**A Comprehensive Review of Recent Advances in Silk Sericin**

**ABSTRACT**

Originally a silk industry waste, sericin has emerged as a multipurpose biomaterial with numerous uses in the food, cosmetic, biomedical and environmental sectors in recent years. It has moisturizing, antibacterial, anti-inflammatory and antioxidant qualities due to its unique biochemical makeup, which includes a high concentration of hydrophilic amino acids and functional groups. Due to concerns about sustainability and the circular bioeconomy, green extraction and purification techniques have made it possible to preserve the high molecular weight fractions in recent decades. Sericin-derived hydrogels, films, nanoparticles and bioinks offered promising properties for drug release, tissue engineering, wound healing, cosmetics and nutraceuticals. Mechanisms have revealed its role in reducing inflammation, oxidative stress, microbial metabolism and cell matrix interactions. Low toxicity and good biocompatibility have been found in safety evaluations; nevertheless, there are currently no clear physiological mechanisms or clinical approval for pharmaceutical use. The value of natural biomaterials and their journey toward the next generation of industry and healthcare is mirrored in sericin, which combines sustainable feedstock recovery with cutting-edge biomedical innovation.

**Keywords:** Sericin,cosmetic, biomedical, silk gland, industry

**INTRODUCTION**

Many thousands of years ago, the Chinese began using silk, one of the world's oldest natural fibers, to make textiles. Fibrin, the structural protein found in the centre of silk strands, is managed in the production of silk, while sericin, the outside gummy protein is disposed of as trash during the degumming process. However, as science and technology have advanced in recent decades, sericin has garnered a lot of attention because of its distinct biochemistry and physicochemical properties as well as its wide range of potential applications in the industrial, biomedical and cosmetic sectors. The use of byproducts in the sericulture industry and growing concern in the sustainable use of natural resources are the causes of this shift, which is considered an environmental contribution.

About 20–30% of a silk cocoon's weight is made up of a collection of water-soluble glycoproteins called silk sericin, which wraps around fibroin fibers. It contains polar amino acids with strong hydrophilicity and antioxidant properties, including glycine, aspartic acid and serine. The complicated molecular structure of sericin varies depending on the cocoon layer, silkworm species and processing circumstances. Its ability to be flexible is crucial to its operation and possible uses in tissue engineering, wound healing, medicines, cosmetics and the creation of eco-friendly biomaterials. The antioxidant, antibacterial, anti-inflammatory and moisturizing properties of sericin have been highlighted as supporting its ongoing interest in both industry and health (Cherdchom, S. et al., 2021, Silva et al., 2022).

One of the topics that have been studied the most recently is the use of silk sericin in biomedicine. It is highly appropriate for tissue engineering scaffolds, drug carrier systems, and wound dressing materials because of its superb biocompatibility and exceptional biodegradability. For instance, it has been reported that sericin-derived hydrogels and films accelerate wound healing by stimulating collagen synthesis and cell proliferation (Qi et al., 2018; Baptista-Silva et al., 2021; Yazarlu et al., 2023).

Silk sericin’s performance extends beyond biomedical applications to cosmetics, where its natural anti-aging, moisturizing, and side-effect-free qualities make it highly desirable. Topical sericin formulations have been shown to improve skin hydration, reduce transepidermal water loss, and protect against oxidative stress induced by UV radiation (Padamwar et al., 2005; Das et al., 2015). As a cosmetic ingredient, sericin represents a promising alternative to synthetic derivatives in a consumer market that favors natural and eco-friendly products.

Recent studies have focused on sericin's effects on environmental sustainability. Previously, sericin which has a significant organic content posed a hazard to the environment and was expelled as a wastewater effluent during degumming. In order to reduce pollution and make the silk business more environmentally friendly that is moving toward a circular economy sericin is now converted into value-added biomaterial biodegradable films, hydrogels and composites (Kumar et al., 2024). Functional industrial uses are indicated by its use in water treatment, biosensing and as an environmentally acceptable packaging material (Soe et al., 2021).

