3D PRINTED DRUG DELIVERY IMPLANTS FOR INNER EAR THERAPIES

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Background: In the UK, greater than 11 million people suffer from hearing loss. With hearing loss affecting a large proportion of the population, the cost of treatment for the healthcare industry is large. Due to the complicated structure of the inner ear, drug delivery can be quite difficult, with ear drops being used as a common method of treatment. A prolonged method of delivery would be more ideal for patient compliance and ease of use. 3D printing (3DP), in particular Fused Deposition Modelling (FDM), could be a viable method of fabrication, as it provides the potential to create personalized devices catering to the winding anatomy of the inner ear. Previous studies of implantable devices using FDM have also proved the potential for prolonged drug delivery. In this study, we explore the incorporation of drug into Thermoplastic Polyurethane (TPU) using Hot-Melt Extrusion (HME), followed by 3DP of implants for the ear of varying designs.

Methods: Drug loaded TPU filaments were created using HME, by combining TPU pellets along with Levofloxacin drug powder. Filaments were created with 3 drug loads of 0.25%, 0.5% and 1% w/w Levofloxacin. These drug loaded filaments were then used to print 3 different designs of implants for inner ear therapy. Designs were created on Free online, computer aided design (CAD) software (TinkerCAD, USA). Designs were downloaded onto Ultimaker Cura software for pre-processing of designs prior to being sent to Ultimaker 2 FDM Printer (Ultimaker B.V., Geldermalsen, Netherlands) for printing. Designs were printed in triplicate for all further characterization methods. Implants were analysed using Fourier Transform infrared (FT-IR) spectroscopy and Scanning Electron Microscopy (SEM). Drug release studies were also carried out by placing the implants in 5 mL of phosphate buffered solution (PBS) and placing in an incubator at 37°C. Implants were removed, sample of solution taken and implants placed into a fresh solution of 5 mL of PBS. Sampling was done at 1, 2, 4, 24, 48, 72 and 96 hrs. Extracted solutions were analysed under UV-Vis Spectroscopy at a wavelength of 292 nm.

Results: Drug loaded filaments were successfully created using HME, with Levofloxacin Powder well distributed throughout the filament. FDM was able to printer successfully 3 designs of implantable ear devices at 0.25, 0.5 and 1% of drug concentrations. Surface morphology analysed using SEM showed that there were no visible drug aggregates present, indicating that Levofloxacin was well distributed within the TPU matrix. FTIR analysis of Levofloxacin loaded filaments showed no clear peak shift which is due to the low levels of drug added to the polymer. Release studies indicated an initial burst release of drug in the first 2 hrs of release followed by a period of sustained release.

Conclusions: This proof of concept study has been able to show that implants for the inner ear can be successfully printed using FDM. Drug loaded filaments were created with homogenous dispersion of drug within the filament. 3 different designs were successfully printed using these drug loaded filaments. Release studies showed that after an initial burst release in the first 2hrs, sustained delivery was possible for a period of 4 days. Longer release study and further characterization of the implants are required. However, this study shows the potential for a new quick, cheap and efficient method of fabrication of implants for the inner ear.