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Pavithra MR
Young Professional, Central Silk
Board, Bengaluru, Karnataka,
India

Vishaka GV
Scientist-C, Central Silk Board,
Bengaluru, Karnataka, India

Ashrith S
Post graduate, Department of
Sericulture, University of
agricultural Science, GKVK,
Bengaluru, Karnataka, India

Sericin as a Multifunctional Biomaterial: A Comprehensive Review of Structure, Properties, Extraction and Application

Pavithra MR, Vishaka GV and Ashrith S

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Abstract

Sericin a natural silk protein secreted by the middle silk gland of the silkworm (*Bombyx mori*), is emerging as a valuable biomaterial in the fields of biomedical science. Once considered a waste product and discarded during the silk degumming process, sericin is now recognized for its exceptional physicochemical and biological properties, including biocompatibility, biodegradability, antioxidant activity, UV protection and strong moisture-retaining capacity. Composed of 18 amino acids-particularly rich in serine, glycine and aspartic acid-sericin exhibits a wide molecular weight range (20-400 kDa), allowing for functional versatility in both low- and high-molecular-weight forms. These properties enable sericin to serve multiple roles in cosmetic formulations such as moisturizers, anti-aging creams, sunscreens and hair care product, where it enhances skin hydration, elasticity and protection against oxidative stress and photoaging. In biomedical applications, sericin is gaining ground as a key ingredient in wound healing dressings, tissue engineering scaffolds, drug delivery systems and biofilms due to its ability to promote cell adhesion, proliferation and collagen synthesis. Advanced extraction methods-such as hot water treatment, enzymatic hydrolysis, microwave-assisted processes and eco-friendly solvents-allow for the recovery of sericin in its active form, further expanding its use. Recent research has also demonstrated sericin potential in developing hydrogels, nanofibers and biodegradable composites for regenerative medicine. As innovation in sericulture broadens to include not just silk fiber but also high-value bioactive byproducts like sericin, the industry is undergoing a transformative shift toward a sustainable, circular bioeconomy. This article reviews the structure, composition, extraction technologies, functional properties and innovative uses of sericin, highlighting its role in redefining sericulture as a multidisciplinary biotechnology sector with applications far beyond traditional silk production.

Keywords: Sericin, *Bombyx mori*, Silk protein, Silk fibroin, Biomaterial

1. Introduction

Sericulture has historically been centered on silk fiber production, with fibroin-the structural core protein of silk-being the primary component of economic value (Alipanah *et al.*, 2020) [2]. Fibroin, known for its exceptional mechanical strength, luster and biocompatibility has long dominated commercial and research interest. However, a significant byproduct of silk processing is sericin the gummy, water-soluble glycoprotein that binds fibroin filaments within the silkworm cocoon. Despite accounting for nearly 20-30% of the cocoon total weight, sericin was traditionally discarded during the degumming process, treated as a low-value waste due to its solubility and lack of direct use in fiber production.

This disposal, primarily through reeling wastewater, has posed environmental concerns, particularly in silk-producing countries like India and China. The biochemical oxygen demand (BOD) and chemical oxygen demand (COD) of sericin-rich effluent are significantly high, leading to water pollution and eutrophication in nearby water bodies. Paradoxically, what was once treated as a pollutant has now emerged as a valuable biomaterial, attracting attention from biotechnologists, cosmetic chemists and medical researchers due to its unique structure and diverse bioactivity. Sericin is composed of 18 amino acids, particularly rich in serine, threonine, alanine and aspartic acid, which impart high moisture-retaining, antioxidant and UV-protective properties. Its biocompatibility, biodegradability and non-toxic nature make it ideal for topical

Corresponding Author:
Pavithra MR
Young Professional, Central Silk
Board, Bengaluru, Karnataka,
India

and internal biomedical applications. Additionally, the presence of multiple functional groups (-OH, -COOH, -NH₂) provides opportunities for chemical modification and drug conjugation, essential for advanced medical formulations like hydrogels, scaffolds and controlled drug delivery systems (Altman *et al.*, 2003)^[3].

Driven by this newfound relevance, recent innovations in sericulture have expanded beyond cocoon productivity. The industry now focuses on holistic utilization of all silk components, embracing a "waste-to-wealth" approach. Techniques have been developed to recover sericin in bioactive form using green extraction methods such as enzymatic hydrolysis, supercritical fluid extraction and subcritical water technology, thereby minimizing chemical usage and aligning with environmentally sustainable practices. This revalorization of sericin is opening up a new paradigm in biocosmetics and biomedicine. In skincare, it is used in anti-aging creams, moisturizers, sunscreens and shampoos due to its moisturizing, film-forming and UV-absorbing capabilities. In biomedical research, sericin is being developed into wound dressings, tissue engineering scaffolds, antimicrobial coatings and bioactive drug carriers. Studies have shown that sericin accelerates wound healing, supports fibroblast and keratinocyte proliferation and possesses anti-inflammatory and immunomodulatory properties, making it highly suitable for clinical and therapeutic applications (Kongprayoon *et al.*, 2022)^[16].

