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Biowaste Transformation to Functional Materials: Structural Properties, Extraction Methods, Applications, and Challenges of Silk Sericin

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This review underscores the novelty of silk sericin, often regarded as a byproduct in silk production. Comprising approximately 30% of silk, sericin possesses valuable properties that have been largely overlooked in favor of silk fibroin. This work focuses on innovative extraction methods to convert sericin, typically considered waste, into a valuable resource. By examining these extraction techniques alongside diverse applications, the review aims to enhance the recognition and utilization of silk sericin in research and industry. Various extraction processes where the traditional methods, and some new techniques, are all discussed. In detail, the advantages, limitations, and strategy optimization associated with each extraction method are highlighted. For instance, silk sericin has shown promise as a wound treatment agent, a scaffold for tissue engineering, a carrier for drug delivery, and a biomaterial for regenerative medicine in the field of biomedical science due to its biocompatibility, biodegradability, and nontoxicity. Additionally, it also finds application in the cosmetic industry, where it is used in skincare products due to its moisturizing, antioxidant, and antiaging properties. Eventually, the challenges, limitations, and prospects of silk sericin are intensively discussed. This comprehensive review is expected to serve the growing body of knowledge surrounding silk sericin and foster further research and development of silk sericin-related fields.

1. Introduction

Sericulture, a complex and ancient trade, has contributed to the worldwide textile industry and cultural legacy.[1] This art of sericulture involves the cultivation of silkworms, harvesting their cocoons, and extracting the silk fibers. According to the Food and Agriculture Organization (FAO), the global production of silk fibers was around 175,000 tons in 2020 and valued at approximately $7 billion.[2] Silk fiber is an ancient textile fiber with a rich history, dating back to the 27th century BC in China. Ancient China was a leading producer of silk fiber, accounting for approximately 66% of global production. China is responsible for approximately 60% of the worldwide silk trade, making it the largest silk exporter.[9] India has become the world's second-largest silk producer, producing approximately 23,000 tons in 2020. The silk industry plays a crucial role in the economies of many countries, offering jobs to numerous individuals and boosting their export earnings.[3] Using silk sericin as a renewable resource makes the silk industry more sustainable and environmentally friendly. The industry may lessen its influence on the environment and advance circular economy principles by turning sericin, which is frequently regarded as waste, into useful biomaterials. The utilization of sericin's biodegradable qualities in conjunction with waste minimization contributes to more sustainable manufacturing across a range of applications.[4]

Commonly, sericin is considered a bio-waste protein and comprises 20%–30% of the cocoon weight. It should be noticed that the composition of sericin comprises a total of 18 amino acids, the majority of which are considered essential. For instance, it contains a sizable proportion of serine (32%) and hydroxyamino acids (45.8%) and comprises a substantial percentage of polar (42.3%) and nonpolar (12.2%) residues.[5–8] The principal role of sericin is to prevent damage and reinforce the fibroin fibers, imparting their durability and resilience. Following the elimination of sericin, the fibroin fibers exhibit a soft and lustrous appearance. An amorphous and disordered coil structure

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characterizes the predominant conformation of sericin, while a minor fraction of the protein adopts a β-sheet arrangement. However, the disordered configuration of sericin can be easily converted into a β-sheet configuration because of the recurrent moisture uptake and mechanical extension.[9,10]

As a result of recent scientific developments, a large body of literature has emerged analyzing the many facets of silk, particularly sericin, and its uses. Just a quick search on the Web of Science will turn up dozens of articles covering everything from the use of sericin in biomaterials to aesthetic applications. Aramwit et al. investigate the use of sericin in wound healing,[11] and Hu et al. investigate its bioactive qualities in the beauty industry.[12] Researchers like Saad et al.[13] and Gupta et al.[14] are among those looking for new ways to efficiently extract sericin from silk cocoons. Despite the wealth of published research, most are too narrow in scope or use outdated methods of extraction. Silk sericin interacts effectively with polymers and nanoparticles, enhancing material functionality in several key ways. These composites are perfect for tissue engineering scaffolds that encourage cell adhesion and proliferation because sericin enhances mechanical characteristics, biocompatibility, and biodegradability when combined with polymers like polycaprolactone (PCL) or chitosan. Furthermore, sericin can encapsulate metal nanoparticles, such as gold or silver, strengthening their antibacterial and stable characteristics. With sericin serving as a carrier and enhancing drug release profiles and targeting abilities, this synergy is very advantageous in drug delivery systems.[15,16] Moreover, sericin can cross-link with other polymers to generate hydrogels, which enable controlled release and moisture retention—important properties for use in medication administration and wound healing. Finally, sericin alters surface characteristics of biomedical implants and smart fabrics to enhance adherence and compatibility. The aforementioned interactions establish silk sericin as a flexible element in the creation of multifunctional materials in several sectors.[17] Therefore, it is urgently required to write a comprehensive review paper, and its primary focus is on learning everything about silk sericin, with a special focus on new methods for extracting it and intriguing but less well-known uses for the protein.

