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| **Electrospun riluzole-loaded, radially aligned dural substitutes for the treatment of spinal cord injury** |
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| **Background:** Currently, the lack of curative treatments for spinal cord injury (SCI) results in paralysis, disability and life-long neuropathic pain. Following SCI an emergency decompression surgery is usually performed. Dural substitutes can be then implanted to provide a scaffold for the regeneration of the dura mater, which envelops the spinal cord and prevents cerebrospinal fluid leakage. Pharmacological interventions are uncommon, but recent studies have shown the neuroprotective potential of riluzole, a glutamate release inhibitor, in patients with traumatic SCI. We hypothesise that delivering the drug locally by implanting riluzole-loaded dural substitutes during neurosurgery could increase the efficacy and decrease the risk of side-effects currently associated with systemic administration. Additionally, the radial morphology of electrospun implants could facilitate accelerated wound healing by promoting cell elongation and migration along the fibres. |
| **Methods:** Radially aligned riluzole-loaded polycaprolactone (PCL) fibres were prepared by electrospinning of a polymer-drug blend onto a bespoke collector. Electrospinning conditions, such as distance, volume and voltage were optimized to achieve the best possible alignment. The fibres were characterised using scanning electron microscopy (SEM). A drug release study was performed over 24 days. Cell tests were performed in cell culture on SH-SY5Y cells to verify the pharmacological effect of riluzole and to determine the optimal drug concentration. Cytocompatibility studies were performed with fibroblasts (L929) to test the growth of cells on the fibres, and data were gathered at three time points. The cells were stained with Hoechst and Phalloidin, and images were acquired using confocal microscopy.  |
| **Results:** The produced PCL fibres were shown to be radially aligned under the SEM. The drug-release study showed sustained release of riluzole with minimal burst release over 24 days. Cytocompatibility studies showed preferential growth and elongation of L929 cells along the radially aligned fibres, compared to randomly aligned fibres, and a preferential growth on the drug-loaded fibres, compared to the non-drug-loaded fibres. Riluzole eluted from electrospun fibres was proven to remain pharmacologically active in the SH-SY5Y glutamate-induced cytotoxicity model.  |
| **Conclusions:** This study has shown that radially aligned electrospun fibre patches loaded with riluzole are able to direct growth and elongation of fibroblasts, but also to increase cell viability in excitotoxic conditions. This dual activity of the fibres could therefore be promising for the treatment of SCI. Future work includes testing the material in human-derived meningeal cells and neuron-optimised 3D scaffolds.  |