Consequently, the sericulture industry is undergoing a strategic transformation from a fiber-centric to a biocomposite-centric model. This shift is not only enhancing the economic viability of sericulture by creating new market avenues but is also contributing to sustainable development goals by reducing industrial waste and promoting green innovation. By integrating biotechnology and traditional silk farming, sericulture is being redefined as a multidisciplinary biotech enterprise poised to play a significant role in the next generation of bioproducts and therapeutics.

2. Structure and composition of sericin

Sericin is a natural, water-soluble glycoprotein produced by the silkworm during cocoon formation. It acts as a cementing material, enveloping and binding the two fibroin filaments (brins) that constitute the silk fiber (Fig.1). Unlike fibroin, which is the inner structural protein of silk threads, sericin makes up the outer coating and is often removed during the degumming process in silk reeling (Omenetto FG *et al.*, 2010)^[28].

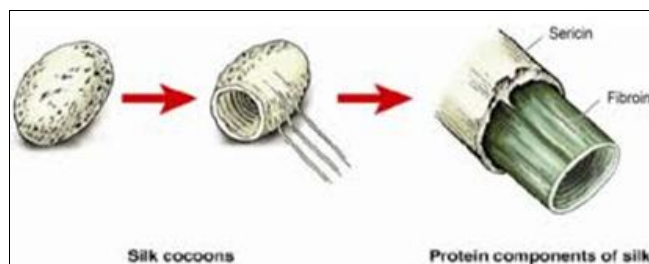


Fig1: Structure of Sericin Layer

2.1 Chemical composition and structure of sericin

Sericin is a globular protein extracted from silk, with a complex of two fibroin filament together, amorphous and loosely packed structure compared to the crystalline structure of fibroin. It consists of random coil and beta-sheets. Its structure is influenced by the silkworm genetics, the location of silk gland and environmental conditions like temperature, humidity, rainfall

(Rony aad *et al.*, 2024)^[30]. Sericin exhibits water solubility at temperatures above 50 °C; however, its solubility progressively declines at lower temperatures. This reduction in solubility promotes the structural transformation of sericin from a random coil to β -sheet conformation, ultimately leading to gel formation (Kunz *et al.*, 2016)^[21]. (Kweon *et al.*, 2000)^[22] investigated the influence of poloxamer, a polymeric surfactant, on sericin gelation and observed that its addition significantly accelerated the transition from random coils to β -sheets. Furthermore, they reported that sericin gelation occurs more rapidly at elevated temperatures and higher sericin concentrations. In a chromatographic study, (Takasu *et al.* 2002)^[23] explained that sericin remains water-soluble within the silk gland, but loses this solubility upon spinning and drying. This loss is attributed to the formation of β -sheet structures during the drying process, which reduces sericin's solubility compared to its amorphous, random coil state.

Sericin is a hydrophilic protein rich in hydroxyl, carboxyl groups, and polar amino acids. While serine is the dominant amino acid, sericin also comprises 17 other amino acids (alanine, arginine, aspartic acid, cysteine, glutamic acid, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, threonine, tryptophan, tyrosine and valine). This diverse amino acid composition contributes to the formation of distinct sericin variants SER-1, SER-2 and SER-3 each differing in amino acid profile and molecular weight. Morphologically and functionally, the silk gland is divided into three distinct regions i.e, anterior, middle and posterior (secreted mainly by the middle and anterior parts) each playing a specialized role in sericin production.

- **Sericin 1:** The outermost layer, rich in serine and acidic amino acids.
- **Sericin 2:** The middle layer, located between sericin A and fibroin; it contains more hydrophobic amino acids.
- **Sericin 3:** The innermost layer in direct contact with fibroin, relatively less hydrophilic.

These layers differ in their biochemical and solubility properties, making them functionally distinct and useful in various applications.