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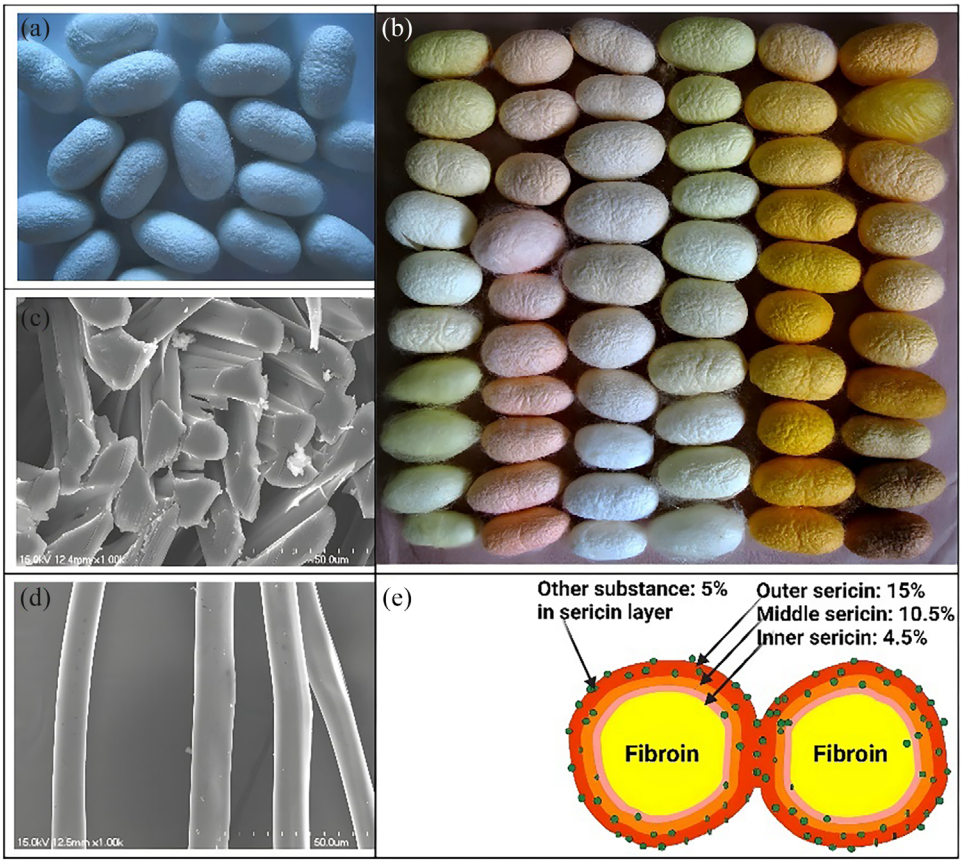


Figure 1. Various visual representations of *B. mori* cocoons, including both (a) white and (b) colored cocoons, (c,d) SEM image of the degummed silk fiber, and (e) a schematic diagram of layered sericin of silk fiber. Reproduced with permission from Ref. [23]. Copyright 2015, Elsevier B.V.

In this review paper, we will firstly introduce the basic information of silk sericin, including its unique structure and various properties. Secondly, the extraction methods of silk sericin will be discussed. Various techniques including alkaline, acidic, urea, enzymatic extraction and boiling will be presented in detail. Then, the highlight of this review will be the exploration of sericin's potential as a biomaterial for various biomedical and pharmaceutical applications like tissue engineering, wound healing, and drug delivery. Eventually, we will summarize and talk about the challenges, limitations, and prospects of silk sericin.

