Sodium dodecyl sulfate-induced rapid gelation of silk fibroin

Xilong Wu,a Jing Hou,a Mingzhong Li,a Jiangnan Wang,a David L. Kaplanb, Shenzhou Lu,a,*

a National Engineering Laboratory for Modern Silk, College of Textile and Clothing Engineering, Soochow University, Suzhou 215123, People’s Republic of China
b Department of Biomedical Engineering, Tufts University, Medford, MA 02155, USA

Abstract

The in situ formation of injectable silk fibroin (SF) hydrogels have potential advantages over various other biomaterials due to the minimal invasiveness during application. Biomaterials need to gel rapidly under physiological conditions after injection. In the current paper, a novel way to accelerate SF gelation using an anionic surfactant, sodium dodecyl sulfate (SDS), as a gelling agent is reported. The mechanism of SDS-induced rapid gelation was determined. At low surfactant concentrations, hydrophobic interactions among the SF chains played a dominant role in the association, leading to decreased gelation time. At higher concentrations of surfactant, electrostatic repulsive forces among micellar aggregates gradually became dominant and gelation was hindered. Gel formation involves the connection of clusters formed by the accumulation of nanoparticles. This process is accompanied by the rapid formation of β-sheet structures due to hydrophobic and electrostatic interactions. It is expected that the silk hydrogel with short gelation time will be used as an injectable hydrogel in drug delivery or cartilage tissue engineering.

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1. Introduction

Interest in the study of hydrogels is growing. Some attractive hydrogel-based biomedical applications include controlled drug release and tissue engineering as scaffolds for the repair and regeneration of defective tissues and organs [1–7]. Minimal invasiveness, targeted delivery at the specific site and encapsulation of bioactive molecules or cells by mixing before injection are the main advantages of injectable in situ-forming medical hydrogels [1,7]. As an ideal injectable hydrogel, gelation must be induced under mild conditions within a short time after injection [1].

Silk fibroin (SF) is a biosynthesized fibrous protein extracted from cocoons of the domesticated silkworm (Bombyx mori). SF-based injectable hydrogels have found recent biomedical application because of their good biological compatibility and biodegradability by enzymatic or oxidative processes [1,8,9]. However, the clinical application of SF is limited because its gelation time (GT) is often too long, unless nonphysiological treatments are utilized (e.g. low pH and high temperature) [8,10,11]. SF solution pretreatments (e.g. extrusion, ultrasonication, and vortexing) [12–14] prior to injection may also increase the risk of in vitro contamination, although the GT could be controlled and shortened. Some studies [10,15] have reported the use of polyethylene oxide (PEO) and Pluronic® (Poloxamer) polymeric surfactants as additives to shorten the GT. However, PEO and Pluronic® only reduced the time in a limited fashion [10], and Pluronic® is nonbiodegradable [1,16]. Hence, these materials are not ideal additives for forming injectable and biomedically relevant silk hydrogels.

Gelation of SF is accompanied by a structural transition from a random coil in the sol into β-sheets. The β-sheets then assemble into a physically cross-linked gel network [4,9,10,17]. SF hydrogels may also consist of agglomerated micron-sized protein-rich particles, possibly caused by the formation of β-sheet structures [11,17]. Freshly prepared aqueous silk solutions, which are colloidal dispersion systems, maintain kinetic stability to a certain extent and thermodynamic instability. From the perspective of dynamics, SF particles slowly cross the potential or energy barrier to aggregate and form a three-dimensional gel network. The hindrances are Brownian motion and the repulsion among negatively charged protein particles at neutral pH (fibroin isoelectric point = 3.8–3.9 [10,17,18]). However, this steady state is eventually destroyed by hydrophobic interactions and/or van der Waals forces, which favor the aggregation of fibroin colloidal nanoparticles. Therefore, fresh SF solutions can ultimately transform into solid hydrogels after passing through changes from clear to turbid solutions. However, this sol–gel transition occurs within a relatively long time (5–15 days at fibroin concentrations of 0.6–7.2 wt% [%] [9]).

In the present work, a new method for SF gelation was developed using sodium dodecyl sulfate (SDS) as the gelling agent. The purpose was to accelerate fibroin aggregation and gelation under mild conditions (37 °C and pH 7.0 ± 0.2). Focus was given to the interactions between SF and SDS to elucidate the mechanism of SDS-induced rapid gelation. SDS, a commonly used inactive ingredient for the US Food and Drug Administration–approved drug products, is mainly utilized as an excipient in solid formulations. It...