DOI: 10.15825/1995-1191-2024-4-157-165

BIODEGRADABLE SILK-BASED PRODUCTS FOR REGENERATIVE MEDICINE

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Silk is becoming one of the key materials in contemporary bioengineering and medicine due to its unique physicochemical and biological properties. This review article discusses the main components of silk, fibroin and sericin, their structure and functional characteristics, as well as their importance in the production of biocompatible and biodegradable materials. Modern methods of modifying silk to enhance its mechanical and biological properties are considered, including physical, chemical, and genetic manipulation. The use of silk in tissue engineering, development of medical implants, controlled drug delivery systems, and biosensors is given particular consideration. In conclusion, the prospects for further silk research targeted at creating innovative biomaterials for medical applications are discussed.

Keywords: silk, silk fibroin, tissue engineering, regenerative medicine.

Silk has captivated scientists and researchers for centuries due to its remarkable properties and wide range of applications. In the modern scientific landscape, interest in silk has grown substantially owing to its unique biological, chemical, and mechanical characteristics. Its exceptional biocompatibility, biodegradability, mechanical strength, and ability to be functionalized have positioned silk as a highly valuable material in the development of medical devices and bioengineered constructs.

COMPLEX CHARACTERISTICS

As a natural biopolymer, silk stands out for its superior physical and chemical properties, distinguishing it from other natural fibers. Its two primary components – fibroin and sericin – are integral to its structure and functionality. The chemical composition and interaction between these proteins play a key role in determining silk's properties and its wide-ranging applications.

Fibroin is the primary structural component of silk, responsible for its strength and elasticity [1]. Chemically, fibroin is a polypeptide composed of long chains of amino acids that form highly ordered structures known as β-sheets. These β-sheets are stabilized by strong hydrogen bonds between adjacent polypeptide chains, contributing to fibroin's distinctive mechanical properties [2]. In addition to these beta sheets, amorphous domains may also be present within the fibroin structure, providing enhanced flexibility to the material.

The structural integrity of fibroin is further reinforced by intermolecular hydrogen bonds that stabilize its three-dimensional structure and adds to its mechanical resilience.

Fibroin's amino acid composition is predominantly glycine (~50%), alanine (~30%), and serine (~10%) [3]. The high content of glycine and alanine is crucial to its structural properties. Glycine, with its minimal side chain (a single hydrogen atom), allows for tight packing of polypeptide chains, enabling the formation of compact and stable structures. Alanine, with a slightly larger methyl side chain, further stabilizes these structures, enhancing the overall strength of the material.

The high tensile strength of fibroin makes it an ideal material for creating sutures and biocompatible implants that must endure mechanical stress within the body [4]. Its notable elasticity enhances user comfort and enables implants and sutures to adapt to tissue movement and physiological changes [5].

The physicochemical properties of fibroin are critical to its broad range of biomedical applications. These properties include hydrophobicity, chemical resistance, and the capacity to be processed into diverse structural forms. Notably, fibroin exhibits low hygroscopicity [4], which contributes to its mechanical integrity and durability in moisture-rich environments – a characteristic particularly advantageous in reducing the risk of infection in medical settings.

Its chemical stability is another significant attribute; fibroin demonstrates resistance to a wide spectrum of chemical agents, including certain acids and alkalis. This resilience enhances its suitability for use in medical devices and materials that may encounter harsh chemical conditions. Furthermore, fibroin can be fabricated into a variety of formats – such as films, gels, and sutures – thereby extending its applications [6].

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Sericin is the second major protein in silk and plays a critical role as a water-soluble binding agent that holds fibroin fibers together. Unlike the highly ordered structure of fibroin, sericin has an amorphous and less organized structure, rich in polar amino acids such as serine, tyrosine, and aspartic acid. These amino acids facilitate the formation of hydrogen bonds and strong interactions with water molecules, giving sericin its distinctive hydrophilic properties [7, 8].

Due to its high content of hydrophilic amino acids, sericin readily interacts with water, enabling it to retain moisture and form hydrogels. This property enhances its function as a natural adhesive, securing fibroin fibers and contributing to the overall integrity of silk.

The interaction between fibroin and sericin results in a cohesive and functionally efficient silk structure [9]. In natural silk cocoons, fibroin forms the structural core, while sericin coats and binds the fibers, adding strength, stability, and protection against environmental stressors.