**Why Sericin Now**

Due to its exceptional blend of bioactivity, processability and sustainability silk sericin has recently seen resurgence as a biomaterial of significant scientific and industrial interest.

a) **Intrinsic bioactivity:** It has already been proved that sericin possesses intrinsic anti-oxidant, anti-inflammatory, antimicrobial activities with increasing evidence of anti-biofilm promise. Its skin moisturizing and skin barrier supporting function lead it attractive for cosmeceutical and dermatological application (Aramwit, 2021; Mondal *et al.,* 2023).

b) **Processability:** In contrast to most protein-based polymers, sericin is water soluble and can be readily mixed with natural and synthetic polymers to generate films, hydrogels, scaffolds and nanoparticles. Its compositional flexibility enables crosslinking by physical ways of β-sheet promotion (Yao *et al.,* 2023) and chemical approaches to regulate mechanical properties, stability and degradation rates (Dash *et al.,* 2022).

c) **Circular economy:** Sericin is mostly released as degumming effluent during the silk processing process in the textile and sericulture industries, which raises the need for BIOX in the liquid effluent. A sustainable waste upcycling method that adheres to the circular economy concept and green biomanufacturing principles is the valorization of this waste into valuable biomaterials (Kundu *et al.,* 2022; Tomita *et al.,* 2023). Therefore, sericin has recently drawn more attention to the nexus of bioengineering, healthcare and green/sustainable materials applications, positioning it as a possible contender to spearhead the next wave of biomedical and cosmetic revolutions.

**Chemistry, Structure and Variability**

Silk sericin's clean amino acid compositional structure, hierarchical structure and processing make it a very heterogeneous protein in terms of its physical characteristics. This uncommon polymer's distinct polar side chain-rich chemistry and fractionated nature are essential components of both its bioactivity and structural adaptability in biomaterials.

a) **Primary structure.** The remarkable quantity of serine-amino acid residues found in sericin which normally make up 30–35% of an amino acid gives it its strong hydrogen bonding potential and water absorbency. Furthermore, aspartic acid and glutamic acid which contribute to anionic and metal complexing potential make up about 18–25% of the residues. In addition to being a bioactive component sericin can also serve as a flexible conjugation substrate thanks to its proteinaceous, amide-rich structure made up of repeating polar themes (Aramwit and Sangcakul 2007; Teramoto and Miyazawa 2005; Zhang et al. 2021).

b) **Architecture and fractionation.** Sericin is a mixture of fractions (often referred to as S1, S2, and S3) that differ in molecular size, solubility, and fibroin-binding properties; it is not a single protein in terms of structure. The reported molecular weight (MW) differs significantly from the prepared extraction protocol's MW of 300 kDa. While low molecular weight fractions of sericin occasionally show improved diffusivity and antibacterial properties, high molecular weight fractions of sericin are good at preserving its antioxidant and moisturizing properties (Kunz et al. 2016; Lamboni et al. 2015).

c) **Functional groups and reactivity.** The side chains of these proteins expose a rich tapestry of reactive groups-- amine (–NH2), carboxyl (–COOH) and hydroxyl (–OH) -- offering a wide range of chemical modification. These are carbodiimide (EDC/NHS) coupling, aldehyde Schiff-base reactions, genipin natural crosslinking, Ag + coordination, and even photo-crosslinking. This chemical versatility is the basis for the applicability of sericin in hydrogels, films, scaffolds and nanocarriers (Wang et al. 2022; Gholipourmalekabadi et al. 2019).

**d)** **Heterogeneity and variability.** The biological and processing parameters have a significant impact on the biochemical and functional properties of sericin. Depending on the type of silkworm (e.g., Bombyx mori versus non-mulberry silk), the larval food and even the cocoon layer, the sericin component may vary. It is crucial to remember that the degumming process alters the molecular weight distribution and bioactivity of the proteins associated to mustard seeds, regardless of whether it is enzymatic, soap-based, alkaline or heated. Extensive oxidative or alkaline treatments frequently cause structural loss, glycation or fragmentation, which can reduce biological activity. Conversely, high molecular weight sericin and its biofunctionality are retained during crude aqueous degumming or aqueous extraction [Shanmugasundaram et al. 2018; Aramwit et al. 2010; Altman et al. 2003].

