INTRODUCTION

Traumatic brain injuries (TBI) are a major cause of death and disability worldwide, especially in children and young adults. In the United States, the mortality rate is estimated to be 21% thirty days after a TBI [1]. Brain trauma occurs as a result of focal impact upon the head, which produces alterations in cerebral blood flow and pressure within the skull. These changes lead to a variety of negative symptoms, including: repeated nausea or vomiting, convulsions or seizures, slurred speech, weakness or numbness in the arms and legs, dilated eye pupils, etc. [1].

One method that has been utilized to treat traumatic brain injuries are chronic electrode implants. These implants can be surgically implanted in the site of local brain damage to reduce brain swelling and inflammation. Electrode implants can be coated with anti-inflammatory drug-loaded polymers. Through controlled time-release mechanisms, the drug dosage and release rate can be controlled, again with the goal of reducing brain inflammation and stabilizing the neural interface.

A current issue with electrode implants lies in the cellular reactivity of the brain to the implantation of an electrode [2]. Magnesium electrodes are of high interest in the exploration of chronic electrode implantation research, because of their known biodegradable characteristics from literature. Magnesium alloys are non-toxic, have low density, and have a high strength to weight ratio [3]. Magnesium also has a natural ability to biodegrade due to corrosion when placed in aqueous substances [3], which is of interest in the field of drug delivery research. This corrosion process could potentially be used to increase drug delivery by increasing the amount of drug-loaded polymer degradation. The corrosion occurs as the magnesium is oxidized in aqueous solution. The oxidation process releases electrons which can directly act on drug-loaded polymer to increase the amount of polymer degradation, and thus the amount of drug released.

A novel idea which will be further tested and discussed involves the direct coating of a magnesium electrode with a conducting polymer, PEDOT/graphene oxide, loaded with the anti-inflammatory drug dexamethasone. These magnesium electrodes will be tested in vitro through electrochemical testing, and released drug will be measured in solution. The electrodes will also be tested with varying levels of exposed bare magnesium, through the process of passive diffusion. This test will determine the effect of increased corrosion on drug release.

OBJECTIVE

The objective of this study is two-fold. The first objective is to prove that dexamethasone release from the magnesium electrodes is controllable and replicable. The second objective is to test the effect on drug release of varying the level of exposed uncoated magnesium to aqueous solution.

Results for both tests will be quantified through the analytical technique of absorption spectroscopy.

HYPOTHESIS/SUCCESS CRITERIA

The study will be deemed successful if, by graphical analysis, regular peak absorbance values are observed for the electrically-powered release. For the passive diffusion study, my hypothesis is that increasing the amount of uncoated magnesium exposure will increase the amount of drug released, due to the increased amount of magnesium corrosion. The goal is to obtain six consistent release profiles for each test, the electrically-powered release and the passive diffusion release.

METHODS

Both tests in the study were conducted in vitro. The electrically-powered release was conducted with a three-electrode system. The magnesium electrode functioned as the working electrode, a platinum electrode functioned as the counter electrode, and a silver chloride electrode functioned as the reference electrode. Current flowed from the working electrode to the counter electrode, and current was measured relative to the reference electrode. The three-electrode system was suspended in a solution of phosphate-buffered saline (PBS). Electric current was passed through the system via repeated chronoamperometry, which allowed the stepping of an applied potential to measure current as a function of time. The repeating chronoamperometry method involved 10 continuous cycles of stepping the voltage from 0 to 0.5 volts. The potential was stepped once every 200 seconds, to model in vivo conditions where the electrode releases drug in a time-released mechanism. After each repeating chronoamperometry run, 100 µL of the PBS solution was removed and tested via absorption spectroscopy. Absorption spectroscopy allows the quantification of drug release, as a generated beam of radiation is directed at the sample, and the intensity of absorbed radiation is measured. To analyze the 100 µL sample, the 100 µL of solution was pipetted into a 96-well plate and then measured utilizing a computer system that ran the absorption spectroscopy test. The returned absorption values were compared to literature values. As high absorption values correspond to high radiation absorbed by the sample, high absorption values correspond to more drug present in the sample. After measuring the absorbance over a time interval of 1200 seconds, the results were plotted, absorbance values versus time in solution in seconds, and observed graphically.

For the passive diffusion, a 12-well plate set-up was utilized. Two types of magnesium electrodes were tested: electrodes with uncoated magnesium exposed to PBS in addition to the coated portion of the electrode, and electrodes with only the coated portion of the electrode exposed, with no uncoated magnesium exposure. Six of each electrode was placed in the bottom of separate wells, and 2 mL of PBS was
pipetted into each well. Diffusion periods were equally spaced at 100 seconds for 1000 seconds, and after each diffusion period, 100 µL of solution was removed and tested through absorption spectroscopy. Results were again plotted absorbance values versus time in solution in seconds.

RESULTS

Plotted results from each test are shown below. One electrode is shown in the electrically-powered release figure, and two electrodes are shown in the diffusion release figure.

Figure 1. Absorbance values (measured at 242 nm) for the powered drug release over a time interval of 1200 seconds. Peak absorbance values were observed at the 200, 400, 600, 800, and 1000-second marks.

The electrically-powered release shows 5 release cycles every 200 seconds. Peak absorbance values were 0.108, 0.088, 0.076, 0.077, and 0.079 at 200, 400, 600, 800, and 1000 seconds, respectively. The release profile has an initial spike at 200 seconds and then begins to flatten out at 600 seconds.

Figure 2. Absorbance values (measured at 242 nm) for the passive diffusion release over a time interval of 1200 seconds. Exposing uncoated magnesium to aqueous solution produced additional dexamethasone release from 200 to 600 seconds.

The diffusion release profile shows that the electrode with additional uncoated magnesium exposure produced higher absorbance values than the electrode without uncoated magnesium exposure. This increase in absorption occurs from the initial diffusion up to around 700 seconds, when the results begin to overlap.

DISCUSSION

The study can be deemed successful because the graphical results for the electrically-powered release show a controlled, predictable time-release pattern. The diffusion release graph also matches the hypothesis that having additional uncoated magnesium exposure in solution increases the amount of drug release.

The initial spike in the electrically-powered drug release shows that most of the drug is released with an initial step in applied potential, as expected. At around 600 seconds, the release begins to flatten, which makes sense because only a limited amount of drug is loaded onto the electrode, so the spike in release will grow smaller over time. The increase in absorption values for the diffusion release graph are also logical, as most of the corrosion that influences drug release occurs in the first 600 seconds of submersion in PBS. Eventually, even if the magnesium continues to corrode, there is no longer drug remaining in the polymer, so that explains the overlap in absorption values on the plot.

In the short term, more successful electrically-powered release and diffusion trials with the magnesium electrodes need to be completed to verify the results. The biggest limitation involves cracking the drug-loaded polymer coatings, which can happen from bumping or scratching the electrode. This limitation can be resolved by carrying out the experimentation carefully, and regularly checking the coating before removing solution for absorption spectroscopy testing. Overall, the study shows promise and magnesium corrosion looks to be a potentially effective method for driving drug release.

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REFERENCES