2.2 Physical properties

Sericin A, B, and C each localized in different layers of the silk that vary in its composition and solubility. Sericin A, found in the outermost layer, is water-soluble at warm temperatures and contains approximately 17.2% nitrogen. Its amino acid profile is predominantly composed of serine, threonine, glycine, and aspartic acid. Sericin B, located in the intermediate layer, contains 16.8% nitrogen and shares a similar amino acid composition with Sericin A, with the additional presence of tryptophan. Sericin C, residing in the innermost layer adjacent to fibroin, is insoluble in hot water, possesses the lowest nitrogen content (16.6%), and includes all the amino acids of A and B along with proline. It can be selectively removed from fibroin by treatment with hot acidic or alkaline solutions. Despite its beneficial properties, sericin is highly susceptible to thermal and pH-induced degradation, as well as solvent sensitivity, making the preservation of its native structure a major challenge. This structural instability is primarily due to conventional degumming processes, which often involve high temperatures, elevated pressures, or alkaline treatments, all of which accelerate sericin degradation and limit its functional applications in sericin-based material synthesis. Color and texture of the sericine is yellowish to light brown and gummy texture (Das *et*

et al., 2021) [10].

2.3 Biological property

Sericin has gained recognition as a multifunctional biomaterial due to its wide array of beneficial properties that support its application across diverse domains. One of its most important features is biocompatibility, which denotes the material's capacity to interface with biological tissues without eliciting harmful immune responses. This attribute is particularly crucial for medical and therapeutic uses, as sericin demonstrates minimal immunogenicity when in contact with living cells, thereby lowering the likelihood of inflammation or rejection. This makes it an excellent candidate for integration into biomedical fields, including wound repair, regenerative medicine, and targeted drug delivery systems (Hu *et al.*, 2018) [14]. Another defining quality of sericin is its biodegradability, which aligns with environmentally conscious biomedical design. In biological environments, sericin can be enzymatically degraded by proteases into smaller peptides and amino acids making it a sustainable and non-toxic material. However, while its short-term safety is well-supported, the long-term biological fate of sericin and its degradation products remains insufficiently understood. Comprehensive research is still required to determine how these breakdown components interact with bioactive molecules within the body, and whether they might produce unintended physiological effects (Holland *et al.*, 2019) [13].

Beyond its biocompatibility and biodegradability, sericin also displays a wide spectrum of functional activities. It exhibits anti-inflammatory, antibacterial, antioxidant, and UV-protective effects, which make it valuable in fields ranging from dermatology to food preservation and textile technology. The anti-inflammatory potential of sericin is linked to its regulatory effect on pro-inflammatory cytokines like interleukin-1 (IL-1) and tumor necrosis factor- α (TNF- α), both central players in inflammatory responses. Its antimicrobial effect is largely attributed to its cysteine content. The sulfhydryl group of cysteine is capable of forming weak hydrogen bonds with nitrogen and oxygen, disrupting essential enzymatic and metabolic activities in microbial cells (Silva *et al.*, 2022) [32]. Sericin antioxidant capacity further enhances its utility, especially in skincare and anti-aging products. This function is

driven by its ability to neutralize reactive oxygen species (ROS). Amino acids such as serine and threonine contribute to this activity by chelating transition metals like iron and copper, which are catalysts for oxidative damage. By reducing oxidative stress, sericin helps delay cellular aging processes. Moreover, the presence of arginine and alanine enhances its anti-tyrosinase properties, as these amino acids can bind to tyrosinase enzymes, inhibiting melanin production—a key application in skin whitening and pigmentation control.

2.4. Molecular weight

Sericin molecular weight which is influenced by various factors that extracted from natural source or biotechnology techniques and also from extraction methods, pH and processing time (Aramwit *et al.*, 2007) [4]. It exists in various molecular weight forms (from 20 kDa to 400 kDa) which are classified into:

- High molecular weight: >200 kDa - viscous, less soluble
- Medium molecular weight: 50-200 kDa most bioactive
- Low molecular weight: <50 kDa easily absorbed, used in cosmetics and biomedical applications

3. Extraction techniques

Sericin, the gummy protein coating the fibroin filaments in silkworm cocoons, is typically removed during the degumming process of silk reeling. Traditionally discarded as waste, sericin is now recognized for its bioactive properties and extracted through various methods to preserve its functional integrity for industrial, cosmetic, pharmaceutical and biomedical applications (Rockwood *et al.*, 2011) [29]. These extraction methods have distinct advantage and disadvantage and limitation.

3.1 Conventional extraction methods

a. Hot Water Extraction

- **Principle:** Sericin is soluble in hot water, especially at temperatures above 90°C.
- **Process:** Cocoons or silk waste are boiled in distilled or deionized water for 30-120 minutes.
- **Advantages:** Simple and lower environmental impact, chemical-free, preserves bioactivity.
- **Limitations:** Low yield and extraction efficiency; some protein degradation, especially at high temperatures or with prolonged exposure (Fig.2) (Chirila *et al.*, 2016) [9].