2. Silk Fiber

Silk is one of the most precious and luxurious natural fibers, and an absolute meaningful change with centuries of history behind its use in various applications thanks to its unparalleled physical and chemical properties.[18] The domesticated silk moth (*Bombyx mori*) produces silk fiber through its larva and some other insect species, such as spiders, moths, and butterflies, also naturally generate silk fiber.[19] The silk fiber possesses a distinctive and delicate architecture, which consists of two primary protein constituents, that is, fibroin and sericin (see Figure 1).[20,21] Fibroin constitutes the predominant structural protein component of silk fiber, whereas sericin is an adhesive protein that surrounds and holds the fibroin together in the silk fiber.[22]

3. Basic Information of Silk Sericin

3.1. Chemical Composition

Sericin is a type of compound protein that is easily soluble in water and is comprised of a multifaceted incorporation of proteins, encompassing sericin I, II, and III alongside several subordinate proteins. The structure of sericin comprises two distinct layers, namely Layer A and B.[24] Layer A is comprised of high-molecular-weight proteins that include sericin I and III, which exhibit a high degree of glycosylation, with carbohydrate fractions comprising 60% of their overall mass.[25] The water solubility and regulation of silk fiber properties are attributed to the glycosylation of sericin. Layer B is constructed with proteins with low molecular weight, among which is sericin II. It exhibits a lower degree of glycosylation in comparison to those presented in layer A. The primary function of layer B is to facilitate the adhesion between sericin and fibroin.[25] The variability of the molecular weight of sericin also depends upon the origin of silk fibers.[26] In general, sericin is composed of 18 amino acids,[27] and a comprehensive analysis of these amino acids is presented in Table 1.

Table 1. The structure and function of various amino acids that existed in the silk sericin.

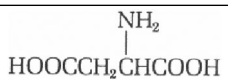
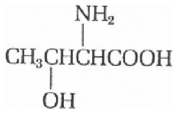
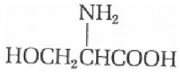
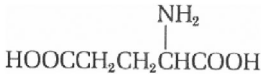
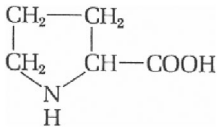
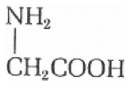
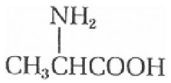
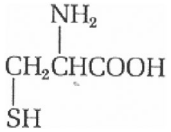
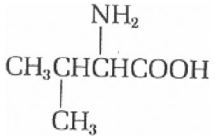
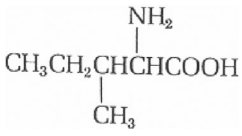
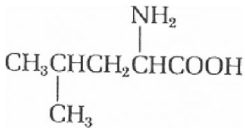
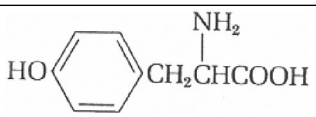
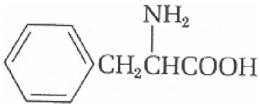
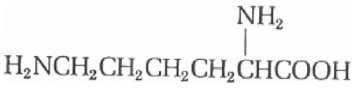
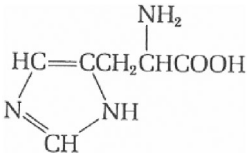
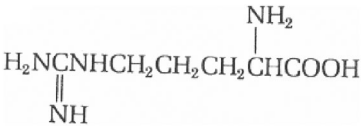
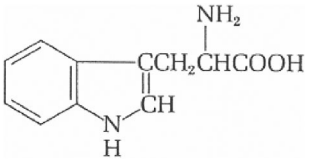
Amino acid	Structure	Functions
Aspartic acid		Involved in the synthesis of proteins and the production of neurotransmitters in the brain.
Threonine		Used to build proteins and is important for the proper functioning of the immune system and nervous system.
Serine		Used to build proteins and is also involved in the synthesis of several important molecules, including neurotransmitters and phospholipids.
Glutamic acid		Involved in the synthesis of proteins and the production of neurotransmitters in the brain.
Proline		It helps to form strong bonds within proteins and is important for the structure of collagen and other connective tissues.
Glycine		A building block for proteins and important to produce collagen, which provides structural support for tissues.
Alanine		Used to build proteins, and can also be converted into glucose for energy
Cysteine		It helps to form strong bonds within proteins and is also involved in the synthesis of important molecules like glutathione, which acts as an antioxidant.
Valine		Valine is an essential amino acid involved in protein synthesis, energy production, muscle metabolism, and neurotransmitter synthesis.
Methionine		Used to build proteins and is important to produce several important molecules, including glutathione and SAMe.
Isoleucine		A branched-chain amino acid that is involved in energy production and the synthesis of proteins.
Leucine		A different amino acid with a branched chain structure is significant for muscle development and restoration.