**e) Design note.** The variability of sericin is an opportunity rather than a constraint from the perspective of biomaterials design. With low glycation and maintained high molecular weight fractions, biofunction frequently scales. This emphasizes how crucial it is to follow optimal extraction and purification procedures in order to customize the molecular profile of sericin for particular uses. For example, reduced molecular-weight sericin may be purposefully used for drug distribution due to its solubility and diffusion advantages, whereas extraction techniques that avoid structural degradation often boost antioxidant efficacy and wound healing (Shao et al. 2019; Aramwit 2021).

Silk sericin is a very versatile protein that connects intrinsic bioactivity with functional engineering opportunities thanks to its combination of structural and chemical characteristics. To advance its transformation from an industrial byproduct to the preferred biomaterial in medicinal, cosmetic, and environmental applications, it is crucial to comprehend its diversity.

**Extraction and Green Valorization**

**Conventional Extraction Routes**

There are various methods that have been proposed to extract sericin from silk cocoons each with a different effect on yield, MW retention and environmental load:

* **Soap/alkali boiling (Na2CO3, NaOH):** It has been extensively used for the efficiency in sericin elimination but known to induce the peptide chain’s hydrolysis and the production of effluent with high alkaline and salt contents.
* **Urea/thiourea:** As chaotropic factors, they can destroy hydrogen bonds uphold a high MW fraction of sericin. The process does require high levels of dialysis to remove salts left over.
* **Heat/pressurized water (autoclaving):** An additive free, logistically simple process, generating moderate MW sericin. Division-2: The light color will decay with long time use while partial emuchroma disappears.
* **Enzymatic degumming (proteases):** Provides selective hydrolysis of sericin and conserve fibroin structure to improve fiber quality. Despite these merits, cost and scalability are the critical bottlenecks.
* **Microwave and ultrasound-assisted extraction:** These are new techniques to intensify mass transfer, shorten the time and decrease the amount of energy used. They are considered as of more green nature but large scale production efficiency is still under way.

**Emerging “green” strategies (2021–2025)**

Recent research has placed a strong emphasis on the environmentally responsible and sustainable extraction and recovery of sericin. Other quick methods like pressurized water degumming and microwave-assisted steam degumming have also shown that minimal chemical inputs can retain more antioxidant activity and result in a lower effluent burden (Kumar *et al.,* 2022; Li *et al.,* 2023). Target-directed adjustment of the most crucial parameters (temperature, time, and solvent ratio) to achieve the highest possible yield and preserve molecular weight distribution and bioactivity is made possible by statistical optimization techniques such as Box Behnken designs and response surface methodology (Ahmed *et al.,* 2021; Chen *et al.,* 2024).

#### Closed-loop aqueous degumming systems with inline ultrafiltration have been proposed for industrial scale, supported by numerous studies. In these systems effluent water is continually recycled to the greatest extent possible to minimize residue (Park et al., 2022; Singh and Bhat, 2024). Concurrently, these initiatives also emphasized the idea of circular economy models, in which sericin is extracted directly from textile effluents and then refined into biopolymers of food or cosmetic quality (Rahman et al., 2023; Wu et al., 20255; Wu et al., 2025). These advancements integrate high-value utilization, energy efficiency and waste reduction in accordance with the green valorization framework.

#### Table 1. Comparison of extraction strategies (recent advances)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Route** | **Typical conditions** | **Yield** | **MW retention** | **Pros** | **Cons** | **Scale readiness** |
| Water/autoclave | 100–121°C, 20–60 min | 10–20% | ◕ | Additive‑free, simple | Coloration, moderate MW | Pilot |
| Alkali (Na2CO3) | 0.05–0.5% at 90–100°C | 15–25% | ◔ | Rapid, established | Chain scission, salt effluent | Industrial |
| Urea (6–8 M) | 60–90°C | 12–22% | ◕◕ | High‑MW preservation | Dialysis burden | Lab–pilot |
| Enzymatic | Protease, 40–60°C | 10–18% | ◕◕ | Selective, fiber quality | Cost/enz reuse | Pilot |
| Microwave‑assisted | 600–900 W, ≤30 min | 12–23% | ◕ | Energy‑efficient | Equipment | Pilot |
| Ultrasound‑assisted | 20–40 kHz | 12–20% | ◕ | Faster | Potential oxidation | Lab |

Legend: MW retention ◔ low, ◕ moderate, ◕◕ high.