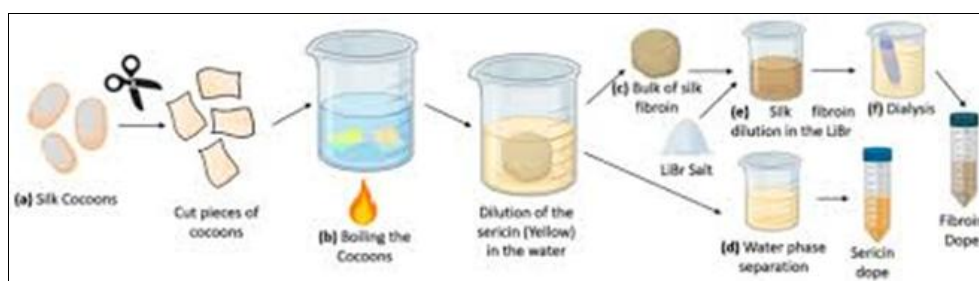


Fig 2: Extraction of Sericin by Hot Water Method

3.2 Chemical extraction

b. Alkaline Extraction

- **Agents Used:** Sodium carbonate (Na_2CO_3), sodium hydroxide (NaOH) or mild soaps.
- **Process:** Cocoons are boiled in dilute alkali (e.g., 0.5-1% Na_2CO_3) for 30-60 minutes.
- **Advantages:** Commonly used in silk degumming, higher yield than hot water.
- **Limitations:** May cause partial degradation of sericin; requires pH neutralization and proper disposal.

c. Acid Extraction

- **Agents Used:** Citric acid, acetic acid, hydrochloric acid (HCl), etc.
- **Process:** Cocoons are treated with dilute acid solution under controlled temperature and time.
- **Advantages:** Can yield low-molecular-weight sericin useful for cosmetics.
- **Limitations:** Risk of hydrolysis; may require pH adjustment and purification.

3.3 Biological extraction method

d. Enzymatic Extraction

- **Enzymes Used:** Proteases such as papain, trypsin, alcalase and bromelain.
- **Process:** Cocoon material is incubated with specific enzymes at optimal pH and temperature.
- **Advantages:** Eco-friendly preserves functional groups, selective extraction.
- **Limitations:** Cost of enzymes; longer processing time.

3.4 Modern Extraction Method

e. Ultrasound-assisted extraction (UAE)

- **Principle:** High-frequency ultrasonic waves disrupt silk fiber matrix, enhancing sericin release.
- **Process:** Cocoons are sonicated in water or buffer solution.
- **Advantages:** Accelerated extraction, better yield and low temperature.
- **Limitations:** Equipment cost is high, scale-up challenges.

f. Microwave-assisted extraction

- **Principle:** Microwave radiation heats the sample rapidly, breaking molecular bonds and enhancing protein release.
- **Process:** Cocoons are treated in a microwave system with water or mild solvents.
- **Advantages:** Fast, energy-efficient and minimal chemical use.
- **Limitations:** Potential for thermal degradation at high power or prolonged exposure.

g. Autoclaving (Pressure cooking)

- **Process:** Cocoons are autoclaved at 121°C and 15 psi for 15-30 minutes in distilled water.
- **Advantages:** High-temperature sterilization, quick and effective for large-scale processing.
- **Limitations:** Can denature high-molecular-weight sericin; recovery of functional proteins may be reduced. Sericin extracted through autoclaving lacks α -helical structures (Kumar *et al.*, 2017) ^[19].

h. Supercritical CO₂ extraction (Emerging technique)

- **Principle:** Uses supercritical carbon dioxide with co-solvents to extract biomolecules.
- **Advantages:** Non-toxic, solvent-free residues and controlled extraction.
- **Limitations:** High operational cost; still under research for sericin.

Comparison table of techniques

S No.	Method	Yield	Eco-Friendliness	Cost	Preservation of Bioactivity
1	Hot Water	Low	High	Low	Moderate
2	Alkaline	Moderate	Moderate	Low	Moderate
3	Acid	Moderate	Moderate	Low	Low-Moderate
4	Enzymatic	High	High	High	High
5	Ultrasound	High	High	Moderate	High
6	Microwave	High	High	Moderate	Moderate-High
7	Autoclave	Moderate	High	Low	Moderate
8	Supercritical CO ₂	Moderate	Very High	Very High	Very High

The method used to extract sericin significantly influences its structural and functional properties, which in turn affect its suitability for biomedical applications. Extraction techniques

such as hot water, alkaline, acidic, and acidic treatments yield sericin with varying amino acid compositions and structural conformations. For instance, hot water extraction tends to preserve higher levels of sulfur-containing amino acids like methionine and cysteine, which are crucial for promoting cell proliferation and collagen synthesis. These amino acids contribute to the formation of β -sheet structures, enhancing the protein's stability and bioactivity. Conversely, harsher chemical extraction methods can lead to the degradation of sericin's secondary structures, such as β -sheets and β -turns, potentially diminishing its biological efficacy. Maintaining the integrity of these structures is essential, as they influence cell behavior, including adhesion and proliferation (Das *et al.*, 2021) ^[10].