The chemical composition of silk largely determines its suitability for various applications [10, 11]. Fibroin fibers, known for their high tensile strength and resistance to external stressors, are widely used in the production of wound dressings, medical implants, sutures, and other biomedical materials. Sericin's hydrophilic nature makes it ideal for cosmetic and medical products aimed at enhancing moisturization and adhesion.

One of silk's key advantages is its biocompatibility, a critical factor for materials used in medical and surgical procedures [5]. Silk fibroin (SF), in particular, integrates seamlessly into biological systems with minimal adverse reactions, largely due to its natural origin and favorable structural properties. As a natural protein, SF is readily recognized by the body, reducing the likelihood of inflammatory responses or immune rejection [12].

When in contact with living tissue, fibroin does not induce severe immune reactions such as inflammation or allergic responses. Its biocompatibility is further supported by its low toxicity and minimal mechanical irritation [13]. Moreover, SF actively supports tissue healing and regeneration. For example, fibroin-based films and scaffolds can function as temporary substrates that facilitate cell attachment, proliferation, and differentiation, thereby creating optimal conditions for tissue repair [14, 15].

BIODEGRADATION

Biodegradation is a crucial property of silk as it determines how silk behaves after implantation. Biodegradation refers to the process by which silk is naturally broken down and eliminated from the body through enzymatic and other biological mechanisms that degrade its polypeptide chains [16].

This property makes silk an ideal material for medical implants and other biodegradable biostructures, as it can be gradually absorbed and replaced by natural tissue. Consequently, this reduces the need for repeated surgical procedures and promotes faster patient recovery.

In addition, the biodegradation of silk products minimizes the risk of long-term inflammatory responses and other adverse effects. As a biodegradable material, silk is well-suited for creating temporary scaffolds that support tissue function until the body regenerates its lost tissue.

SF undergoes controlled biodegradation, allowing for precise regulation of the degradation timeline and rate [17]. Various processing techniques are employed to manipulate this process, including structural modifications and incorporation of specific additives [52, 53]. The biodegradation rate can also be influenced by environmental factors such as temperature, humidity, and enzymatic activity within body tissues.

It is also important to note that sericin, the second protein component of silk, is prone to biodegradation as well. Research has demonstrated that, unlike fibroin, which has a denser and more stable structure, sericin is water-soluble and, therefore, more readily biodegraded [54]. This property makes sericin particularly suitable for applications where a faster degradation rate is desired.

APPLICATION OF SILK FIBROIN IN TISSUE ENGINEERING AND REGENERATIVE MEDICINE

SF is widely used in tissue engineering, primarily to create biocompatible scaffolds that support tissue growth and regeneration [18]. Thanks to its structural strength and flexibility, SF-based matrices can be fabricated into various forms – films, scaffolds, and hydrogels – that closely mimic the natural extracellular matrix of tissues. These matrices facilitate cell adhesion, proliferation, and differentiation, making them effective in regenerating skin, bone, cartilage, and other tissues.

Research has shown that SF scaffolds promote the growth and migration of various cell types, including fibroblasts, osteoblasts, and chondrocytes, thereby aiding in the regeneration of damaged tissues [14, 15, 19]. Furthermore, SF can be modified with bioactive molecules, such as growth factors, to enhance its interaction with cells and further accelerate the regenerative process.

Examples of SF applications in tissue engineering include the creation of skin coatings for treating burns and wounds, as well as bone and cartilage substitutes [10, 14, 19]. Silk-based scaffolds and hydrogels can serve as temporary implants to support tissue regeneration following surgical procedures. In some cases, these materials are combined with other biomaterials, such as collagen or hyaluronic acid, to enhance both their mechanical strength and biological properties. Additionally, ongoing research focuses on creating three-dimensional printed structures made from silk proteins, which could be used for precise reconstruction of complex anatomical structures [20].

MEDICAL IMPLANTS

Silk is also widely employed in the production of medical implants [21]. A well-known example is surgical suture materials, which offer high tensile strength and minimal immune response [22]. Beyond sutures, silk proteins are used in developing a range of implants, including skeletal fixators, vascular prostheses, and devices for nerve tissue repair. The biocompatibility and mechanical strength of these silk-based implants ensure their stable integration with biological tissues and reliable long-term function.

For instance, SF-based skeletal fixators are used to stabilize and support bone structures in the treatment of fractures and other bone injuries [23, 24]. Unlike traditional metal fixators, silk-based structures are immune to corrosion and can be fully bioresorbable once the healing process is complete. This property reduces the risk of long-term complications and eliminates the need for additional surgeries to remove the fixators.

