

CHITOSAN HYDROGEL CONTAINING BIOACTIVE GLASS AIMING AT 3D PRINTING FOR PERIPHERAL NERVE REGENERATION

Larissa Lourenço¹, Roger Borges^{1,2}, Danilo Carastan³, Carlos Silva¹, Mônica Beatriz Mathor⁴,
Juliana Marchi^{1,*}

¹CCNH/UFABC, Brazil

²School of Biomedical Engineering/Faculdade Israelita de Ciências da Saúde/Hospital Albert Einstein, Brazil

³CECS/UFABC, Brazil

⁴CETER/IPEN, Brazil

*Corresponding author: julina.marchi@ufabc.edu.br

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Introduction and objective: Peripheral nerve lesions are a challenge in the context of regeneration. Tissue engineering strategy can increase repair success using biomaterials and cells. Chitosan is a biocompatible natural polymer, with good cost-effectiveness and rheological properties that has been shown to be suitable for nerve regeneration. Bioactive glasses exhibited the ability to increase the production of neurotrophic substances in *in vivo* experiments that could assist nerve repair. 3D printing presents the possibility of building complex and patient-specific structures. Thus, the development of chitosan hydrogels with different concentrations of bioactive glasses for 3D printing is proposed for future application in peripheral nerve regeneration.

Methodology: Chitosan hydrogel was produced with different concentrations of bioactive glass (0, 0.5%, 1%, 2%, and 5%). The rheological characterization of the hydrogels was carried out by shear sweep and creep-recovery experiments. Printability and shape fidelity were evaluated after the 3D printing process through the comparison of the theoretical CAD model and printed structure. Indirect cytotoxicity assay using PC12 cells was performed to evaluate the biological properties of the scaffolds.

Results and discussion: The presence of glass affects the rheological properties of chitosan hydrogel. The shear sweep results showed that the viscosity of the chitosan containing bioactive glass decreases at the lowest shear rate compared to pure chitosan hydrogel. However, the viscosity of hydrogels containing higher concentrations of glass (2% and 5%) increases when compared to the other composites. Such behaviour is a consequence of two events: the presence of the bioactive glass particles and the ions release, caused by glass dissolution in the material, which can interact with the polymeric chains and disrupt the formation of intermolecular interactions. Furthermore, the incorporation of the ceramic particles increased the recovery percentage of the material. This raise is caused by the interactions between the bioactive glass surface and chitosan chains, increasing the hydrogel's stability. These rheological characteristics improved shape fidelity of the material and possible use as ink for 3D printing. Biologically, the extracts of the materials had a non-toxic effect on the PC12 cells.

Conclusions: The presence of glass affects the rheological properties of chitosan hydrogel to improve its use as 3D printing ink. The biological experiments showed that the materials do not have cytotoxic effects and could be used in tissue engineering. Therefore, chitosan hydrogel with bioactive glass particles are promising materials for application in peripheral nerve regeneration.

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