4. Properties of Sericin

Sericin, the outer protein coating of silk fibers secreted by the silkworm, is gaining significant attention for its diverse biological properties (Rony aad *et al.*, 2024) ^[30]. Previously considered a waste product during silk processing, sericin is now valued for its biocompatibility, bioactivity and environmental sustainability. These biological attributes make it an important biomaterial in pharmaceuticals, cosmetics, agriculture and biomedical engineering (Franco *et al.*, 2019) ^[12].

Key Biological Properties of Sericin

1. Biocompatibility

- Sericin is non-toxic, non-immunogenic, and biodegradable, making it safe for use in contact with living tissues.
- It promotes cell adhesion, growth and proliferation especially fibroblasts and keratinocytes.
- Due to its biocompatibility, sericin is widely used in wound healing, tissue engineering scaffolds and drug delivery systems.

2. Antioxidant Activity

- Sericin contains amino acids like serine, threonine and tyrosine, which scavenge free radicals and inhibit oxidative damage.
- It protects skin and tissues from UV radiation, pollutants and aging
- This property is crucial for cosmetic formulations such as anti-aging creams and sunscreens.

3. Antimicrobial and Antibacterial Activity

- Sericin exhibits broad-spectrum antimicrobial effects against bacteria like *Staphylococcus aureus*, *E. coli* and *Pseudomonas aeruginosa*.
- Its natural antimicrobial property helps in wound dressing materials and medical textiles.
- It reduces microbial contamination in cosmetic and pharmaceutical formulations.

4. Anti-inflammatory Activity

- Sericin inhibits the release of pro-inflammatory cytokines and reduces inflammation in damaged tissues.
- It is effective in treating burns, wounds, and skin irritations by accelerating healing and reducing redness/swelling.

5. Moisturizing and Hydrating Effects

- High hydrophilicity due to abundant polar amino acids (*e.g.*, serine) helps retain moisture on skin.
- It forms a thin film that prevents water loss, making it suitable for moisturizers lotions, and hair conditioners.

- Helps manage dry skin eczema, and dermatitis.

6. UV Protection

- Sericin absorbs ultraviolet (UV) radiation, preventing photo-damage to skin.
- Acts as a natural UV barrier, useful in sunscreens and protective skincare products.

7. Anticancer and Antitumor Activity

- Some studies suggest sericin may inhibit tumor cell proliferation, particularly in colon and skin cancers.
- It induces apoptosis (programmed cell death) in cancer cells without affecting normal cells.
- More clinical research is required to confirm its therapeutic role (Blake *et al.*, 2021) ^[6].

8. Hypcholesterolemic and Anti-obesity Effects

- Animal studies show that dietary sericin may reduce cholesterol levels, inhibit lipid absorption, and control weight gain.
- Potential application as a functional food or nutraceutical ingredient

9. Wound Healing and Regeneration

- Enhances collagen synthesis angiogenesis (new blood vessel formation), and tissue remodeling
- Accelerates wound closure and improves skin regeneration in burn and surgical wound treatments.

10. Anticoagulant and Blood Compatibility

- Sericin shows minimal blood clotting effect, ensuring compatibility in blood-contacting medical devices.
- Helps prevent thrombosis in vascular grafts and stents.

The biological properties of sericin reflect its potential as a natural, safe, and multifunctional biomaterial. Its diverse therapeutic and cosmetic roles make it a powerful ingredient in modern sericulture innovation, extending the value chain far beyond silk fiber production. By transforming this once-discarded protein into a high-value bioproduct, sericulture is evolving into a more sustainable, health-conscious, and economically rewarding enterprise.

5. Applications in Biomedical Fields

Sericin, the silk glue protein secreted by the silkworm, is rapidly gaining significance in biomedical sciences due to its biocompatibility, biodegradability, non-toxicity, and bioactivity. Traditionally discarded as a waste product during silk reeling in sericulture, sericin is now being harnessed for various therapeutic, pharmaceutical, and tissue-engineering applications, transforming sericulture into a biotechnology-oriented sector.

5.1 Wound Healing

Silk fibroin, a biodegradable protein derived from the cocoons of sericulture, is emerging as a versatile and biocompatible biomaterial for advanced wound care. Its remarkable mechanical strength, low immunogenicity, and ease of processing into multiple formats make it ideal for facilitating tissue regeneration and supporting skin repair (Borges A *et al.*, 2024) ^[7].