Table 1. (Continued)

Amino acid	Structure	Functions
Tyrosine		It builds proteins and produces serotonin, a neurotransmitter that regulates mood and other functions.
Phylalanine		Used to build proteins and is a precursor to several important molecules, including dopamine, norepinephrine, and epinephrine.
Lysine		Used to build proteins and is also involved in calcium absorption and collagen synthesis.
Histidine		Used to synthesize histamine, which is involved in the immune response and acts as a neurotransmitter.
Arginine		Protein synthesis, wound healing, and immunity. Lowers blood pressure too.
Tryptophane		It builds proteins and produces serotonin, a mood-regulating neurotransmitter.

3.2. Mechanical Properties

Sericin exhibits extraordinary mechanical properties, and it is notable for its high tensile strength, which allows it to withstand significant forces of stretching without fracturing. This characteristic makes it a compelling biomaterial and is especially useful in tissue engineering, where materials must withstand mechanical stresses while providing structural support.[28] Tensile strength increased significantly from 25 to 50 MPa when sericin concentration was increased from 5% to 15%, as shown by Meerasri et al.[29] The effects of different sericin concentrations on the mechanical characteristics of sericin films were the main focus of the investigation. Findings showed a significant relationship between concentration and tensile strength, underscoring the significance of processing variables in the creation of biomaterials. Integrating sericin with additional biopolymers, such collagen or chitosan, can improve its mechanical characteristics. According to a study by Tuwalska et al.,[30] sericin-chitosan composites showed increased flexibility and tensile strength, which qualified them for use as scaffolding in tissue engineering. Ran et al.[31] synthesized chitosan-tussah silk fibroin/hydroxyapatite composites, with a range of around 250–400 MPa for the elastic modulus and 45–100 MPa for the cracked strength. The composite material indicated above can serve as a scaffold for the implantation of bone repair cells.

In addition, sericin exhibits remarkable elasticity, allowing it to revert to its original form after being deformed. This resilience makes it suitable for various biomedical applications in which materials must maintain their form and function under dynamic conditions.[32]

3.3. Chemical Properties

Solubility: Sericin is soluble in water and some organic solvents, which is another desirable property for its application in drug delivery. The manipulation of pH and temperature parameters has been observed to have large effects on the solubility of sericin.[32,33]

Gelling Properties: The ability of sericin to form gels has garnered considerable attention due to its potential utility in the fields of delivering drugs and tissue engineering. The modulation of pH and temperature of the mixture can regulate the sol-gel transition of sericin.[34] Sericin is a globular protein with β-sheets and random coils as its structural components. Temperature, where the sol-gel transition takes place, moisture absorption,

and mechanical stretching qualities all readily cause changes in the random coil topology of β-sheets. Protein takes on its soluble form in water that is heated to 50–60 °C or more. A gel forms at lower temperatures when the solubility decreases and the random coil structure transforms into β-sheets.[35] Moreover, the process of gelation exhibits great reversibility, thereby enabling the regulated discharge of pharmaceuticals or bioactive molecules.[26,36]

Isoelectric Point: The isoelectric point of sericin is approximately 4.5, which is an important property for its application in drug delivery. At low pH values, sericin has a positive charge and can interact with negatively charged drugs, enabling sustained drug release.[26,37]

Thermal Properties: *The thermal stability of sericin is a crucial characteristic of its use in biomedical engineering*. The sericin is found to exhibit good stability up to a temperature of 240 °C, surpassing the melting point of most synthetic polymers.[38,39]

UV Absorption Properties: The absorption of UV radiation has been widely demonstrated, which is attributed to the existence of tryptophan that can absorb UV light. Sericin is found to have a UV absorption rate of 65% at 280 nm, which is like that of synthetic UV-absorbing polymers.[40]

3.4. Biological Properties

Sericin is a hydrophilic macromolecular protein that is extracted from the cocoon of the silkworm Bombyx mori, as previously mentioned. Its structure, which is typified by a high concentration of hydrophilic amino acids, makes it easier for it to interact with biological molecules and water, which boosts its biological activity. Sericin's notable antibacterial, anti-inflammatory, and antioxidant qualities can be attributed to its abundance of polyphenols, flavonoids, and β-carotene.[41] Because of these structural characteristics, sericin can scavenge free radicals, lower oxidative stress, and strengthen the immune system. Furthermore, as numerous studies have shown, sericin's special makeup promotes wound healing, provides protection from UV rays, and has antihyperglycemic, antidyslipidemic, and antitumor properties.[42]

