Implementing Projection Stereolithography (PSLA) 3D Printing for the Long-Term Release of Biomacromolecules

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Background: Biomacromolecule therapeutics are of increasing interest for treatment in a number of chronic areas, including cardiovascular and metabolic illnesses. It is desirable to tailor treatments and delivery to specific patient group needs, and to help address this our research focuses on the investigation of 3D printing approaches as a pathway to bespoke production. Past success has been documented in literature for tuning small biomolecule release (Da) from 3D printed multi-material delivery devices. Hence, the overall research project purpose considers how additive manufacturing methods could also be implemented to deliver biomacromolecules (kDa). This is challenging for sustained delivery periods requiring methods allowing encapsulation, elution and activity retention.

Methods: Projection stereolithography (PSLA) 3D printing was selected for the fabrication of 10 x 10 x 2 mm structures with encapsulated model proteins of varying nominal sizes. Alkaline phosphatase (ALP) from bovine intestinal mucosa, bovine serum albumin (BSA) and lysozyme (LYZ) were selected due to their differing characteristics such as molecular weight (~14 – 160 kDa) and nominal size (~4 – 15 nm). Release from different polyethylene glycol diacrylate (PEGDA) based formulations in phosphate buffer solution (PBS) at 37 °C were assessed using a Bradford protein assay. Swelling and theoretical matrix mesh size for printed samples was calculated using the Peppas-Merrill model and compared in relation to each encapsulated model protein size to determine the importance of matrix mesh size influence on dictating release.

Results: Swelling ratio increased with increasing PEGDA molecular weight, corresponding with increased theoretical matrix mesh size calculated, ranging from ~0.3 to 7.5 nm, for the formulations evaluated to date. Further PEGDA MWs will be trialed to conclude the study. For lower MW PEGDA formulations, prepared with PEGDA 575 and PEGDA 700 50 v/v% in PBS, release was not observed. The associated theoretical matrix mesh sizes calculated of these two formulations were ~0.3 and 0.5 nm, considerably lower than the 4, 7, 15 nm approximate nominal sizes of LYZ, BSA and ALP respectively. For a formulation comprised of 20 w/v PEGDA 10,000 in PBS, the associated theoretical matrix mesh size was ~7.5 nm. For this formulation, burst release of low quantities was seen for LYZ and BSA encapsulated samples (32.9 ± 9.0 and 26.5 ± 2.4 ug respectively after 24 hours), within minimal/no release after this point.

Conclusions: Matrix mesh size of crosslinked polymer networks appears to dictate entrapment or release of the model proteins encapsulated in the PSLA 3D printed PEGDA based samples. Results aligned with past literature whereby release is expected when matrix mesh size is comparable or greater than the encapsulated protein size. For samples where release was achieved an associated burst release characteristic before plateau was observed, which is undesirable for long-term applications. This indicates the majority of protein loaded could be entrapped/bound, likely due to the chain growth polymerisation mechanism with free radicals produced under UV exposure during printing. The proposal moving forward is to trial step growth polymerisation reactions, which are highly tunable and favourable for efficient printing using minimal photoinitiator additions.