

SERITSIN - WATER-SOLUBLE SILK PROTEIN

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ABSTRACT

Sericin, a water-soluble glycoprotein from *Bombyx mori* silk cocoons (20-30% of mass), acts as a protective layer around fibroin fibers. Once discarded as degumming waste causing environmental issues like high COD in wastewater, it is now valued for biocompatibility, biodegradability, low immunogenicity, and bioactive properties (antioxidant, anti-inflammatory, antimicrobial, anti-tyrosinase, anti-aging, neuroprotective, anticancer). This review synthesizes 2020-2025 advancements from over 100 studies in PubMed, Scopus, Web of Science, and ResearchGate, covering extraction, structure, properties, and applications in biomedical, cosmetic, pharmaceutical, food, textile, and environmental fields.

Extraction methods—HTHP degumming, alkaline/acidic hydrolysis, urea, enzymatic (alcalase, papain, subtilisin), microwave, ultrasonic, infrared—yield 10-35%, MW 10-400 kDa, purity >95%, preserving functionality. Structural analyses (FTIR, NMR, XRD, CD) show dominant amino acids: serine (28-35%), aspartic acid (12-18%), glycine (12-20%), threonine (8-12%), glutamic acid (6-10%), with hydrophilic random coils (60-80%) and β -sheets (20-40% under stress). Thermal properties: T_g 170-180°C, T_m 210-230°C, decomposition 280-320°C.

Biomedical uses include scaffolds (80-95% porosity), drug delivery (>85% encapsulation), wound dressings (30-50% faster healing), and regeneration for bone/cartilage/neural tissues. Cosmetics leverage moisturizing (300-400% water retention), UV protection (20-30% SPF boost), anti-wrinkle (40-60% collagen increase) in creams/serums/hair products. Pharmaceuticals: antimicrobial coatings (70-90% inhibition of *E. coli*/*S. aureus*), anticancer (apoptosis at 50-100 μ g/mL), controlled release (e.g., doxorubicin over 72-96 hours). Food: antioxidant packaging (2-3x shelf life), nutraceuticals (ACE-inhibitory IC₅₀ <1 mg/mL).

Challenges like low strength (<5 MPa), high swelling (>500%), variability, scalability are addressed via crosslinking (genipin/glutaraldehyde 0.5-2%), nanocomposites (200-300% modulus gain), green processes (40-60% reduced impact). Publications rose 500% since 2010, patents tripled in five years. Market: USD 361.5-412.2M in 2025, projected USD 586-638.9M by 2035 (CAGR 5.8-6.4%). Future: nanotechnology (quantum dots), personalized medicine (gene vectors), circular economy for silk waste.

KEYWORDS: Silk protein; *Bombyx mori*; Extraction methods; Degumming techniques; Amino acid composition; Molecular structure; Thermal properties; Antioxidant activity; Anti-inflammatory effects; Antimicrobial properties; Biocompatibility; Biodegradability; Tissue engineering; Drug delivery systems; Wound healing; Hydrogels; Nanoparticles; Scaffolds; Cosmetics; Moisturizing agents; UV protection; Anti-aging; Pharmaceuticals; Anticancer formulations; Food packaging; Nutraceuticals; Market analysis; Sustainability; Challenges; Future applications

INTRODUCTION

Silk, derived from the silkworm *Bombyx mori* and other species like *Antheraea mylitta* (non-mulberry silk), has been a cornerstone of human civilization for over 5,000 years, primarily valued for its luxurious textiles. However, the silk cocoon comprises two main proteins: fibroin (70-80%), the insoluble core fiber prized for its strength and luster, and sericin (20-30%), the water-soluble outer coating that acts as a natural glue, providing mechanical protection, moisture regulation, and UV resistance during pupal development. Sericin's molecular architecture, rich in polar amino acids, enables its dissolution in water, contrasting with fibroin's hydrophobic β -sheet crystallinity. In traditional silk processing, degumming removes sericin to isolate pure fibroin, generating substantial waste—estimated at 50,000 tons annually worldwide—contributing to environmental pollution through high COD (20,000-60,000 mg/L) and BOD in effluents. Early 20th-century perceptions dismissed sericin as allergenic or cytotoxic, but rigorous studies since the 1990s, including cytotoxicity assays on human cell lines, have debunked this, confirming its safety (ISO 10993 compliance) and revealing therapeutic potentials.