Silk vascular prostheses are being developed as replacements for damaged or blocked blood vessels [25–27]. Due to its excellent mechanical properties, silk can be processed to replicate the elasticity and strength of natural blood vessels. Furthermore, these silk prostheses can be modified to enhance anticoagulant properties, which helps reduce the risk of thrombosis.

In nerve tissue repair, silk scaffolds are being developed to support the growth and directed repair of nerve fibers [28]. Silk can be used to create microtubules and other structures that guide axon growth, promoting functional recovery from peripheral nervous system injuries. Experimental studies have shown that silk-based implants can significantly enhance nerve fiber regeneration, restoring both sensory and motor functions in animal models [29–32].

CONTROLLED DRUG DELIVERY

Controlled drug delivery is another significant application of silk proteins in medicine. SF microspheres and nanoparticles can be used to encapsulate and deliver a range of drugs, including antibacterial agents, anticancer drugs, and proteins. The unique properties of fibroin allow for the regulation of drug release rates, enabling sustained and controlled therapy [33, 34].

For example, fibroin nanoparticles can be used to deliver anticancer drugs directly to tumor cells, minimizing damage to healthy tissues and reducing side effects [35]. Additionally, fibroin microspheres are ideal for vaccine delivery, providing a gradual release of antigens and stimulating a sustained immune response [36, 37]. This approach is particularly valuable for the development of vaccines targeting chronic infections and cancers, where long-term and stable immune system activation is essential.

BIOSENSORS AND DIAGNOSTIC DEVICES

Recently, researchers have been exploring the use of silk in the development of biosensors and diagnostic devices. Thanks to its biocompatibility and functionalizability, silk provides an ideal foundation for sensors that can detect biomolecules, pathogens, and other critical analytical targets [38]. These sensors have potential applications in disease diagnosis, treatment monitoring, and the development of personalized medical strategies.

Examples of silk-based biosensors include devices designed to monitor glucose levels in diabetic patients, detect specific biomarkers for early cancer diagnosis, and track the condition of wound surfaces to prevent infections [39, 40]. These sensors are not only useful in medical settings but can also be employed in home care, making diagnostics more accessible and convenient for patients. Furthermore, they can be integrated into wearable medical devices, enabling continuous monitoring of a patient's condition and facilitating early detection of any changes [55].

MODIFIED SILK

Genetically modified silkworms can produce silk enriched with functional peptides and proteins, such as antibacterial agents or growth factors [41]. These genetically modified silks may exhibit enhanced mechanical and biological properties compared to natural silk. For instance, the incorporation of genes encoding elastin-like peptides can improve the elasticity and strength of silk fibers [56]. Additionally, the addition of antimicrobial peptides can make silk more resistant to bacterial infections [57].

Silk proteins are also used in the fabrication of composite materials with enhanced properties. By combining SF with other biomaterials, such as collagen, chitosan, or carbon nanotubes, it is possible to create materials with unique mechanical and biological characteristics [42–44]. These composites have applications in medical implants, tissue engineering, and biosensors. For example, composites made from SF and carbon nanotubes show potential in cardiac tissue engineering for heart repair [45].

Chemical modification of fibroin involves adding various functional groups and molecules to its surface [46]. For instance, incorporating antibacterial agents can make fibroin resistant to bacterial infections [47]. Additionally, modification with growth factors and other bioactive molecules enhances the interaction of silk fibroin (SF) with cells, promoting regenerative processes. Chemically modified fibroin has been shown to significantly improve tissue engraftment and regeneration [48].

Physical modification of silk focuses on altering its structure and morphology to enhance its mechanical and biological properties. For example, creating porous structures can improve permeability and biocompatibility, which is crucial for tissue engineering applications [49, 50]. Nanotechnology enables the fabrication of silk nanostructures with unique properties, such as increased strength and elasticity. Furthermore, physically modified SF has been shown to improve cell adhesion and proliferation, which aids in tissue regeneration and wound healing.

COMPARATIVE CHARACTERISTICS OF SILK-BASED MATERIALS AND THEIR APPLICATIONS

To clearly compare the characteristics of silk-based materials in various fields of application, Table provides an overview of key properties and benefits. It summarizes the use of fibroin and other silk components in tissue engineering, medical implants, biosensors, and drug delivery systems.

