoxy and shrink tube were used to seal the back end.
6. As seen in Figure 3, the house made electrodes recorded an accurate reading of a known signal in a KCl solution.

PREVALENCE OF TYPE 2 DIABETES

- In 2012, 27.85 million Americans were diagnosed with type 2 diabetes.
- 2010 to 2012 saw the emergence of 3 million cases of diabetes.
- Diabetes remains the 7th leading cause of deaths in the United States.

COST OF TYPE 2 DIABETES

- In patients diagnosed with type 2 diabetes at age 25-44, the lifetime cost of medical treatment is $124,700 and $130,800 for men and women respectively.