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Crosslinked Porous 3-Dimensional Cellulose Nanofibers/Gelatin Based Biocomposite Aerogels for Tissue Engineering Application

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Abstract : Recent advances in biomaterials have led to utilizing biopolymers to develop 3D scaffolds in tissue regeneration. One of the major challenges of designing biomaterials for 3D scaffolds is to mimic the building blocks similar to the extracellular matrix (ECM) of the native tissues. Biopolymer based aerogels obtained by freeze-drying have shown to provide structural similarities to the ECM owing to their 3D format and a highly porous structure with interconnected pores, similar to the ECM. Gelatin (GEL) is known to be a promising biomaterial with inherent regenerative characteristics owing to its chemical similarities to the ECM in native tissue, biocompatibility abundance, cost-effectiveness and accessible functional groups, which makes it facile for chemical modifications with other biomaterials to form biocomposites. Despite such advantages, gelatin offers poor mechanical properties, sensitive enzymatic degradation and high viscosity at room temperature which limits its application and encourages its use to develop biocomposites. Hydrophilic biomass-based cellulose nanofibrous (CNF) has been explored to use as suspension for biocomposite aerogels for the development of 3D porous structures with excellent mechanical properties, biocompatibility and slow enzymatic degradation. In this work, CNF biocomposite aerogels with various ratios of CNF:GEL) (90:10, 70:30 and 50:50) were prepared by freeze-drying technique, and their properties were investigated in terms of physicochemical, mechanical and biological characteristics. Epichlorohydrin (EPH) was used to investigate the effect of chemical crosslinking on the molecular interaction of CNF: GEL, and its effects on physicochemical, mechanical and biological properties of the biocomposite aerogels. Ultimately, chemical crosslinking helped to improve the mechanical resilience of the resulting aerogels. Amongst all the CNF-GEL composites, the crosslinked CNF: GEL (70:30) biocomposite was found to be favourable for cell attachment and viability. It possessed highly porous structure (porosity of ~93%) with pore sizes ranging from 16-110 µm, adequate mechanical properties (compression modulus of ~47 kPa) and optimal biocompatibility both in-vitro and in-vivo, as well as controlled enzymatic biodegradation, high water penetration, which could be considered a suitable option for wound healing application. In-vivo experiments showed improvement on inflammation and foreign giant body cell reaction for the crosslinked CNF: GEL (70:30) compared to the other samples. This could be due to the superior interaction of CNF with gelatin through chemical crosslinking, resulting in more optimal in-vivo improvement. In-vitro cell culture investigation on human dermal fibroblasts showed satisfactory 3D cell attachment over time. Overall, it has been observed that the developed CNF: GEL aerogel can be considered as a potential scaffold for soft tissue regeneration application.

Keywords : 3D scaffolds, aerogels, Biocomposites , tissue engineering
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