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Injectable and dual-stimuli-responsive silk fibroin hydrogels for tissue engineering and regenerative medicine applications

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Hydrogels have been attracting increasing attentions, since they mimic the extracellular matrix environment and can be used as delivery systems for cells or bioactive agents. Silk fibroin is a well recognized and compatible biopolymer for tissue engineering applications. The traditional methods to prepare silk fibroin (SF) hydrogels take advantage of the conformation transition from amorphous to β-sheet in aqueous SF solution. During this procedure, the gelation time normally varies from hours to months depending on the methods used. The relative long gelation time of those methods limits their practicality as in situ injectable systems for incorporation of cells or drugs. Furthermore, most of these approaches are not suitable for cell/drug incorporation in the silk hydrogel. The current study provides an approach to develop a new SF hydrogel within a few minutes in physiological conditions via peroxidase mediated cross-linking. The influence of silk concentration, and the content of peroxidase and hydrogen peroxide on the physicochemical properties of the hydrogels were studied. The results showed that the gelation time of the silk hydrogel decreased with increasing silk and peroxidase content, and can be tuned between 4 to 50 minutes. The storage moduli of the hydrogels improved via increasing the hydrogen peroxide content and silk concentration, ranging from 0.25 to 5.20 kPa. The fast formed hydrogels showed extreme elasticity and transparent appearance. There were no differences of the silk hydrogel in the visible light absorbance, before and after the gelation. The dominant conformation of the formed silk hydrogels was amorphous, confirmed by Fourier Transform Infrared Spectroscopy. Interestingly, the prepared hydrogels were of ionic strength and pH responsive properties. Its size or wet weight increased in solutions of low ionic strength or basic pH, and vice versa. Cells could be incorporated into the hydrogels and were viable up to 11 days. Cytotoxicity results demonstrated that these hydrogels were non-cytoxic. After subcutaneous implantation in mice for 2 and 4 weeks, the SF hydrogels induced no inflammation reactions in vivo. This study provides a facile approach to prepare injectable SF hydrogels with dual stimuli-responsive properties. The unique properties of these hydrogels exhibit innumerous potential applications, such as for oral drug delivery, adipose tissue regeneration, artificial cornea, wound dressing, and cartilage regeneration.

Reference:
Le-Ping Yan, Ana L. Oliveira, Joaquim M. Oliveira, Diana Ribeiro Pereira, Rui A. Sousa, Rui L. Reis. Hydrogels derived from silk fibroin: Methods and uses thereof. National Patent Nr. 106041, priority date: 06-12, 2011.

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