**Physicochemical Properties Relevant to Formulation**

A unique high adhesion and hydrophilic property that can be utilized for coatings and films with exceptional hydration ability is produced by silk sericin's high water solubility, which is caused by the predominance of polar amino acids and an isoelectric point of roughly pH 4 (Zhang et al., 2022, Pereira et al., 2023). When dry, its glass transition temperature is between 200 and 220 °C. The induction of β-sheet structures during processing significantly improves mechanical strength and water stability both of which are critical for packaging and biomedical scaffolds (Lee et al., 2021, Wang et al., 2024). Both molecular weight and concentration have a significant impact on the rheological characteristics of sericin solutions. In complex blends and bio-inks, it typically exhibits shear thinning behavior, which improves processability in hydrogel formulations and 3D bioprinting (Kim et al., 2022, Saha et al., 2023).

Along with a variety of other bioactivities, such as potent radical scavenging as determined by DPPH and ABTS assays, metal-ion chelation and antimicrobial activity, particularly against Staphylococcus aureus and Escherichia coli, it also demonstrates anticancer activities, such as inhibiting collagen biosynthesis in absorption tissues and suppressing the formation of solid tumors. The former is primarily explained by the regulation of an activated reactive oxygen species and activated cationic peptide domains (Chen et al., 2021, Colloids and Surfaces B: Biointerfaces; Reddy et al., 2024).

#### Table 2. Typical ranges

|  |  |
| --- | --- |
| Property | Range (recent reports) |
| MW distribution | 5–300+ kDa (extraction‑dependent) |
| Zeta potential (pH 7) | −5 to −25 mV |
| Water uptake (films) | 100–600% |
| Tensile strength (cast films) | 5–40 MPa (blend/crosslink dependent) |

**Hydrogels & Film-Forming Gels**

Silk sericin-based hydrogels and film-forming gel systems have experienced increasing popularity in the past 5 years because of their biocompatibility, water solubility and natural bioactivities.

**Denaturation strategies:** By using a diverse range of physical and chemical crosslinkers, sericin has been reported to have been effectively stabilized into hydrogel matrices. These agents often include genipin, EDC/NHS, citric acid, dialdehydes and metal ions (e.g., Ag⁺) that provide the advantages of enhancing structural integrity as well as antimicrobial activities. Very recently, photo-initiated crosslinking systems that allow for spatially controlled gelation as well as tunable mechanical properties were developed.

**Smart wound-healing functions:** sericin is formulated beyond the classic hydrogel and the whole hydrogel shows stimuli-responsive functions. Such as ROS-responsive oxygen-generating sericin microneedles for treating diabetic wounds that combines the intrinsic antioxidant property of sericin with augmented oxygen supply for wound healing. Harboring antioxidant activity within hydrogels (such as sericin gels incorporating high levels of resveratrol) similarly provides a synergistic protection against the oxidative stress associated with infection.

**Film-forming applications:** sericin gels having sprayable or spreadable type which upon application instantly give a protective film on either the skin or wound bed. These conformal dressings integrate barrier with moisture retention while still allowing controlled release of the therapeutic agents into the wound bed. These innovations in combination demonstrate a paradigm shift of sericin from an inactive excipient to an active multi-functional agent in novel hydrogel and film-forming wound dressings.

**Electrospun & Printed Structures**

Silk sericin (SS) has been combined with other biodegradable polymers, such as polycaprolactone (PCL), polylactic acid (PLA), chitosan and alginate to create asymmetric electrospun dressings that provide moisture balance and an antibacterial protective barrier. Their sericin rich shells provide an appealing environment for cell adhesion, migration support and inflammatory response modulation and these hybrid mats have demonstrated enhanced biocompatibility and adjustable degradation. These findings point to a great potential for these materials in wound healing and cell/tissue engineering applications (Wang et al., 2021; Chen et al., 2022, Li et al., 2023). According to Zhang et al. (2024), certain 3D printing techniques have also been applied to sericin blends in order to create customized scaffolds and bioinks for regenerative medicine.

**Particles and Nanocomposites**

Particles based on sericin that are produced by ionic gelation, desolvation, and spray drying have been investigated as possible bioactive carriers. Using charge interactions and peptide ligands, some of these systems have been developed to selectively target and release natural antioxidants, anticancer drugs (doxorubicin and curcumin), and antibiotics (gentamicin) (Aramwit et al., 2021, Singh et al., 2022, Liu et al., 2023).

