Enhancing Mechanical Properties of Hydrogel Materials through Peptide-Polymer Conjugation: A Novel Approach for Tissue Engineering Applications

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Designing synthetic hydrogel materials that recapitulate the dynamic properties of natural systems, including stimuli-responsive motifs to modulate chemistry and interpenetrating networks of multiple polymers to augment mechanical properties is an area of significant technological interest (1). Recent advancements in hydrogel design have focused on developing innovative polymers, polymer-protein, and polymer-peptide conjugates to enhance biological activity and avoid immune detection in vivo (2). The peptide-based hydrogels, characterized as supramolecular materials, exhibit self-assembling capabilities into nanostructures and can respond to microenvironmental stimuli. The combination of these two networks creates hybrid hydrogels with improved stiffness, pore size, and extracellular matrix hierarchical mimicry (3). Recently, our group designed a Trpzip motif-based peptide hydrogelator that self-assembles into a nano- and micro-structured material with unique mechanical and biological properties such as yield-stress fluid behaviour, high-density cell ink support, antimicrobial activity, etc., all useful characteristics for biofabrication and tissue engineering applications (4). However, the designed tryptophan zipper peptides display low stiffness and yield points which are not appropriate for some applications. The present study aimed to develop hydrogel materials based on Trpzip peptide (q5) and its conjugation as a distinctive tool offering optimized properties for biofabrication and scaffolding for tissue engineering. To do this, we synthesized Trpzip peptide- 4-arm PEG-Mal conjugate (conj) using Trpzip peptide with the sequence of SWTWQGNVWTWVC and cysteine residue and 4 Arm-PEG-Mal through click chemistry, Michael-type addition reactions (5). We prepared Trpzip-based hydrogels through ionic-triggered gelation, achieved by dissolving lyophilized peptides in Milli-Q water and conjugated material in high glucose Dulbecco's modified Eagle's medium (DMEM). The results of the linear viscoelastic measurements through the oscillatory time sweep test showed that by adding only 0.22% w/v conjugated materials to 2% w/v Tripzip peptide, the stiffness increases, and the gelation time decreases significantly (Figure 1a). The amplitude sweeps test results (Figure 1b) reveal that the double network hydrogel sample of 2% w/v q5/0.22% w/v conj exhibits a higher yield point at 1.2% shear strain when compared to the 2% w/v q5 hydrogel which shows a yield point of 0.4% shear strain suggesting a more stable structure, gel-like characteristics, with increased stiffness (6). These properties make this hybrid network material a good candidate for diverse applications spanning three-dimensional (3D) bioprinting/organ printing to loading cells for tissue engineering and cell therapy.

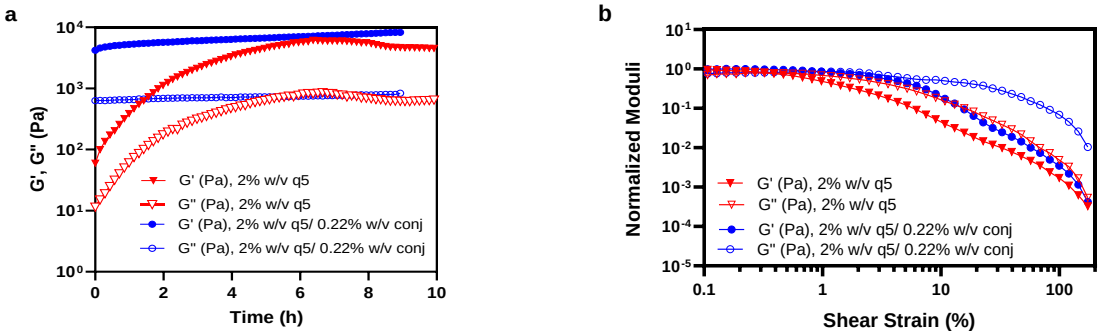

Figure 1. Mechanical characterization of Trpzip-q5-based hydrogel samples at 37 °C. **a** Oscillatory time sweeps and **b** strain sweeps

References

[1] Li Y.; Kilian KA. Adv. Healthcare Mater. **2015**, *4*, 2780–2796.
[2] Holz E.; Darwish M.; Tesar DB.; Shatz-Binder W. Pharmaceutics **2023**,*15, 600*, 1-54.
[3] Liu YS.; Chakravarthy RD.; Saddik AA.; Mohammed M.; Lin HC. RSC Adv. **2022**, *12(22)*,14315–20.
[4] Nguyen AK.; Molley TG.; Kardia E.; Ganda S.; Chakraborty S.; Wong SL.; et al. Nat Commun. **2023**, *14(1),* 1-13.
[5] Hamley IW. Biomacromolecules **2014**, *15(5)*, 1543–59.
[6] Schwab A.; Levato R.; D'Este M.; Piluso S.; Eglin D.; Malda J.; Chem Rev. **2020**,*120(19)*,11028–55.