Biodegradability: Sericin is biodegradable and can be degraded by proteases, enzymes that break down proteins. A study reported that sericin films degraded completely within 21 days in the presence of proteases.[43]

Anti-inflammatory Properties: Studies have demonstrated that sericin possesses anti-inflammatory characteristics through the inhibition of pro-inflammatory cytokines, including interleukin-1β and tumor necrosis factor-α. According to a study, the administration of sericin resulted in a significant reduction of the expression of cytokines by 57% and 47% in macrophages that were subjected to lipopolysaccharide treatment.[44]

Antimicrobial activity: Antimicrobial activity refers to a comprehensive term encompassing all active agents that impede bacterial growth, hinder the formation of microbial colonies, and potentially eradicate microorganisms.[45] The antibacterial efficacy of sericin has been exhibited against both Gram-positive and Gram-negative bacterial strains.

Antibacterial properties: Sericin may have antimicrobial properties against a variety of microorganisms, including *E. coli, Staphylococcus aureus, Candida albicans, Aspergillus flavus*, and *Streptococcus pneumoniae*, according to the studies described. In the study by Wang et al.,[46] a composite film of sericin and agar exhibited encouraging antimicrobial activity against microorganisms, as determined by inhibition zone and bacterial growth assays. In addition, sericin was used as a reducing agent to synthesize silver nanoparticles with potential antimicrobial activity in the study by Tahir et al.[47] These results presented in Table 2 that sericin could be a beneficial material for future antimicrobial product development.

Antioxidant property: Antioxidant activity in silk means that sericin can suppress the growth of germs that cause disease. The cosmetic industry makes use of low-molecular-weight sericin peptides and sericin hydrolysates. Medical biomaterial, biodegradable biomaterial, functional biomaterial, and functional fibers are just some of the applications for high molecular weight sericin peptides.[53,54] Excessive accumulation of reactive oxygen species (ROS), a consequence of normal cellular metabolism, can be detrimental. Diseases including cancer, cirrhosis, and ischemia-reperfusion can all be triggered by a cascade of cellular or tissue damage brought on by free radicals and reactive oxygen species (ROS). The antioxidant effects of sericin are well-known. Kato et al.[55] showed that it scavenges reactive oxygen species, inhibits lipid peroxidation, and acts as an anti-tyrosinase and anti-elastase agent. In addition, sericin's potential to boost the activity of antioxidant enzymes such as superoxide dismutase, catalase, and glutathione peroxidase has been suggested by research published by Li et al.[56]

The antioxidant effects of silicon sericin have been the subject of extensive research. Takechi et al.[66] used 1,1-diphenyl-2-picrylhydrazyl (DPPH), chemiluminescence, and oxygen radical absorbance capacity (ORAC) assays to determine the antioxidant capability of sericin isolated from the yellow-green cocoon. The results indicated that a flavonoid pigment present in the sericin layers was responsible for this characteristic. More than that, the inclusion of sericin powder enhanced the bread's antioxidant property, since all sericin was discovered to have good antioxidant activities against several types of free radicals. Due to the detrimental effects of free radicals on the human body, the antioxidant activity of dietary antioxidants has gained considerable study. Sericin has been shown in in vitro research by Kato et al.[55] to prevent the development of malondialdehyde, a chemical connected to several cardiovascular risk factors, by inhibiting lipid peroxidation in rat brain homogenate. The browning reactions in foods and the manufacture of melanin are controlled by the enzyme tyrosinase, which sericin effectively suppresses. This may have consequences for cancer and neurological illnesses. These results suggest that silk sericin may be beneficial as a dietary antioxidant.

Because it detects both hydrophilic and lipophilic antioxidants, the FRAP test is regarded as the gold standard for assessing the antioxidant capabilities of silk sericin. In the FRAP assay, antioxidants in the sample are used to reduce Fe (III) to Fe (II), which is then detected through spectrophotometry. The FRAP assay has an advantage over the DPPH• scavenging activ-

Table 2. Antimicrobial properties of sericin.