Simultaneously, sericin has been studied in the construction of metal and oxide nanohybrids as a green reductant and stabilizer. Additionally, sericin-derived silver, gold and zinc oxide nanoparticles showed synergistic antibacterial and antioxidant activities that enhance wound healing effectiveness and reduce the formation of biofilms (Kumar et al., 2021, Das et al., 2022, Huang et al., 2024). In biomedical applications using nanotechnology, these innovative sericin-metal composites may offer a more environmentally friendly alternative to the conventional chemical stabilizer.

**Bioinks & Adhesives**

Recent advances led to further application of silks sericin in bioink formulations and tissue adhesive making it an appealing candidate in the advanced biomedical engineering field.

**Bioinks for 3D bioprinting:** GMA-grafted sericin (and sericin-containing protein blends) for 3D SSB bioinks40. Being characterized by increased compressive strength, improved thermal stability protease resistance as well as improved structural fidelity these are ideal candidates for extrusion-based bioprinting (Zhao et al., 2022)

**Multi-functional:** Sericin has been incorporated into UV-curable polyurethane-acrylate (PU-A) adhesives for sternal closure after open-heart surgery. They display record adhesion strength (~4.3 MPa), excellent mechanical stability, biodegradability in vitro biocompatibility (on L-929 cells) and antimicrobial efficacy against E. coli, P. aeruginosa and S. aureus (Patel *et al.,* 2023).

Hemostatic and tissue sealant scaffolds Composite alginate aalo vera–sericin scaffolds exhibit hemostatic efficacy, blood absorption, antimicrobial activity and hemocompatibility. They are believed to have potential as natural tissue sealants due to rapid blood clotting and vessel formation potential in vitro assays (Reddy *et al.,* 2024).

#### Table 3. Representative formulations and outcomes (selected studies, 2023–2025)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Year** | **Platform** | **Additives/Drug** | **Model** | **Key outcomes** |
| 2025 | Robust sericin hydrogel | — | diabetic wound | Enhanced antioxidative/antimicrobial properties; accelerated closure vs. control |
| 2025 | Film‑forming gel (SS–PVA) | — | full‑thickness wound | Faster re‑epithelialization, collagen deposition |
| 2024 | ROS‑responsive SS microneedles | O2 generators | diabetic wound | Improved angiogenesis; reduced inflammation; scarless healing |
| 2024 | SS–resveratrol hydrogel | resveratrol | infected wound | Reduced bacterial load; improved granulation |
| 2025 | SS–gentamicin microparticles | gentamicin | in vitro/in silico | Controlled release; validated by modeling |

**Biomedical Applications**

**Hemostasis & Wound Management**

Silk sericin's many hydrophilic groups have a natural hemostatic action can activate platelets and absorb water quickly. It speeds up wound closure by encouraging keratinocyte and fibroblast migration. In diabetic and infected wound models, sericin based dressings also showed faster closure rates, improving by more than 20–40% by days 10–14 post-treatment. They also decreased the production of biofilms and modulated inflammatory cytokines, such as TNF-α IL-6. In chronic wound models, sericin-containing hydrogel and nanofiber systems exhibited enhanced collagen remodeling and angiogenesis. Prasong and associates, 2023.

**Tissue Engineering**

**Skin:** These Sericin Rich Scaffolds lead to better re-epithelialization, granulation tissue formation and control the, I/III collagen ratio to achieve decrease in scar formation and restoration of function.

**Bone/Cartilage:** Mineralized sericin composites enhanced osteoblast proliferation and differentiation after a combination with hydroxyapatite or bioactive glass. Sericin poassing the affinity for calcium ions along with growth factor binding capacity ayud to osteoinduction and cartilage regeneration.

**Nerve:** Hydrophilic surface decorated with peptide motifs promoting neurite outgrowth and Schwann cell migration to support peripheral nerve regeneration (sericin conduits and electrospun fibers)

**Cornea:** Transparent and non-transparent sericin films and hydrogels suitable for human corneal epithelial cells possess great potential for the application of on-corneal stent as well as in vitro contact lens coatings essential for visual restoration.

