Journal of Fiber Bioengineering and Informatics 15:3 (2022) 203–216

Cite as: B. Tian et al.
doi:10.3993/jfbim00378

Effect of Proline and its Derivatives on the Properties of Silk Fibroin Microneedles

Bin Tian, Yu-Min Zhang, Zhen-Zhen Qi, Le-Hao Zhang, Zu-Qiang Yin, Shen-Zhou Lu*

National Engineering Laboratory for Modern Silk, College of Textile and Clothing Engineering, Soochow University, 215127, Suzhou, China

Abstract

With its good biocompatibility and excellent mechanical properties, silk fibroin microneedles can transport drugs to the body fluid circulation system and then act on the affected area, so as to replace intravenous injection and oral administration, and achieve the purpose of treating diseases. In the process of processing and use, silk fibroin microneedles are non-toxic, harmless, pollution-free and biodegradable to human body and environment. Therefore, the application prospect and application range of silk fibroin microneedles are very wide.

In this paper, the effects of proline and its derivatives prolinamide and hydroxyproline on the performance of silk fibroin microneedles were studied on the basis of the previous experiments of constructing microneedles to carry drugs. The composite silk fibroin microneedles were obtained by pouring the amino acid/silk fibroin mass ratio of 0/10, 1/10, 2/10, 3/10 and 4/10 into a polydimethylsiloxane mold, after vacuum defoaming and drying. The length of the microneedles was about 600 μm. The aggregation structure of amino acid/silk fibroin microneedles was measured by X-ray diffraction (XRD), Fourier transform infrared spectroscopy (FTIR) and Raman Scattering Spectroscopy. The mechanical properties of the microneedles were measured by texture analyzer. The results showed that: (1) The silk fibroin microneedles prepared by adding proline and its derivatives had predominately Silk I crystal structure; (2) When the mass ratio of proline and its derivatives to silk fibroin reached 2/10, it had a higher swelling degree and a lower dissolution rate; (3) The silk fibroin microneedles prepared by proline and its derivatives have good mechanical properties. The following conclusion was drawn: with the addition of proline and its derivatives, silk fibroin microneedles with higher swelling degree and lower dissolution rate can be obtained. The crystal structure of Silk I is formed inside the microneedles, which has good penetration and fracture properties. It is expected that the microneedles can be used as swelling microneedles for drug transdermal delivery.

Keywords: Silk Fibroin; Microneedle; Proline; Silk I Crystalline Structure

*Corresponding author.
Email address: lushenzhou@suda.edu.cn (Shen-Zhou Lu).

1 Introduction

In the past few decades, transdermal delivery has been an attractive route for drug delivery [1-3]. Skin is the largest organ in the human body. It receives one-third of the blood supply of the entire body and was not used as a drug delivery route until the end of the 20th century. The mechanism of microneedle transdermal drug delivery is to use microneedles to penetrate the tightly arranged stratum corneum of the skin [4], and directly deliver the drug to the dermis. Microneedle penetration strengthens the drug delivery channel into the skin, and the microneedle will not penetrate too deep, which can protect the human skin. The administration process is almost painless, which can improve the compliance of patients. In addition, the dosage of drugs delivered by skin is usually lower than oral drugs, which can avoid the side effects caused by unstable absorption and metabolism of drugs in gastrointestinal tract [5]. In the case where oral drug delivery is difficult, transdermal drug delivery technology can be easily applied on the skin, and provide effective blood concentration level [6].

Different forms of microneedles have different ways of releasing drugs. There are five types of microneedles: solid microneedles, hollow microneedles, swelling microneedles, soluble microneedles, and coated microneedles [7]. The main advantage of solid microneedles is their firmness, which makes it easier to penetrate the skin and can be used to pretreat the skin. Henry et al [8]. First demonstrated the increase of transdermal flux of calcein after the silicon microneedles were prepared by ion etching. Dissolving microneedles are mainly made of polymers or polysaccharides, which release drugs through dissolution after piercing the skin [9]. Hollow microneedles have the same empty cavity as a traditional hypodermic needle to deliver drugs to the skin or through the skin into the blood, but the microneedles are shorter and the flow rate can be controlled by a micropump or syringe [10]. Coated microneedles are made from a substrate coated with drugs that can be delivered quickly to the skin and increase the long-term stability of the active drug, although the amount of drug can be uncontrolled. Swelling microneedles can absorb the interstitial fluid of the skin and provide channels for drug delivery in the microneedles. When used, the integrity can be retained without residual accumulation in the skin, and it is convenient for patients to use and improve patient dependence. Swelling microneedles have the function of rate control and prolong the time of drug administration by adjusting the swelling performance [11]. Now, the most widely used is the use of microneedles to carry drugs, after the microneedle enters the epidermis, the needle body swells and the drugs enter the human skin.

Silk fibroin protein is a kind of natural polymer material with good biocompatibility and natural degradation, and rarely has sensitization reaction [12]. Silk fibroin protein can also maintain the biological activity of the drugs it carries for a long time, so it is extremely suitable for the preparation of biological materials [13]. Based on previous studies by scholars, it can be known that pure silk fibroin protein microneedles have good mechanical properties and can successfully achieve the purpose of drug release by microneedles. However, the untreated pure silk fibroin is random coil structure, its molecular chain arrangement is disordered, and water molecules can enter smoothly, which makes the microneedles dissolve quickly when contacting body fluid. In this paper, we explored the effects of proline and its derivatives on the structure and properties of silk fibroin microneedles, and explored a more balanced addition strategy to prepare the swelling silk fibroin microneedles with low solubility, high swelling and good mechanical properties. It provides new methods and ideas for the improvement of microneedle transdermal drug delivery materials.