Designing High Performance Gelatin–Based Hydrogels for Tissue Engineering Applications

Abstract:

Tissue engineering aims at replacing or reconstructing fully functional substitute for damaged or diseased or lost tissues and organs. Biomaterials play a vital role in this field by acting as synthetic platforms referred as scaffolds or matrix, providing and maintaining a well-defined healthy microenvironment to encourage cells to enhance repair or generate new tissue. Hydrogels, as scaffolding substrate, have emerged as the most promising candidate for tissue engineering application due to their remarkable properties and cell-friendly perspective. Towards optimal performance, hydrogel development has been witnessing the emergence of a powerful set of new exciting design parameters to improve their ultimate utility. There's little doubt that creating complex scaffolding substrate using high-tech (over-engineering devices) is often plagued by financial considerations and less likely to clinical translation. As such, we developed a novel 'softly-cum-simply' synthesis approach to fabricate hydrogels that were targeted to assist tissue regeneration. We exploited the synergy contribution between natural (gelatin (G), chitosan (CH) and hydroxyethyl cellulose (HEC)) and synthetic polymer (polyethylene glycol (PEG)) while keeping the threshold quantity of latter to avoid biocompatibility issue. A series of hydrogels, namely, G/PEG, G/PEG/HEC and G/PEG/CH were prepared via a green, simple, scalable and cost-effective synthesis procedure which mainly consists four sequential steps of gelation, unidirectional freezing, freeze-drying and post curing process. The collective mechanical behaviour of all hydrogels was resemblance to the mechanics of soft tissues. All

hydrogels showed significant level of cells viability for both L6 rat myoblasts and human foreskin fibroblasts, indicating that they were biocompatible. The hydrogel scaffolds splendidly demonstrated both osteogenic and chondrogenic differentiation of human mesenchymal stem cells (hMSCs). More importantly, the developed synthesis approach was versatile enough to accommodate a range of different polymers and nanomaterials without perturbing the benign process conditions. We incorporated conductive nanomaterials, carbon black (CB) or functionalized graphene nanoplatelet (GnP), into G/PEG/CH hydrogels system for imparting electrical conductivity and improving mechanics. Overall, the obtained nanocomposite hydrogels showed superior mechanics and improved electrical conductivity, an essential pre-requisite for electro-responsive cells for cell-cell coupling, and they deserves potential applications for tissue engineering scaffolds, biosensors, actuators, and drug delivery systems.

Finally, this developed simple, sustainable and scalable synthesis approach to design degradable and cell-compatible hydrogels with tailorable morphological, mechanical and chemical properties, along with versatility to ensemble various polymers and nanomaterials to ensure optimal performance toward clinically relevant endpoints, would offer great promise, but not limited to, in the tissue engineering application.