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In vitro biocompatibility panel for PEGDA intraocular drug delivery devices

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Abstract

Purpose : PEGDA drug delivery devices (PDDD) have potential for the treatment of chronic vitreoretinal diseases, surpassing the ocular barriers, and sustaining the drug release. *In vivo* models are the most used to analyze the potential of PDDD. However, there are cellular biomarkers that can be analyzed *in vitro* to prevent non desired effects in preclinical studies. Here, we analyzed the acute cell response *in vitro* in terms of cell viability, cytotoxicity, apoptosis, and necrosis in cells exposed to PDDD.

Methods : PDDD were 3D bioprinted at Lawrence Livermore National Laboratory. Endothelial cells SVEC 4-10 (ATTC®) were used in three groups: control (non-treated), negative control (treated with 15% DMSO), and treated (exposed to PDDD). For the cytotoxicity test, a second negative control was used (treated with 5% DMSO). SVEC 4-10 cells (5,000/100mL per well) were incubated in a 96-well plate with or without a ~2.4 mg piece of PDDD for 24h to determine cell viability (with Cell Titer Blue, Promega) and cytotoxicity (with LDH assay kit, Pierce). For apoptosis analysis (with Annexin V kit, ThermoFisher Scientific), 200,000 cells/well in a 12-well plate were used. The results were analyzed using GraphPad Prism 8.01 software.

Results : The viability of cells exposed to PDDD was 70.9%, with significant difference when compared to the control (p = 0.0383). The cytotoxicity measured by LDH activity was 2.17% (p = 0.0123). The early apoptosis was 24.1% in the treated cells and 15.9% in the control, while the late apoptosis was 3.4% and 2.7% respectively. There was no difference in the necrosis analysis (0.1% in treated and non-treated cells).

Conclusions : The exposure to PDDD decreased the cell viability and increased the cytotoxicity near to the acceptable treshold. The apoptotic activity increased in 10% in the treated cells, however, the viability decrease is not attributed to necrotic events. This *in vitro* biocompatibility panel allows the adjudgment making in the composition of the PDDD before using it in preclinical models. Additionally, this panel can be complemented with the analysis of oxidative stress, genotoxicity, and inflammatory markers.

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