Table

Silk application in medicine and biotechnology

Area of application	Material	Product	Result	Manufacturing method	Article
Tissue engineering	Fibroin	Corneal regeneration membranes	Stimulates cell growth, supports cell functional activity	Irrigation method	[14, 15]
Tissue engineering	Natural silk fabrics	Tissue regeneration scaffolds	Supports tissue regeneration	Chemical treatment of silk fabrics	[18]
Tissue engineering	Fibroin	Bone regeneration scaffold	Supports cell growth and regeneration	Irrigation method, freeze-thaw	[19]
Medical implants	Silk threads	Surgical threads	Minimal body reaction	Antibacterial treatment, thread tube weaving	[22]
Medical implants	Silk threads	Vascular prostheses	Enhanced tissue integration, excellent biocompatibility	Electrospinning	[25]
Medical implants	Silk threads	Endovascular prostheses	Reliability and long-term stability	Thread tube weaving, chemical treatment	[26]
Medical implants	Silk threads	Elastic vascular prostheses	Reduced risk of thrombosis	Thread tube weaving, chemical treatment	[27]
Neuroregeneration	Fibroin	Nerve regeneration hydrogels	Enhanced regeneration	Chemical modification	[29]
Neuroregeneration	Fibroin	Regeneration nanofiber tubes	Directed growth support	Electrospinning	[30]
Neuroregeneration	Fibroin	Nerve scaffolds	Accelerated regeneration	3D printing	[31]
Neuroregeneration	Fibroin	Hydrogels loaded with stem cells for brain regeneration	Function restoration after stroke	Cell integration into hydrogels	[32]
Drug delivery	Fibroin nanoparticles	Encapsulation of anticancer drugs	Precise delivery, minimization of side effects	Encapsulation	[35]
Drug delivery	Fibroin	Microspheres for DNA vaccine delivery	Improved immunogenicity	Encapsulation	[36]
Drug delivery	Fibroin	Microneedles for transdermal vaccine delivery	Efficient and painless delivery	Chemical treatment, casting of needle molds	[37]
Biosensors	Fibroin	Electrochemical glucose biosensors	Continuous glucose monitoring	Chemical treatment, casting of needle molds	[39]
Biosensors	Fibroin	Colorimetric biosensors on stable platforms	Accurate diagnosis, reuse	Chemical modification	[40]
Genetically modified silkworm	Fibroin	Components for enhancing mechanical properties	Enhanced mechanical properties	Use of transgenic silkworms	[41]
Tissue engineering	Fibroin	Composite matrices for bone regeneration	Enhanced cell adhesion and proliferation	Modification with nano-hydroxyapatite and gelatin	[42]

End of table

Area of application	Material	Product	Result	Manufacturing method	Article
Tissue engineering	Fibroin	Cardiomyocyte matrices	Enhanced cardiomyocyte function	Electrospinning	[45]
Chemical modification	Fibroin	Modified fibroin	Enhanced properties	Serine-based chemical modification	[46]
Tissue engineering	Fibroin	Hydrogels for growth factor delivery	Growth factor delivery	Chemical treatment, UV irradiation	[48]
Tissue engineering	Fibroin	Hydrogels for bone tissue engineering	Enhanced properties	Sequential addition and porogen leaching	[50]
Medical implants	Fibroin Antheraea pernyi	Modified implants	Increased resistance to degradation	Acylation by succinyl anhydride	[52]
Pharmacology	Fibroin-based nanoparticles	Nanocapsules for drug delivery	Controlled drug release	Self-organization of fibroin into nanostructures	[53]
Biosensors	Fibroin	Biosensors and wearable devices	Continuous health monitoring	Formation of flexible fibroin films	[55]
Genetically modified silkworm	Transgenic silk with antibacterial peptides	Antibacterial sutures	Resistance to bacterial infections	Genetic modification of silkworms	[57]

CONCLUSION

Silk and fibroin continue to be among the most promising materials for research and development across a range of scientific disciplines. The growing scientific interest in silk is driven by its unique properties and broad potential for application in various fields.

A primary area of focus is the development of innovative biomedical materials. For example, biodegradable silk- and fibroin-based implants are being investigated for their potential to repair damaged tissues and organs [51]. Ongoing research aims to create advanced dressings and suture materials that offer enhanced mechanical properties and promote tissue regeneration [18].

The authors declare no conflict of interest.

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The article was submitted to the journal on 13.08.2024