Electrosprayed Minocycline-loaded PLGA Microparticles for the Treatment of Glioblastoma

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Background
Around 12,340 patients in the US are diagnosed with glioblastoma multiforme (GBM) yearly, and despite the current treatment options, such as chemotherapy, radiotherapy, surgical resection, or a combination of them, the median survival is only about 15 months after initial diagnosis. Minocycline, a tetracycline antibiotic, has shown to inhibit U87 glioblastoma cell death and inhibit angiogenesis, or the creation of new blood vessels as is often needed by the tumor to grow. The utilization of biomaterials such as poly lactic-co-glycolic acid (PLGA) can better sustain the release and bioactivity of loaded drugs. The use of polyethylene glycol (PEG), a hydrophilic polymer, may improve the encapsulation of minocycline into the PLGA microparticles, given its hydrophilic nature. Electrospraying may be a promising method to fabricate drug loaded PLGA microparticles with high drug loading and loading efficiency. Therefore, the objective of this project was to develop electrosprayed minocycline-loaded PLGA microparticles for the treatment of GBM.

Methods
Minocycline-loaded PLGA microparticles were fabricated through electrospraying utilizing an 18 cm needle-tip to glass plate distance, 0.9 ml/hr flowrate, and 14 kV voltage. The solution consisted of 1 ml of chloroform as the solvent and 70 mg of PLGA as the polymer with different minocycline amounts and with or without polyethylene glycol (PEG). The amount of drug loaded into the microparticles was determined by dissolving the microparticles in 1 mL of dimethylsulfoxide and then measuring the absorbance of minocycline at 350 nm. Release kinetics studies were performed by placing the microparticles in phosphate-buffered saline and reading minocycline absorbance of the supernatant at various timepoint. Scanning Electron Microscopy (SEM) was used to determine size and morphology of the minocycline-loaded PLGA microparticles.

Results
The amount of drug loading and loading efficiency increased with the addition of PEG (3.23 ± 0.29 vs. 4.02 ± 0.34 and 49.40 ± 4.49 vs. 64.30 ± 5.47%, respectively) and the utilization of higher amount of drug (4.02 ± 0.34 vs. 9.93 ± 0.64 and 64.30 ± 5.47 vs. 70.76 ± 4.57%, respectively). The release kinetics study demonstrated that the different microparticles experienced a burst release within the first hour (67-80%). The microparticles were spherical in shape and ranged between 4-11 μm in size. The addition of PEG resulted in the aggregation of the microparticles, as observed in SEM imaging.

Conclusions
This study demonstrated that electrosprayed minocycline-loaded PLGA microparticles can be successfully fabricated with high drug loading and loading efficiency and have a spherical shape within the micron size range. PEG was able to increase drug loading of the lipophilic drug by increasing the solubility of the drug in the polymer/chloroform solution. However, the utilization of PEG affected the collection of the particles and therefore, further optimization of the electrospraying parameters needs to be done to improve the collection of non-aggregated microparticles. In addition, given their burst release of minocycline, the microparticles may need to be further encapsulated in a scaffold or depot to prolong their release of drug.