Tuning the viscoelastic properties of hydrogels to mimic prostatic cancer microenvironment

Introduction

Three-dimensional hydrogels are increasingly proposed[1] to mimic biological tissues and micromechanical environments, owing to their tunability. Understanding structure–composition relationships is crucial for tailoring their properties. A prostate cancer (PCa) model was developed using an internally crosslinked[2] alginate/gelatin hydrogel, designed to mimic the micromechanical environment and optimized for bioprinting with human PCa cells.

Methods

Hydrogels were prepared by sequentially mixing solutions/suspensions in 22Rv1 culture medium (final composition of 2% w/v gelatin, 6% w/v alginate, 0.7% w/v $CaCO_3$, 3.74% w/v GDL, and $3x10^6$ 22Rv1 cells/ml). Hydrogels were then covered with an equal volume of buffered medium. Frequency sweep tests were performed at 20–0.1 Hz at 20 °C, 37 °C, 50 °C using a rotational rheometer. Gelation time was evaluated by time sweep tests.

Results

The hydrogel formed a semi-IPN showing in frequency sweep tests higher G'' at 20 °C and no G' variations upon temperature changes. The timing of the medium addition (t_{add}) was used to control the viscoelastic properties. At 37 °C, 24 h after crosslinking onset, with t_{add} of 60 min, G' reached 5.5 kPa (at 1.05 Hz), within the PCa stiffness range (5–10 kPa)[3], and G'' was 240 Pa. Printability was *a-priori* assessed by rheological analyses and then with a pneumatic 3D bioprinter[2,4]. The best performance (printability coefficient 1.17) was obtained 30 min after crosslinking onset, with a 25G conical nozzle, 10 mm/s speed, and 70 kPa pressure. After 72 h, cell viability and metabolic activity increased compared to 1 h incubation (slightly below 2- and 1.5-fold, respectively). The initial pH (~6.5) gradually reached neutrality within 2 h (t_{add} 60 min; one medium change after 1 h).

Conclusions

Our study shows how composition and experimental parameters influence the properties of an alginate/gelatin hydrogel, providing a versatile approach for advanced 3D models and other hydrogel-based systems.

Figure 1: Grid (10 mm x10 mm x 0.3 mm) 3D printed at BioX, 30 minutes after the beginning of crosslinking, with printing speed of 10 mm/s and printing pressure of 70 kPa.

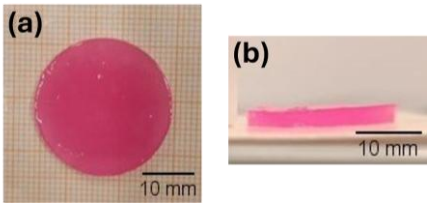

Figure 2: Top (a) and side (b) view of samples tested at the rheometer to measure viscoelastic properties.

References:

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