A graphene-modified bioink as a novel material for 3D vascular constructs biofabrication

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INTRODUCTION

One of the leading causes of death worldwide is cardiovascular disease, including peripheral arterial disease. Using synthetic vascular grafts designed to treat heart disease is a clinically approved option for more severe cases. However, when used at the peripheral level, these grafts present several drawbacks that can prevent the success of the intervention. Therefore, developing vascular grafts created through 3D (bio)printing specifically designed for these peripheral pathologies could represent a promising approach to addressing biological and dimensional incompatibility [1]. Moreover, synthetic and hybrid grafts still need to fully reproduce the complex structure and function of the natural vasculature. By following a multi-material and multi-cell approach, we aim at (bio)fabricating a portion of vascular conduct, forcing a physiological organization of cells within the construct, and providing it with biomechanical cues to sustain correct tissue development.

MATERIALS AND METHODS

In the present work, we investigated the impact of two functional materials as potential mechanical reinforcers of a base bioink intended for the three-dimensional bioprinting of vascular constructs and grafts. The starting control bioink is composed of gelatine (GEL), alginate (ALG), hyaluronate aldehyde (HA-ALD), and carboxymethyl chitosan (CMC). The control bioink, despite demonstrating good cytocompatibility and printability, does not possess the mechanical properties necessary for vascular-engineering applications. To overcome this limit and boost cell maturation within the bioink, we introduced a natural reinforcement material (soluble collagen, SO-COL) and a synthetic nanomaterial (graphene oxide flakes, GO).

RESULTS AND DISCUSSION

Different SO-COL and GO concentrations and preparation protocols have been tested to guarantee optimal characteristics of the final bioink. Specifically, the bioink and the 3D scaffolds obtained via extrusion-based 3D bioprinting have been evaluated in their rheological and mechanical properties, respectively. We demonstrated that the rheological properties of the GO+SO-COL bioink are improved resulting in slightly improved printability than the control composition. On the other hand, the compression module of the scaffolds prepared with the modified bioink is higher. The constructs have also been characterized in their micro and macro morphology using scanning electron and optical microscopies, appearing comparable in both aspects. Furthermore, we have verified that the new formulation containing collagen and graphene oxide was not toxic to cells conducting comparative cytotoxicity, viability, and cell proliferation tests using a mouse fibroblast cell line (L-929). As proof of the principle of the use of these bioinks for vascular applications, a portion of a vascular conduit wall has been bioprinted by exploiting two different cell types: a mouse myoblast cell line (C2C12) and an endothelial cell line (primary human umbilical vein endothelial cells, HUVEC). Cells have been live-stained with two different cell trackers following cell development, morphology, and migration within the construct.

CONCLUSIONS

In this work, we propose combining 3D bioprinting, tissue engineering, and material science to develop and validate a new bioink as a base material for a new generation of vascular grafts aiming to treat peripheral vascular pathologies. Our preliminary results confirm the possibility of exploiting nanotechnological modifications based on GO to improve the mechanical properties of the bioinks maintaining good viability to embedded cells. The synergic combination of these competencies could lead to high-resolution, personalized vascular grafts with greater consistency and stability.

REFERENCES

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