**Drug and Gene Delivery**

An appealing biopolymer for the field of nanomedicine, silk sericin is an amphiphilic protein that allows the simultaneous encapsulation of hydrophobic and hydrophilic therapeutic cargos in a single nanocarrier. Drugs and genetic material can be released in a regulated and targeted manner thanks to sericin nanoparticles' shown pH and enzyme responsiveness. Recent studies have also looked into intranasal and transdermal delivery systems, which could improve permeability and bioavailability while still producing biocompatible sericin-based carriers (Kundu et al., 2023; Bhattacharjee et al, 2022; Mandal et al., 2021). The application of sodium sericin as RNA/DNA biocarriers has been made easier by the use of engineering techniques to create sericin-derived nanocarriers, opening up the possibility of precision medicine and cancer treatments (Huang et al., 2023; Zhang et al., 2022).

**Cosmetics and Dermatology**

In cosmetics, silk sericin is a naturally occurring film-forming ingredient that can also hydrate and strengthen the integrity of the compromised skin barrier. Because of its ability to retain moisture and bind keratin, hyaluronic acid is frequently found in anti-aging products that improve the skin's suppleness and smoothness (Aramwit et al., 2022; Rajput et al., 2023). Additionally, sericin increases UVA/UVB protection when combined with UV filters which promotes photoprotection and lowers oxidative stress (Pham et al., 2022; Kim et al., 2021). Its use in cosmetic and dermatological preparations is supported by laboratory and clinical data that suggest calming, anti-wrinkle, and healing benefits (Kawasaki et al., 2023; Shitole et al., 2021). It has also recently been applied in sericin-based hydrogels and nanoemulsions to enhance its potential as a sustainable cosmetic bioactive (Wang et al., 2023; Bhat et al., 2022).

**Food and Nutraceuticals**

Lastly, silk sericin (SS) has been confirmed as a new source of bioactive chemicals for the food and nutraceutical industries. Because of its antioxidant and antibacterial properties, SS has also been utilized as a natural coating material to extend the shelf life of perishable food by halting oxidative therapy and microbiological spoiling (Aramwit et al., 2020; Li et al., 2022). Because of their excellent mechanical qualities, transparency and water vapor permeability, edible films made from sericin showed promise for use in food packaging and preservation (Kong et al., 2021).

It has also been investigated for application in microencapsulation technology. It has been shown that adding SS to probiotic formulations improves the survivability of bacteria with functional delivery in gastrointestinal settings (Abou El-Nour et al., 2021; Kwertnik and Szafranski, 2014). Similarly, the stability, bioavailability, and controlled release of polyphenols and other nutraceutical components are improved when they are embedded in sericin matrices (Luo et al., 2022; Nair et al., 2023). These qualities of sericin strengthen its capacity to serve as a functional element and protective carrier in food systems. Large-scale commercialization is still pending completion of the gouging process, regulatory approval, customer acceptance, and required safety assessments.

**Mechanisms of Action**

**Antioxidant property:** Silk sericin has strong antioxidant properties because of the presence of high number of hydroxyl, carboxyl and amine groups that can act directly on the free radical scavenging along with transition metal chelating property of the silk sericin. Moreover, it has been shown to modulate the redox sensitive signaling pathways particularly through Nrf2/HO-1 axis activation hence increasing the cellular defense against oxidative stress (Kunz *et al.,* 2016; Lamboni *et al.,* 2015; Zhang *et al.,* 2020).

**A series of antibacterial effects sericin**: sericin exerts an antibacterial effect by binding to microbial membranes, disrupting permeability, leaking intracellular contents. Again, its antimicrobial activity increases in a combination with, or as a stabilizer of metallic nanoparticles like silver and zinc oxide, showing synergetic inhibition of bacterial growth and biofilm formation (Aramwit et al., 2012; Lamboni et al., 2015; Kasoju & Bora, 2012).

**Anti-inflammatory activity**: Sericin downregulates pro-inflammatory cytokines (IL-6 and TNF-α), hence attenuating inflammatory responses. Other recent findings reveal that it encourages macrophage polarization into the M2 phenotype that facilitates tissue repair and inflammation resolution (Aramwit *et al.,* 2013; Lamboni *et al.,* 2015; Vepari & Kaplan, 2007).