Material Formats & Their Roles

1. Silk Films: Thin peptide-based membranes that conform closely to wounds, acting as protective barriers that maintain

moisture and support cell adhesion. In animal models, they have outperformed collagen films by promoting faster fibroblast attachment and facilitating full-thickness skin healing within seven days, with minimal inflammation.

2. Silk Sponges and Scaffolds: Porous constructs made via gas foaming, salt porogens, lyophilization, or electrospinning. These absorbent matrices support fibroblast and keratinocyte infiltration and guide tissue regrowth, particularly in high-exudate wounds (Biman *et al.*, 2009).

3. Silk Hydrogels: Soft, highly hydrated networks that sustain a moist wound milieu, essential for effective healing. These hydrogels can be loaded with therapeutic agents such as growth factors (e.g., FGF-1) or combined with synthetic collagen-like proteins. One recent innovation-PASCH (Photo-activated Silk fibroin and Collagen-like protein Hydrogel) uses visible blue-light crosslinking and has shown accelerated closure and reduced inflammation in diabetic and burn wound models.

4. Silk Sutures: Natural silk sutures have been used in surgery for centuries. Purified silk fibroin is less inflammatory than traditional sericin-containing silk, offering strong and biocompatible closure for skin wounds (Franco *et al.*, 2019) ^[12].

How Silk Accelerates Healing

Silk fibroin supports healing through multiple synergistic pathways:

1. Moisture Retention & Barrier Function

It creates a moist wound environment that facilitates cellular activities and limits contamination-key to rapid tissue repair and reduced scarring.

2. Cell Proliferation, Migration & Re-epithelialization

SF enhances fibroblast and keratinocyte growth, supporting re-epithelialization and dermal regeneration. Its structural similarity to natural extracellular matrix and controlled release of factors (e.g. VEGF, EGF) further enhance closure.

3. Angiogenesis Promotion

SF can modulate key signaling pathways (NF- κ B, MAPK, AKT/mTOR, TGF- β) to accelerate blood vessel formation and tissue remodeling.

4. Low Inflammation & Immunogenicity

SF triggers minimal immune response and reduces scarring compared to many synthetic or collagen-based dressings.

5. Antimicrobial & Responsive Potential

When combined with antibacterial agents or nanoparticles (e.g. cerium oxide), SF dressings can directly reduce infection risk. Emerging smart hydrogels respond to wound environment cues (like pH, temperature, redox state) to release healing agents as needed (Borges *et al.*, 2024) ^[7].

Key Benefits

- **Reduced Scarring:** By guiding organized tissue regeneration and minimizing excess inflammation, SF enables aesthetically and functionally superior wound repair.
- **Tailorable Therapeutic Delivery:** SF matrices support controlled and sustained release of growth factors, antimicrobials, and other bioactives as the wound evolves.

- **Stimuli-Responsive Features:** Smart SF hydrogels that detect and respond to micro-environmental changes offer next-generation wound dressings that adapt to the wound state.

5.2 Drug Delivery Systems

Sericin is used to prepare nanoparticles, microspheres, and hydrogels for sustained drug release. Its functional groups allow easy conjugation with drugs or targeting ligands (Kundu *et al.*, 2013)^[20].

1. **Silk Nanoparticles:** Silk fibroin nanoparticles can encapsulate drugs-small molecules, proteins, or nucleic acids to safeguard them from degradation and enhance pharmacokinetics. These particles are often engineered to respond to stimuli like pH, temperature, or light, enabling controlled and targeted release in wound environment. For example, silk-fibroin nanoparticles loaded with both plant extract (*Avicenna marina*) and neomycin were aerosolized and applied as a spray. They exhibited potent antibacterial and antioxidant effects and drove complete fibroblast scratch closure in 24 hours, outperforming antibiotic-only controls (Wang *et al.*, 2010)^[34].
2. **Silk Hydrogels:** Silk fibroin hydrogels serve as excellent carriers for localized, sustained delivery of therapeutic agents in tissue repair. They can be formed in situ and tuned for mechanical stability and drug release profiles. Sericin-decorated silk hydrogels have also been formulated to disperse hydrophobic actives like curcumin or silver nanoparticles. The resulting SF/sericin-curcumin/Ag hydrogels reduced oxidative stress and inflammation, provided antibacterial protection, and accelerated healing through improved angiogenesis (Kumar dan *et al.*, 2022)^[17].
3. **Silk Films & Coatings:** Thin silk films can be applied to medical devices, implants, or wound beds to enable localized drug release, prevent infections, and support tissue repair. While specific wound healing film studies weren't located, this form is known for offering protective, drug-eluting coatings in biomedical settings.
4. **Silk Microneedles:** Microneedle arrays made of silk fibroin-especially hydrogel-forming variants-offer minimally invasive transdermal delivery. They can swell and form porous networks in situ, ensuring controlled release of encapsulated molecules through the skin barrier. Silk fibroin/hyaluronic acid interpenetrating-network microneedles loaded with insulin maintained normoglycemia in diabetic mice for around 6 hours, demonstrating effective transdermal delivery and mechanical robustness (Zhang *et al.*, 2009)^[36].
5. **Sericin-Based Systems:** Silk sericin-when integrated into alginate nanoparticles or hydrogels-enhances drug delivery performance. Sericin-loaded alginate nanoparticles (70-90 nm) exhibited biphasic release (initial burst followed by sustained phase) at skin-like pH and temperature, and markedly reduced inflammation in animal models. Such carriers are well-suited for topical delivery of anti-inflammatory drugs or co-loading with antimicrobials in wound dressings.