Sample	Methods	Temperature (°C)	Bacterial Strains	Zone of Inhabitation (mm)	Ref.
Sericin	Disc diffusion	37	*S. aureus*	8.0	[48]
–	–	–	*K. pneumoniae*	8.0	–
–	–	–	*E. coli*	7.5	–
–	–	–	*A. baumannii*	7.5	–
–	–	–	*P. aeruginosa*	7.0	–
SS/Agar	Disc diffusion	37	*E. coli*	11.0	[49]
–	–	–	*S. aureus*	11.0	–
PDA-SS/Agar	–	–	*E. coli*	11.0	–
–	–	–	*S. aureus*	11.0	–
AgNPs-PDA-SS/Agar	–	–	*E. coli*	16.3 ± 0.3	–
–	–	–	*S. aureus*	19.1 ± 0.11	–
Silver zinc sulfadiazine with sericin cream	Standard cup–plate	37 ± 0.2	*B. subtilis*	8.80 ± 0.08	[11]
–	–	–	*E. coli*	6.68 ± 0.07	–
–	–	–	*MRSA*	8.49 ± 0.02	–
–	–	–	*P. aeruginosa*	16.29 ± 0.03	–
–	–	–	*S. aureus*	10.05 ± 0.39	–
G. postica sericin solution	Agar Well Diffusion	–	*B. subtilis*	9	[41]
–	–	–	*S. aureus*	11	–
–	–	–	*S. epidermidis*	10.5	–
Sericin solution	Disc diffusion	37	*S. aureus*	–	[50]
Sericin treated cotton	Parallel stream	37	*S. aureus*	42	[51]
–	–	–	*E. coli*	40	–
Sericin treated fabric	Agar diffusion	37	*S. aureus*	30	–
–	–	–	*E. coli*	28	–
Silk sericin	Well diffusion	32	*Micrococcus leutus*	9–12	[52]
Sericin-conjugated silver nanoparticles	Well diffusion	4	*E. coli*	14.9 ± 0.10	[47]
–	–	–	K. pneumoniae	14.8 ± 0.25	–
–	–	–	S. aureus	15.9 ± 0.25	–
–	–	55	E. coli	15.3 ± 0.25	–
–	–	–	K. pneumoniae	15.4 ± 0.10	–
–	–	–	S. aureus	17.3 ± 0.10	–
–	–	37	E. coli	15.1 ± 0.20	–
–	–	–	K. pneumoniae	14.9 ± 0.15	–
–	–	–	S. aureus	16.9 ± 0.35	–

G. postica, Gonometa postica; E. coli, Escherichia coli; S. aureus, Staphylococcus aureus; C. albicans, Candida albicans; K.pneumoniae, Klebsiella pneumoniae; B. cereus, Bacillus cereus; A. nigar, Aspergillus niger; B. subtilis, Bacillus subtilis; S. epidermidis, Staphylococcus epidermidis.

ity assay and the ABTS•+ scavenging activity assay because it measures the sample's reducing capacity, which is indicative of its ability to contribute electrons to decrease oxidants. It has also been established that the FRAP assay correlates highly with other types of antioxidant assays (see Table 3). The FRAP assay relies on a single electron transfer reaction, which may not be representative of the antioxidant capacity of some substances and has other limitations. Even if the FRAP assay is helpful for gauging a sample's total antioxidant capacity, it is not sufficient for determining a sample's antioxidant activity on its own. Instead, it should be used in conjunction with other assays, such as the DPPH• scavenging activity test and the ABTS•+ scavenging activity assay, which measure distinct elements of antioxidant activity. In addition, you need to think about the constraints of each assay and pick the right procedure according to the characteristics of the material.

4. Extraction and Recycling of Sericin

The process of silk degumming involves eliminating sericin, a protein with gum-like properties that naturally envelops silk fibers and is soluble in water. Sericin is produced by the silk gland and serves as a protective coating for the delicate silk

Table 3. Antioxidant activity of sericin.

