Development of Cell-laden Bioink based on Blood-derived Proteins for Tissue Engineering

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INTRODUCTION

Today, one of the key challenges in reconstructive surgeries is to restore or replace the damaged tissue caused by diseases and accidents with a suitable graft. One of the leading reconstruction methods is biological grafts (allografts and autografts) [1]. Although these biological grafts can promote bioactive tissue, they have a high incidence of complications. For example, rejection, non-union, delayed union, and infection [2]. Recently, 4D bioprinting has been regarded as the next generation of tissue repair technology. This technology, which is based on bioink that combines biomaterials, living cells, and bioactive factors, has the ability to create dynamic, personalized, and precise tissue-engineered grafts through complex structure and functional maturation [3]-[5]. The overall goal of this research is to develop a novel bioink based on blood-derived proteins and human cells that will be 4D-printed into functional, personalized tissue grafts.

MATERIALS AND METHODS

The bioink composition, in terms of material selection and concentration, and the optimal printing parameters were determined by testing the printability, structural stability, and biodegradability of the hydrogels. The models were printed using CELLINK Bio-X6 bioprinter with a pneumatic 3mL printhead with a 22G nozzle. The bioink's optimal printing parameters were 200 kPa pressure, and 2 mm/s printing speed with a 50% infill rectilinear pattern. Then, the mechanical properties of the optimal bioink were evaluated by compression and rheology testing. An indirect cell viability test was performed according to ISO10993-12. Further biocompatibility testing was carried out by seeding cells into the bioink-printed models using a syringe pump printhead with an extrusion rate of 1 μL/sec at a print speed of 1 mm/sec to obtain 100K cells per model. Then, the printed grafts were incubated in standard cell conditions (37 °C, 5% CO_2). The biological evaluation included the deposition of the extracellular matrix by the cells.

RESULTS AND DISCUSSION

The obtained results demonstrate a highly mechanically stable bioink over time with an elastic modulus similar to biological tissue. Furthermore, the bioink has shear-thinning properties suitable for printing. In terms of biocompatibility, the bioink presented high cell viability according to the indirect cell viability test and non-toxic properties. Additionally, the 4D-printed grafts exhibit the deposition of extracellular matrix induced by the cells over time.

CONCLUSIONS

The proposed novel bioink has shown promising biocompatibility as well as the ability to successfully promote tissue remodelling, with suitable mechanical and rheological properties. This bioink could be used in various applications as an alternative to current biological graft solutions. Since this bioink is comprised of blood-driven proteins and cells, it could potentially be constructed entirely from components derived from the patient for enhanced personalisation treatments.

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