**Cell–matrix signaling:** Sericin, by being hydrophilic and having the presence of bioactive peptide motifs promotes cell adhesion in an integrin-mediated manner. Thus, β-sheet content can be altered through processing and altered material stiffness can effect stem cell differentiation and tissue integration (Kundu *et al.,* 2014; Lamboni *et al.,* 2015; Numata & Kaplan, 2010).

**Safety, Biocompatibility and Regulatory Landscape**

Recent studies reported that SS possesses low acute and sub-chronic toxicity in rodent and in vitro models, potentially rendering SS as an ideal candidate in biomedical and nutraceutical fields (Zhang *et al.,* 2021). Nonetheless, the inherent safety of these materials is highly dependent on the purification process as endotoxins from microbial sources or residual solvents and crosslinkers used in the processing can change the safety profile and need to be monitored very closely (Aramwit *et al.,* 2013).

Cytotoxicity, sensitization and genotoxicity assays are increasingly reported as per the ISO 10993 testing panel where the biocompatibility of sericin have generally been found to be favorable for mammalian cells (Dash *et al.,* 2022). However, up to now no sericin-based drug products have been registered by FDA or EMA giving their utmost preference to preclinical datum.

However, in the cosmetic and skincare industry, sericin is a common ingredient for moisturizing and anti-aging (Nagai *et al.,* 2018). A few wound dressings and tissue repair formulations containing SS have also been found to be promising in terms of skin regeneration and scar reduction (Aramwit & Sangcakul, 2007; Kumar *et al.,* 2020), and such formulations are under preclinical or early clinical evaluation in the biomedical domain.

**Manufacturing, Scale-up and Circular Bioeconomy**

The degumming fluid produced during silk reeling and textile processing serves as the primary feedstock for sericin recovery. Silk sericin is produced via the most widely used conventional chemical degumming, which is most likely alkaline or soap-based, however it will have negative environmental effects. In addition to reducing the use of harsh chemicals, new methods such as hot-water or microwave degumming improve sericin recoveries and reduce environmental impacts (Sothornvit et al., 2010; Zhang et al., 2020). TFF, dialysis, ultrafiltration and chromatographic procedures are a few of these techniques that can be used to remove minor impurities while keeping the sericin fractions with the appropriate molecular weights (Martins et al., 2018). In order to obtain pharmaceutical grade, which necessitates strict control over molecular homogeneity and bioburden for regulatory approval, several tactics are required.

Integration of circular bioeconomy models for industrial scale-up is also highlighted. Since sericin is a waste by-product of the manufacture of silk, it can account for up to 25–30% of the weight of a cocoon. By valuing this by-product, waste is reduced and value-added products for the sericulture industries are produced (Kundu et al., 2008). Although it has been demonstrated that pilot recovery units near textile mills are feasible, downstream purification that is both economical and efficient remains a major obstacle. In conclusion, sericin can function as a circular bioeconomy product that links the traditional silk industries to the profitable biomaterial markets of the twenty-first century through sustainable manufacture and the use of ecologically acceptable extraction techniques.

**CONCLUSION**

As reported in recent literature, silk sericin has changed from being an effluent of the silk reeling process that had little value to becoming a high-value biomaterial for the health care and cosmetic industries. It has also emerged as a potential candidate for biomedical, cosmetic and industrial applications. It is perfect for a number of uses, such as hemostatic wound dressings, regenerative scaffolds, nutraceutical coatings and cosmetic formulations because of its inherent biological activity, infinite variation of forms and ease of processing. Its application so far is outstanding as an active therapeutic agent and an excipient as indicated by the advances in smart hydrogels, Nano carriers and bioinks. In the meantime, its standing as a leader in sustainable biomaterials is strengthened by eco-friendly extraction techniques and circular economy concepts. Regulatory approval for pharmaceutical applications and large-scale production with sufficient safety and quality assurance, however are particularly problematic. To effectively utilize sericin's potential, further study bridging transnational research and molecular design mechanistic understanding will be crucial. Tinuvin sericine Sericin Ceramic digitalization method based on PCR that is not heated. Silk and sericulture have a long and rich history and we are excited about silk sericin as a biomaterial substance that bridges the gap between old customs and contemporary biomaterial science for sustainability, industry and health.

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