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# Graphene oxide as an additive to dECM-based bioink for tissue engineering applications

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## INTRODUCTION

Tissue engineering is one of the fastest growing fields in modern medicine. Due to the very high demand of organs for transplantation, many methods are being developed to enable the preparation of functional three-dimensional (3D) structures that mimic the native tissue and can be used as scaffolds for cell culture [1-3]. The biggest challenge in material engineering is to develop a cell-safe biomaterial with significant utility in fabrication technologies such as 3D bioprinting. The main goal of this work was to optimize the composition of a new bioink based on graphene oxide (GO) and decellularized extracellular matrix (dECM) with unique properties, suitable for bioprinting of functional scaffolds.

## MATERIALS AND METHODS

Bioinks were composed of dECM paste and GO-based hydrogel. The GO-based hydrogel was prepared by mixing methacrylated gelatin (GelMa), methacrylated hyaluronic acid (HaMa), photoinitiator (Lithium phenyl-2,4,6-trimethylbenzoylphosphinate - LAP) and GO (all the biomaterials were provided by Polbionica Ltd.). The dECM paste was fabricated by dissolving the appropriate amount of dECM in hydrochloric acid and pepsine. The solution was stirred for 72 h at room temperature and then neutralized. After neutralization, dECM powder was added to the hydrogel and mixed until a paste-like consistency was obtained. As a result, 5 different variants of biomaterial were prepared: two hydrogels (HGO1, HGO2) and two bioinks (BGO1, BGO2) containing different concentrations of GelMa, HaMa and supplemented with GO, as well as the reference bioink BREF – a BGO1 variant that does not contain GO.

The experimental work evaluated such functional properties as viscosity and complex modulus, printability, mechanical strength, elasticity, degradation and absorbability. In addition the survival of cells on the materials and cell's immune response as a consequence of cell exposure to the biomaterial were evaluated.

## RESULTS AND DISCUSSION

Printability close to 80% was achieved for all the biomaterials, and the addition of GO slightly affects the assessed printability parameters. The use of GO leads to an increase in Young's modulus and yield strength, and a slight decrease in mechanical strength compared to BREF. All bioinks showed a higher storage modulus (G`) than the loss modulus (G``) in the tested range of oscillation amplitude, which indicates that it can retain the structure after extrusion from the nozzle. Hydrogels have viscosity values 100 times lower than bioinks. The addition of GO compared to BGO1 did not affect the viscosity of the bioink. It can be seen that significantly more water is absorbed by hydrogels compared to bioinks. The degree of degradation after 21 days was 50-90% for non-enzymatic degradation and 80-90% for enzymatic degradation. The bioinks were more resistant to non-enzymatic degradation than hydrogels. The results of the cytotoxicity test for all tested biomaterials showed that they had lack of cytotoxicity effect on the reference cell line (L-929) after 24 h of exposure.

## CONCLUSIONS

The addition of GO did not affect the rheological properties and printability of the bioink, but it increased the mechanical strength. Graphene hydrogels were characterized by a much higher degree of swelling, water absorption and degradation compared to bioinks. The addition of GO has a positive effect on the cytotoxicity of the biomaterial.

## REFERENCES

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