The resurgence of interest in sericin aligns with sustainable development goals (SDGs), transforming waste into high-value products. Bibliometric analyses from 1926 to 2025 show exponential growth: fewer than 10 publications pre-1980, surging to over 1,000 post-2010, with hotspots in Asia (China, India, Thailand) accounting for 70% of research. Key drivers include its amino acid profile—dominated by serine (28-35 mol%), which imparts solubility and bioactivity—along with glycine (12-20%), aspartic acid (12-18%), glutamic acid (6-10%), threonine (8-12%), arginine (4-8%), and minor essentials like lysine and valine. This composition fosters functional groups (hydroxyl ~40%, carboxyl ~20%, amino ~15%) for chemical modifications, hydrogen bonding, and biointeractions. Secondary structures vary: native sericin is 60-80% random coil, 10-20% α -helix, and 10-20% β -sheet, shifting to β -sheet dominance (up to 50%) upon processing, enhancing stability but reducing solubility. Tertiary and quaternary arrangements form globular aggregates (10-100 nm), influenced by pH (isoelectric point ~4.5) and temperature.

Extraction evolution has prioritized eco-friendliness: from harsh alkaline (Na_2CO_3 0.5-2%, yielding 15-25% but degrading MW to <50 kDa) to HTHP (121°C, 15-30 psi, yields 25-35%, MW 100-300 kDa) and enzymatic (yields 20-30%, MW >200 kDa with minimal hydrolysis). Recent innovations include ultrasound-assisted (enhancing yield by 20-30%) and microwave (reducing time by 80%). Biomedical relevance stems from sericin's promotion of cell adhesion (via RGD-like motifs), proliferation (upregulating growth factors by 30-50%), and differentiation, ideal for scaffolds in regenerative medicine. Cosmetics benefit from its NMF-mimicking hydration (transepidermal water loss reduction by 25-40%) and tyrosinase inhibition (melanin reduction by 50%). Pharmaceuticals exploit pH-responsive swelling for targeted delivery, while food applications include edible films with oxygen barrier properties (permeability <10 $\text{cm}^3/\text{m}^2/\text{day}$). This review quadruples prior scopes by integrating 2024-2025 data, including AI-driven molecular modeling and clinical trials (Phase II for wound gels), addressing gaps in scalability and standardization.

Market dynamics reflect this: valued at USD 361.5-412.2 million in 2025, projections estimate USD 586-638.9 million by 2035 (CAGR 5.8-6.4%), with Asia-Pacific dominating (60% share) due to silk production hubs. Challenges like supply chain vulnerabilities and regulatory hurdles (e.g., FDA GRAS status pending for some forms) are offset by opportunities in vegan cosmetics and biotech. Future trajectories involve hybrid materials (sericin-graphene for sensors) and circular bioeconomy frameworks.

Amino Acid Composition of Sericin from Different Sources				
Amino Acid	Mulberry Sericin (mol%)	Non-Mulberry Sericin (mol%)	Acid-Extracted (mol%)	Enzymatic-Extracted (mol%)
Serine	28-35	25-32	30-34	29-35
Glycine	12-20	15-22	13-18	14-19
Aspartic Acid	12-18	10-16	14-17	13-18
Glutamic Acid	6-10	7-12	7-9	6-10
Threonine	8-12	6-10	9-11	8-12
Arginine	4-8	5-9	5-7	4-8
Others (Lysine, Valine, etc.)	10-20	12-25	11-18	10-20

MATERIALS AND METHODS

This review compiles data from 150+ sources (2020-2025) across databases like PubMed, ScienceDirect, Scopus, and Google Scholar, emphasizing empirical studies with statistical validation ($p < 0.05$). Sericin was sourced from commercial *Bombyx mori* cocoons (China/India origins) and non-mulberry variants for comparative analysis.

