Porous Materials Based on Bombyx Mori Silk Fibroin

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Abstract: Bombyx mori silk fibroin (SF) is one of the most important fibers among biomedical porous materials due to its superior machinability, and biocompatibility. It is also chosen for its biodegradability and bioresorbability. It is a protein-based fiber. In this paper, we have reviewed the key features of SF. Moreover we have focused on the morphous, technical processing and biocompatibility of SF porous materials. We have also dealt with its application in research. Finally, a perspective on potential applications and problems of SF porous materials were provided.

***Keywords*:** Bombyx mori silk fibroin, porous materials, processing, biomaterial, application, biocompatibility, biodegradation.

1. Introduction

Porous three-dimensional materials and the network structure materials are composed of interconnected or closed pores. They possess some excellent characteristics, such as favourable mechanical properties and optic-electrical properties, good perm-selectivity, selective adsorption and chemical activity. Porous three-dimensional biomaterials provide a microenvironment for attachment, increase surface area, support a large cell mass, form an extracellular matrix and play an important role in manipulating cell functions in regenerative medicine [1]. Moreover, tissue engineering is an interdisciplinary and multi-disciplinary field that aims at the development of biological substitutes that restore, maintain, or improve tissue function [2].

Bombyx mori silk is a naturally occurring polymer that has been used in textile production and as clinical suture for centuries [3]. Silk in its natural form is composed of a filament core protein, SF, and a glue-like coating consisting of a family of sericin protein. SF consists of heavy (H) and light (L) chain polypeptides of ~390 kDa and ~26 kDa, respectively, linked by a disulfide bond at the C-terminus of the two subunits, and associates with the H-L complex primarily by hydrophobic interactions [4]. The hydrophobic blocks tend to form β-sheets or crystals through hydrogen bonding and hydrophobic interactions, forming the basis for the tensile strength of SF [5]. These ordered hydrophobic blocks combine with the less ordered hydrophilic blocks to give rise to the elasticity and toughness of SF [6]. SF also exhibits diverse structures, mechanical properties and biocompatibility. Based on these features, interest has arisen in the use of Bombyx mori SFs as starting materials for biomaterials and scaffolds for tissue engineering [7]. Recently, there have been many reports about SF porous materials which have been widely investigated in controlled drug delivery system, anticoagulant blood materials, biosensors, artificial ligaments, artificial tendon and artificial skin, etc [8]. In this paper, we will focus on SF based porous materials derived from Bombyx mori silkworms. Several preparation methods, different morphous of SF porous materials and its applications are reviewed as follows.

2. Silk fibroin processing

2.1 Solution of silk fibroin

Because SF is coated by sericin, degummimg is very important. High-purity SF fiber can be obtained easily from degummed silk [9]. SF can be dissolved in neutral solutions of salts such as LiSCN, LiBr, and $CaCl_2$ [10,11]. In the processing of SF porous biomaterials, preparation of SF-based scaffolds with high porosity and interconnected homogeneous pores has become one of the major challenges. Several methods including salt leaching, freeze-drying, gas forming and freeze-drying/foaming have been developed to fabricate porous fibroin scaffolds [12].

2.2 Non-woven silk fibroin mats

Non-woven SF nets/mats/membranes can be prepared using SF with diameters in the range of several to tens of micrometers in their native or partially dissolved forms [13]. A process for producing non-woven SF

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nets/mats/membranes comprises the following steps [14]: firstly, degumming and removal of the sericin; secondly, by a homogenization and drying step (Figure 1) that yields 3D, nonwoven nets/mats/membranes. Non-woven mats can also be obtained by electrospinning SF fibers with different diameters [15]. Electrospinning uses electrical forces to produce polymer nanofibers with diameters around fifty nanometers and arbitrary length. Electrospinning occurs when electrical force at the surface of a polymer solution or melt overcome surface tension and viscoelastic forces and create an electrically charged jet. When the jet dries or solidifies, an electrically charged fiber remains, which can be directed or accelerated by electrical force and then collected in sheets or other useful shapes [16]. The two methods as mentioned above are the predominant ways to obtain SF-based porous mats.

