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3D TUBULAR HYBRID SCAFFOLDS FOR SPINAL CORD INJURY REPAIR

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INTRODUCTION

Spinal cord injury (SCI) represents a significant health problem. It is estimated that 90 million people around the world currently suffer from some form of SCI. In Europe and United States there are approximately 600,000 paraplegics (20,000 people each year) [1]. Until now, the use biomaterials loaded with grow factors or the injection of cells, on its own, has not allowed the development of an effective clinical therapy, fact that is mainly related with the complexity of SCI. Therefore, only a mustidisciplinary approach such as those presented by tissue engineering concepts, where a 3D porous scaffolds plays a central role, will adequatly tackle the problem. In fact the development of strategies for SCI based in these concepts holds great promise, because includes all the needed aspects for tissue regeneration, from the adequate mechanical support to the basic cellular processes of regeneration. Therefore the objective of the present work was to develop a new range of 3D tubular structures, based on starch biodegradable polymers and rapid prototyping techniques, aimed at inducing the regeneration within SCI sites.

MATERIALS AND METHODS

The materials used in the present work consisted on 70/30% blend of starch with polycaprolactone (SPCL). 3D tubular structures, with different thickness layers as well as different pore geometry and orientation were processed by using 3D plotting, a rapid prototyping technology. Up to six different 3D porous scaffold designs were processed. Following this phase their mechanical properties were assessed by dynamical mechanical analysis (DMA), in both dry and wet conditions and morphology/porosity analysed by micro-CT and scanning electron microscopy Upon characterization a polyssacharide based hydrogel, gellan gum [2], was injected in the central canal of the 3D tubular structures. Biological evaluation of these SPCL/Gellan Gum structures were firstly carried out by determining their cytotoxicity, using for this purpose the MEM extraction and MTS tests as previously described [3]. Second phase of the biological tests consisted on the encapsulation of central nervous system derived cells, namely a cell line of oligodendrocytes (M0 III cell line), being the latter further injected into the central canal of the SPCL structures. Cells were allowed to grow for periods up to seven days, after which their viability was assessed by a cell live/death assays and confocal laser microscopy.

RESULTS AND DISCUSSION

Mechanical tests revealed that scaffolds presented compressive modulus that ranged from 17.4 MPa to 62.0 MPa in dry conditions, and 4.42 MPa to 27.4 MPa in wet conditions. The porosity and morphological analyses showed that scaffolds disclosed a fully interconnected network of pores with porosity ranging from 70%-85%. In both cases, mechanical properties and porosity analyses, the differences observed were mainly related with different number of SPCL layer that composed the SPCL 3D tubular scaffolds. Cytotoxicity assays revealed that the extracts released by the 3D SPCL/Gellan Gum conduits were non cytotoxicity, as they did not cause major alterations on cell morphology, proliferation and metabolic activity. Finally preliminary direct contact assays showed that the 3D guidance conduit developed in the present study could support the *in vitro* culture of oligodendrocyte like cells.

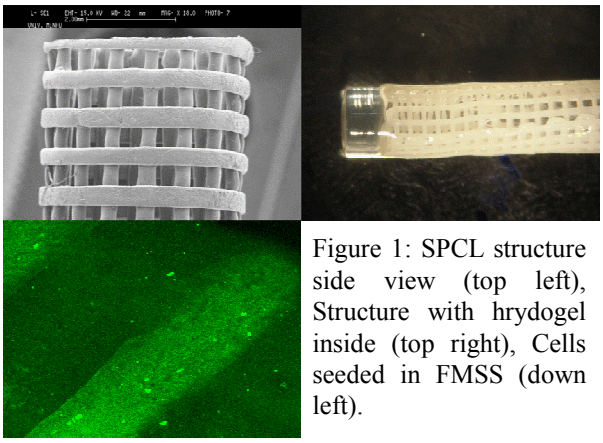

Figure 1: SPCL structure side view (top left), Structure with hrydogel inside (top right), Cells seeded in FMSS (down left).

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CONCLUSIONS

Within the present work it was possible to show that 3D plotting, a rapid prototyping technology, is an adequate processing methodology for the development of tissue hybrids aimed at SCI regeneration. Furthermore it was also possible to demonstrate that the SPCL/Gellan Gum 3D guidance conduits developed with this methology revealed adequate mechanical properties, pore sizes and interconnectivy for the referred applications. Finally it was possible to conclude that the 3D SPCL/Gellan Gum scaffolds discoled a non-cytotoxic behaviour and allowed the culture of oligodendrocyte like cells within its structure. Further work will focus on the behaviour of these scaffolds when implanted in SCI animal models.

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