Why Silk is Ideal for Drug Delivery

- **Prolonged & controlled release:** Silk carriers can deliver drugs over days or even weeks, reducing dosing frequency and improving compliance.
- **Protection of sensitive drugs:** Silk matrices stabilize

fragile molecules like proteins, preventing degradation before they reach their target.

- **Tunability:** By adjusting silk concentration, crosslinking methods, or combining with other polymers (e.g. sulfonated silk, PVA, sericin), release rates and mechanical behavior can be precisely tailored.
- **Stimuli responsiveness:** Silk nanoparticles or hydrogels can respond to environmental cues-like pH shifts or glucose levels-to release drugs on demand. Silk, especially fibroin and sericin, offers a highly versatile platform for advanced drug delivery systems-whether as nanoparticles, hydrogels, films, or microneedles. Each format brings unique advantages in controlling release kinetics, protecting bioactive agents, and enabling minimally invasive dosing. Ongoing research continues to push boundaries by combining silk with other responsive materials and loading strategies to deliver therapeutic agents precisely where and when they are needed most.

5.3 Tissue Engineering

Silk fibroin a protein derived from silkworms, has garnered significant attention in tissue engineering due to its exceptional biocompatibility, mechanical strength, and versatility. Here's an overview of its applications across various tissues (Kasoju *et al.*, 2012)^[15].

1. **Bone Tissue Engineering:** Silk fibroin scaffolds serve as robust frameworks for bone regeneration. When combined with hydroxyapatite, the primary mineral component of bone, these scaffolds enhance osteogenesis and improve integration with native bone tissue. Their mechanical properties and ability to support cell adhesion make them ideal for bone tissue engineering applications (Yao *et al.*, 2016)^[35].
2. **Cartilage Repair:** In cartilage tissue engineering, silk scaffolds support the growth and differentiation of chondrocytes, the primary cells responsible for cartilage formation. Their resilience to mechanical stress and ability to promote cell proliferation make them suitable for repairing cartilage defects.
3. **Skin Tissue Engineering:** Silk-based materials are utilized in wound dressings and skin grafts due to their superior biocompatibility and ability to support cell proliferation and migration. These properties facilitate effective wound healing and skin regeneration (Kumar *et al.*, 2016)^[18].
4. **Nerve Regeneration:** Silk conduits provide a guiding structure for nerve regrowth, supporting the regeneration of peripheral nerves. Their biocompatibility and ability to facilitate cell adhesion make them promising materials for neural tissue engineering.
5. **Vascular Tissue Engineering:** The mechanical properties and biocompatibility of silk make it a promising material for creating vascular grafts. Silk-based scaffolds can support the formation of new blood vessels, essential for tissue regeneration and repair.

Advantages of Silk in Tissue Engineering

- **Natural Origin:** Being a naturally derived protein, silk offers better integration with biological tissues compared to synthetic polymers (Lamboni *et al.*, 2015)^[24]
- **Customizability:** The properties of silk can be tailored through genetic engineering of silkworms or post-processing techniques to optimize it for specific applications. Enhanced Cell Interaction: Modifications to silk's amino acid composition can promote better interaction

with cells, enhancing tissue regeneration. Silk's unique combination of biocompatibility, biodegradability, mechanical strength, and versatility positions it as a promising material in tissue engineering. Ongoing research and technological advancements are expected to expand its applications and improve its performance in clinical settings (Kundu B *et al.*, 2013) ^[20].

5.4 Antimicrobial Coatings

Sericin natural antimicrobial efficacy is attributed to its amino acid composition, which can disrupt bacterial cell walls and inhibit microbial growth. Additionally, sericine can be combined with silver nanoparticles to enhance its antibacterial properties offering a synergistic effect against a broad spectrum of pathogens. Sericine coating is for surgical suture and medical textiles. It reduces infection risks in catheters, bandages, and implantable devices (Al Masud *et al.*, 2021) ^[1].