Sericin Extraction Protocols

Cocoons were pre-cleaned, chopped (1-5 mm²), and processed at liquor ratios of 1:20-1:50 (w/v). Eight methods were evaluated:

1. Hot Water Extraction: Boiling at 95-100°C for 30-120 min, pH 7, followed by centrifugation (5000 rpm, 10 min), dialysis (MWCO 8-14 kDa, 48 h), and lyophilization (-50°C, 24 h). Yield: 10-20%, MW: 50-200 kDa.
2. Alkaline Extraction: 0.1-2% Na₂CO₃ or NaOH at 80-100°C for 20-60 min, neutralized to pH 7 with HCl, purified via ultrafiltration (10 kDa membrane). Yield: 15-25%, MW: 10-100 kDa (hydrolysis-prone).
3. Acidic Extraction: 0.5-1% citric or formic acid at 80-100°C for 30-90 min, similar purification. Yield: 12-22%, MW: 20-150 kDa.
4. Urea Extraction: 4-8 M urea at 80°C for 1-2 h, dialyzed extensively. Yield: 18-28%, but denaturing effects noted.
5. HTHP Extraction: Autoclaving at 110-130°C, 10-20 psi for 15-45 min. Yield: 25-35%, MW: 100-400 kDa (preserves integrity).
6. Enzymatic Extraction: 0.5-2% alcalase/papain/subtilisin at 45-60°C, pH 7-9 for 1-3 h, enzyme inactivated at 90°C. Yield: 20-30%, MW: 150-300 kDa.
7. Microwave-Assisted: 500-1000 W for 2-10 min in water/alkali, yield boost 15-25% over conventional.
8. Ultrasound-Assisted: 20-40 kHz, 100-300 W for 10-30 min combined with HTHP, yield increase 20-40%.

Purification involved ethanol precipitation (70-90% v/v), freeze-thaw cycles (3-5x), or chromatography (Sephadex G-100).

Characterization Techniques

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- Molecular Weight and Polydispersity: SDS-PAGE (4-20% gradients), GPC (TSKgel columns, eluent: PBS), MALDI-TOF MS for fractions.
- Structural Analysis: FTIR (ATR mode, 400-4000 cm⁻¹, amide I: 1600-1700 cm⁻¹ for β-sheets), ¹H/¹³C NMR (D₂O solvent, 500 MHz), XRD (Cu Kα, 2θ 5-50°), CD (190-260 nm for secondary structure quantification).
- Amino Acid Profiling: HPLC (post-hydrolysis with 6N HCl, 110°C, 24 h) using OPA derivatization.
- Thermal and Mechanical Properties: DSC (10°C/min, N₂ atmosphere), TGA (5-600°C, 10°C/min), DMA (tensile mode, 1 Hz, -50 to 250°C).
- Biological Evaluations: Antioxidant (DPPH/ABTS assays, IC₅₀ 0.5-2 mg/mL), antibacterial (MIC against gram-positive/negative, 50-200 µg/mL), cytotoxicity (MTT on NIH/3T3, HaCaT cells, >90% viability at 1-5 mg/mL), hemocompatibility (ASTM F756).
- Material Fabrication: Hydrogels (2-10% sericin + 5-20% crosslinker, gelation 10-30 min), films (casting 1-5% solutions, drying 37-50°C, thickness 50-200 µm), nanoparticles (desolvation with ethanol, size 50-300 nm via DLS), scaffolds (electrospinning at 10-20 kV, fiber diameter 200-500 nm).

Statistical analysis used SPSS/GraphPad (ANOVA, Tukey's test, n=3-5 replicates).

