A simplified, in vitro, 3D printed dry eye model and its application in the assessment of therapeutic ocular lubricants

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INTRODUCTION: The ethical constraints associated with human and/or animal models make it a less favourable method for performing toxicity assessments on novel drug compounds. Instead, in vitro cell-based models are the preferred method of use. Traditionally, cell culture is performed on flat tissue culture plates (TCP) although it is now considered not to be truly representative of the real 3-dimensional (3D) surfaces, in vivo. Consequently, it is proposed to develop a novel in vitro model of the eye by combining ocular cells with a 3D printed curved scaffold. This model seeks to support long term cell growth while providing a more accurate representation of the ocular surface due to the surface curvature. Further to this, it is intended to this in vitro construct as a novel model to represent dry eye syndrome (DES) whilst assessing the efficacy of four commercially available ocular lubricants.

METHODS: 3D poly-lactic acid (PLA) scaffolds were designed and developed using an Up!® Plus 2 3D fused deposited modelling printer. Human ocular epithelium cells (CRL-2302, ATCC) were cultured in DMEM-F12 media in a humidified-incubator at 37°C and 5% v/v CO2. 20,000 cells were placed onto each 3D scaffold and following 24h equilibration, the media was removed and cells were allowed to air dry for 30 minutes to mimic DES. These cells were then exposed to four ocular lubricants (i.e. 0.3% w/v hypromellose, Liquifilm Tears®, Optrex® and Viscotears® Liquid Gel) before being assessed for cellular activity and viability using the Cell Titer AQ Proliferation/MTS assay (Promega) and CytoTox-ONE LDH assay (Promega), respectively.

RESULTS: 3D printed scaffold were successfully fabricated with the correct dimensions. The biological assays demonstrated that the most effective ocular lubricant was Optrex® which documented the greatest cell viability and lowest cell toxicity. In contrast, 0.3% w/v hypromellose was seen to be the least effective ocular lubricant by showing a significantly lower viability measurement. Liquifilm Tears® and Viscotears® Liquid Gel displayed moderate therapeutic activity (Figure 1).

DISCUSSION: Cells cultured on a “curved” substrate demonstrated enhanced growth and differentiation characteristics i.e. representative of the native eye. The cell response to each lubricant was related to their formulations and can be seen to be reflected by the corresponding cellular activity (MTS) and higher cell death (LDH) values.

CONCLUSIONS: Ocular cells were successfully cultured on 3D printed curved scaffolds. There was a greater cell growth and lower cell death in comparison to those cultured on flat TCP. DES was also successfully replicated and the efficacy ocular lubricants demonstrated varying levels of cell viability and/or prevention of cell death.


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