5.5 Antioxidant Therapy

As a reactive oxygen species (ROS) scavenger, sericin is beneficial in:

- Diabetic wound healing
- Liver and kidney protection (in animal models)
- Anti-inflammatory treatments.

6. Innovations and Research Trends

6.1 Recombinant sericin production

- Biotechnological synthesis of recombinant sericin in *E. coli* and *Pichia pastoris* systems allows controlled production without relying solely on cocoons (Mandal BB *et al.*, 2009) ^[5].

6.2 Sericin-based biinks for 3D printing

- Sericin hydrogels are being tested as biinks for 3D bioprinting of tissue scaffolds, owing to their viscoelastic and cell-supportive properties.

6.3 Sericin in ophthalmology

- Hydrogels made of sericin are evaluated for corneal repair and as carriers for intraocular drug delivery, due to their transparency and oxygen permeability (Nagai N *et al.*, 2018) ^[27].

6.4 Hybrid biomaterials

Researchers are combining sericin with:

- Chitosan - for antimicrobial wound dressings
- Hyaluronic acid - for injectable cosmetics
- Hydroxyapatite- for bone repair

6.5 Clinical trials and safety

- Several animal model studies have shown sericin to be safe, non-toxic, and effective. Human trials are underway for skin grafts and anti-aging cosmeceuticals.

7. Environmental and Economic Implications

7.1 Waste utilization: Traditional degumming during reeling releases sericin-rich effluent. Modern extraction reuses this effluent, reducing environmental load and adding economic value to silk processing.

7.2 Sustainable sericulture: The integration of sericin utilization in sericulture promotes waste-to approaches and supports circular bioeconomy models.

7.3 Livelihood diversification

- Startups in green cosmetics
- Contract manufacturing for biomedical textiles
- R&D opportunities in biotech firms

8. Challenges and future directions of sericin utilization in sericulture

Sericin, the hydrophilic silk protein has emerged as a multifunctional biomolecule with diverse applications in biomedicine, cosmetics, and agriculture. Despite its recognized potential, mainstream utilization of sericin remains limited due to various technological, economic, and regulatory challenges. Overcoming these hurdles is essential to fully integrate sericin into the value chain of sericulture and to ensure long-term sustainability and profitability (Ma Q *et al.*, 2025) ^[25].

8.1 Challenges in sericin utilization

1. Lack of standardized extraction techniques

Issue: Extraction methods vary widely in terms of yield, purity and bioactivity.

Consequence: Inconsistent product quality hinders scalability and commercialization.

Cause: Variability in cocoons, degumming conditions, and solvent use (Cao *et al.*, 2016) ^[8].

2. Low awareness among sericulturist and reelers

Issue: Many farmers and silk reelers still treat sericin as waste.

Consequence: Missed opportunity for additional income and rural enterprise.

Cause: Inadequate training and weak linkage with downstream industries.

3. Storage and stability issues

Issue: Sericin is prone to microbial contamination and degradation.

Consequence: Short shelf life restricts transportation and formulation flexibility.

Cause: High protein content and hygroscopic nature.

4. Regulatory and safety hurdles

Issue: Lack of harmonized guidelines for sericin use in cosmetics, foods and drugs.

Consequence: Delays in product registration and limited global market access.

Cause: Gaps in clinical testing, toxicological validation, and documentation (Sahu *et al.*, 2016) ^[31].

5. Underdeveloped market infrastructure

Issue: Absence of organized collection, processing, and supply chains for sericin.

Consequence: Fragmented production, low investor interest.

Cause: Focus of sericulture policies remains fiber-centric.

6. High cost of advanced processing technologies

Issue: Enzymatic, ultrasonic, and nanotech-based methods are expensive.

Consequence: Economically unviable for small-scale rural enterprises.

Cause: Need for specialized equipment and expertise.

7. Intellectual property and technology transfer gaps

Issue: Patents exist for sericin formulations, but access is limited.

Consequence: Slows innovation adoption by MSMEs and

startups.

Cause: Weak industry-research institute collaboration.

Conclusion

Sericin, once considered a low-value byproduct of silk reeling, is now emerging as a biological treasure in the fields of cosmeceuticals, wound healing, drug delivery, and tissue regeneration. Its multifunctional nature, sustainability, and compatibility with human biology make it a 21st-century biomaterial of immense potential. Integrating sericin-based innovations with conventional sericulture not only enhances the economic resilience of silk farmers but also transforms sericulture into a biotechnological enterprise, aligned with the goals of the bioeconomy, sustainability and human wellness.

Disclaimer (Artificial intelligence)

Author(s) hereby declare that NO generative AI technologies such as Large Language Mode (Chat GPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of this manuscript.

Competing Interests

Authors have declared that no competing interests exist.

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