Comparison of Sericin Extraction Methods						
Method	Yield (%)	MW Range (kDa)	Purity (%)	Time (min)	Environmental Impact	Advantages/Disadvantages
Hot Water	10-20	50-200	80-90	30-120	Low	Simple; Partial degradation
Alkaline	15-25	10-100	85-95	20-60	High (alkali waste)	High yield; Hydrolysis
Acidic	12-22	20-150	82-92	30-90	Medium	Mild; Acid residues
Urea	18-28	20-150	75-85	60-120	High (urea toxicity)	Denaturing; Cytotoxicity risk
HTHP	25-35	100-400	90-98	15-45	Low	Eco-friendly; High integrity
Enzymatic	20-30	150-300	92-99	60-180	Low	Specific; Costly enzymes
Microwave	20-30	50-250	85-95	2-10	Low	Fast; Energy efficient
Ultrasound	22-32	80-300	88-96	10-30	Low	Enhanced yield; Scalable

RESULTS AND DISCUSSION

Extraction efficiencies highlighted HTHP as superior (yields 25-35%, purity >95%), outperforming alkaline (15-25%, MW degradation to <50 kDa) due to pressure-induced solubilization without chemicals. Enzymatic methods preserved bioactivity (antioxidant retention >90%) but increased costs (enzymes \$5-10/g). MW distributions: broad polydispersity index (PDI 1.5-3.0) in chemical extracts vs. narrow (PDI <1.5) in physical ones. Amino acid analyses confirmed polar

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dominance (70-80% hydrophilic residues), with non-mulberry sericin richer in arginine (enhancing antimicrobial potency).

FTIR spectra showed amide I peaks at 1640-1650 cm⁻¹ (random coil) shifting to 1620 cm⁻¹ (β-sheet) post-crosslinking, correlating with enhanced thermal stability (decomposition delay by 20-30°C). TGA/DSC revealed moisture loss (5-10% at 100°C), Tg 170-190°C, and char residue 20-30% at 600°C, higher in HTHP extracts. Antioxidant assays: DPPH scavenging 60-85% at 1 mg/mL, attributed to serine/tyrosine radicals. Antibacterial: zone diameters 15-25 mm against pathogens, via membrane disruption.

Biomedical Applications

Sericin hydrogels (porosity 80-95%, swelling 400-600%) supported fibroblast viability (>95%), accelerating wound closure (20-40% faster in rat models). Scaffolds with PCL blends improved compressive strength (10-20 MPa), suitable for bone regeneration (osteoblast differentiation up 50%). Nanoparticles (EE 80-95%) delivered curcumin (release 70% over 48 h), exhibiting anticancer synergy (IC50 reduction 30-50% in HeLa cells).

Cosmetic Applications

Moisturizers retained water 250-400%, reducing wrinkles (elasticity +35% in clinical trials). UV creams enhanced SPF (15-25), anti-tyrosinase activity inhibited melanin (40-60%).

Pharmaceutical and Food Applications

Antimicrobial films inhibited bacteria 80-95%, anticancer gels induced apoptosis (60-80% at 100 µg/mL). Food coatings extended fruit shelf life (2-4 weeks), nutraceuticals showed antidiabetic effects (glucose uptake +40%).

Strain variations: mulberry sericin hydrophilic, non-mulberry bioactive-rich. Crosslinking boosted mechanics (Young's modulus 5-15 MPa).

Thermal Properties of Sericin from Various Extractions				
Extraction Method	Tg (°C)	Tm (°C)	Decomposition Onset (°C)	Char Residue (%)
HTHP	175-185	215-225	290-310	25-30
Alkaline	165-175	200-210	270-290	20-25
Enzymatic	170-180	210-220	280-300	22-28
Microwave	168-178	205-215	275-295	21-26
Applications and Performance Metrics				
Sector	Key Application		Performance Indicator	Improvement (%)
Biomedical	Wound Healing		Healing Rate	30-50
Cosmetics	Moisturizing		Water Retention	300-400
Pharmaceuticals	Drug Release		Sustained Duration (h)	72-96

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Food	Packaging	Shelf Life Extension (days)	14-21
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CONCLUSIONS

Sericin emerges as a versatile, sustainable biomaterial with transformative potential across industries. Optimized extractions like HTHP and enzymatic methods maximize yields and properties, enabling advanced applications in regenerative medicine, smart cosmetics, targeted pharmaceuticals, and functional foods. Market growth to USD 600+ million by 2035 underscores economic viability, though challenges in standardization and scalability persist. Future research should prioritize AI-optimized formulations, clinical validations, and waste-to-value chains for global impact.

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