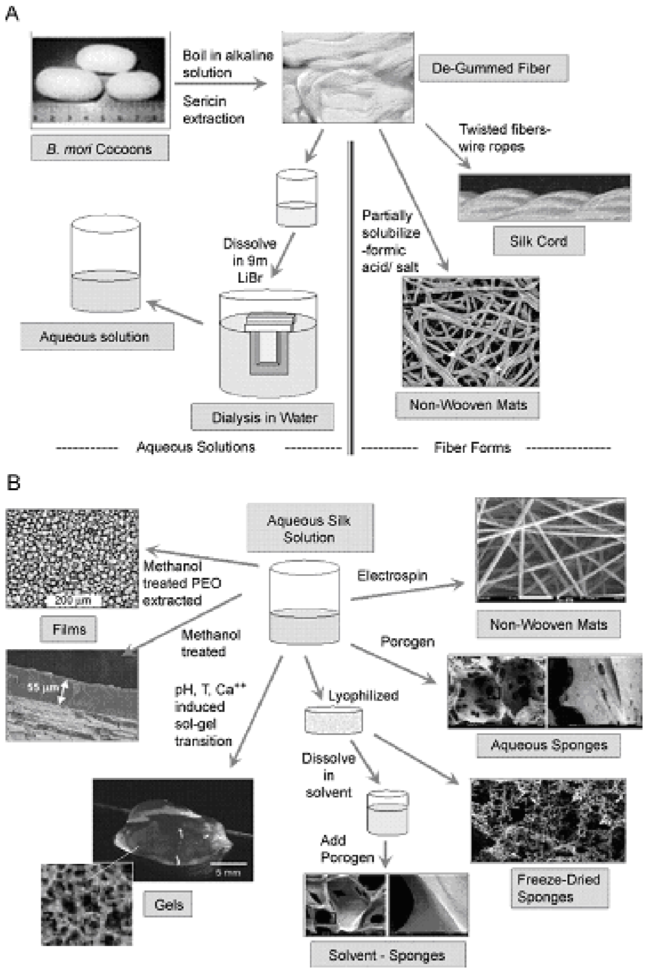

Figure 1. (A) Silkfibroin is purified from sericins via boiling in an alkaline solution. (B) Processing of silk morphologies from aqueous silk fibroin solution [17].

2.3 Silk fibroin hydrogels

Hydrogels are three-dimensional polymer networks which are physically durable for swelling in aqueous solution but do not dissolve in these solution [17]. Hydrogels are formed from regenerated SF solution by a sol-gel transition in the presence of acid, ions, or other additives [18]. During the gelation process, SF experiences a structural transition from random coil to *β*-sheet due to enhanced hydrophobic interactions and hydrogen bond formation [19, 20]. The processes for producing regenerated SF hydrogels are as follows: a) silk is obtained from silk cocoons; b) the sericin layer covering the silk fibers is removed; c) the disulfide bonds are broken in order to obtain aqueous SF solutions; d) the silk aqueous solutions are concentrated; e) some acid, ions, or other additives are added; f) after further processing, such as freeze-drying, microporous SF sponges are formed from hydrogels. Recently, many applications suggest the potential of porous hydrogels for cell culture and in regenerative medicine [21]. Those will be reviewed in later sections.

2.4 Silk fibroin porous sponges

Porous sponges are important tissue engineering materials. SF porous sponges can be obtained using porogens, gas forming, and freeze-drying, freeze-drying/foaming, electrospun fibers [22]. Solvent-based sponges were prepared using salt (e.g., sodium chloride) or sugar as porogen. Porogens such as NaCl were added into SF aqueous solutions in disk-shaped containers, and then the containers were covered and left at room temperature for 24 hours, and then leaching the salt in water at room temperature for 24 hours and drying it [1]. Freeze-drying-based sponges were prepared using crosslinking agent, freezing and drying [9]. The freeze-drying/foaming method was a composite processing method to prepare 3-D SF scaffolds. Unlike the freeze-drying method, the ice/silk composites were firstly placed in the atmosphere at 20°C for different times to make them partly thaw and then lyophilized leaving a porous material [12]. Electrospinning has also been one of the important methods to obtain SF porous scaffolds. There are many ways to prepare the 3-D SF scaffolds. Those mentioned above does not cover all the ways, but rather the predominantly used methods to produce the material.