3D printed triamcinolone acetonide-loaded polycaprolactone implants for the treatment of posterior ocular disease

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Background: Triamcinolone acetonide (TA) is an intermediate-acting synthetic corticosteroid extensively used to treat posterior segment ocular diseases (Pinto *et al.*, 2012). Intravitreal injection of TA is the commonly used route to treat posterior ocular diseases. Nevertheless, this route usually experiences fast clearance from the vitreous humour, so frequent injections are needed to maintain the therapeutic drug levels. As a result, side effects such as endophthalmitis, cataracts, vitreous haemorrhage and retinal detachment are observed (Huang X *et al.*, 2019). A sustained-release system can deliver the drug more efficiently to the targeted ocular tissue, minimise toxicity, reduce administration frequency and improve patient compliance (Lee SS *et al.*, 2010). Three-dimensional (3D) printing is an additive manufacturing technology that has recently increased because of its feasibility to fabricate complex, customised, and personalised dosage forms. This project aims to fabricate TA-loaded polycaprolactone **(**PCL) implants using a 3D-bioscaffold printer and evaluate the properties of the implants.

Methods: The implant was designed using computer-aided design (CAD) software and printed using GeSiM 2.1 Bioscaffolder 3D Bioprinter (Radeberg, Germany). Different ratios of low and high molecular weight of PCL (20:80 and 40:60 v/v) as matrix polymers and different drug loading (5, 10 and 20% w/w) were utilised in this experiment. Characterisation of PCL implants was done using SEM, IR, DSC and HPLC. The in-vitro study used PBS pH 7.4 containing 0.05% sodium azide and 0.5% sodium lauryl sulfate as the release media. The release mechanism of TA from PCL implants also evaluated using various mathematical models. Biocompatibility of the implants was assessed using ARPE-19 cells.

Results: Six formulations of TA-loaded PCL implants were successfully fabricated without using any organic solvent during the fabrication process. Drug content analysis showed good reproducibility, with the recovery between 98.60 to 100.34% at all drug loadings. The characteristics of PCL implants using SEM, IR, and DSC showed that TA is fully incorporated within the implant matrix. The in-vitro study of PCL implants showed that TA was released above the minimum therapeutic levels for six months. The release of TA from PCL implants followed the Korsmeyer-Peppas model with the n-value < 0.5, following Fickian-diffusion. The biocompatibility results revealed that the implants were non-toxic to the ARPE-19 cells.

Conclusions: TA-loaded PCL implants were successfully fabricated with a 3D bioprinter. TA can be released from the implants for six months period. This implant can be an alternative compared to frequent intravitreal injections in the treatment of posterior ocular diseases. However, an in-vivo study needs to be demonstarted further to examine the efficacy and safety of these implants.