Source	Extraction method	Assay	Concentration (mg/mL)	Extraction Temperature (°C)	Scavenging activity (%)	IC_{50}	Ref.
B. mori	Heat	DPPH	1	95	9.67 ± 0.58	5.57	[57]
–	–	–	3	–	26.33 ± 1.52	–	–
–	–	–	5	–	41.33 ± 1.53	–	–
–	–	–	7	–	62.33 ± 2.08	–	–
–	–	–	9.0	–	79.0 ± 1.00	–	–
B. mori	Heat	Superoxide	2.5	95	58.13	–	–
B. mori	Heat	Hydroxyl	5	95	70.14	–	–
G. postica	Heat	DPPH	(2.0–10) × 10^{-3}	–	6.39 ± 4.1	–	[41]
–	–	–	–	–	5.40 ± 1.5	–	–
G. rufobrunnea	–	–	–	–	–	–	–
Argema mimosae	–	–	–	–	2.31 ± 2.1	–	–
Trolox	–	–	–	–	0.70 ± 5.3	–	–
BNES from Bacillus sp.	Na_2CO_3 solution	ABTS	0.075	90–95	9.33 1.53	0.41	[58]
–	–	–	0.15	–	19.47 1.21	–	–
–	–	–	0.3	–	34.34 1.25	–	–
–	–	–	0.6	–	51.96 1.71	–	–
–	–	–	1.2	–	72.59 2.34	–	–
–	–	DPPH	0.075	–	21.78 0.42	*0.38*	–
–	–	–	0.15	–	46.26 0.53	–	–
–	–	–	0.3	–	71.28 0.48	–	–
–	–	–	0.6	–	73.08 0.57	–	–
–	–	–	1.2	–	80.26 0.45	–	–
B. mori	Autoclave	DPPH	10	120	32	–	[59]
–	–	–	20	–	52	–	–
–	–	–	40	–	66	–	–
B. mori	Conventiona	DPPH	0.1 to 0.4	95	40 ± 8	–	[60]
–	–	FRAP	–	–	111.11 ± 39.87	–	–
A. assama	–	DPPH	*0.1 to 0.4*	–	40 ± 8	–	–
–	–	FRAP	–	–	179.1745 ± 38.90	–	–
B. mori	Heat	DPPH	10	95	51.3 ± 2.3	–	[61]
–	–	–	20 × 10^{-3}	–	52.8 ± 5.6	–	–
–	–	–	40 × 10^{-3}	–	74.92 ± 5.4	–	–
–	–	–	80 × 10^{-3}	–	78.306 ± 3.1	–	–
–	–	–	100 × 10^{-3}	–	79.576 ± 4.9	–	–
B. mori L.	Hydrothermal	DPPH	–	220	–	6.41 ± 0.05	[62]
–	–	ABTS	–	–	–	0.79 ± 0.37	–
B. mori	Waste water during reeling process	DPPH	0.02	–	8.1	0.0741	[63]
–	–	–	0.04	–	19.3	–	–
–	–	–	0.06	–	34.6	–	–
–	–	–	0.08	–	55.6	–	–
–	–	–	0.1	–	73.4	–	–
–	–	Super oxide anion	0.02	–	11.2	0.0779	–
–	–	–	0.04	–	15.3	–	–
–	–	–	0.06	–	31.2	–	–
–	–	–	0.08	–	53.6	–	–
–	–	–	0.1	–	69.3	–	–

Table 3. (Continued)

Source	Extraction method	Assay	Concentration (mg/mL)	Extraction Temperature (°C)	Scavenging activity (%)	IC_{50}	Ref.
Nangsew (yellow)	Boiling	DPPH	–	80–100	43.03 ± 1.05	–	[64]
–	–	ABTS	–	–	7.86 ± 0.15	–	–
–	–	FRAP	–	–	3.16 ± 0.24	–	–
Eri (white)	–	DPPH	–	–	2.28 ± 0.18	–	–
–	–	ABTS	–	–	3.25 ± 0.20	–	–
–	–	FRAP	–	–	2.11 ± 0.24	–	–
Control sericin (CS)	Autoclave	ABTS•	–	121	25.78 ± 0.72	–	[65]
–	–	DPPH•	–	–	32.18 ± 4.66	–	–
Hydroquinone-sericin conjugate (HSC)	–	ABTS• +	–	–	52.34 ± 2.66	–	–
–	–	DPPH•	–	–	83.68 ± 2.28	–	–
Pyrogallol-sericin conjugate (PSC)	–	ABTS• +	–	–	76.64 ± 0.74	–	–
–	–	DPPH•	–	–	64.67 ± 5.81	–	–

B. mori, Bombyx mori; *G. rufobrunnea, Gonometa rufobrunnea; A. assama, Antheraea assamensis;* DPPH, 2,2-diphenyl-1-picrylhydrazyl; ABTS• +, 2,2′-azino-bis (3-ethylbenzothiazoline-6-sulfonic acid); ABTS•, 2,2′-azino-bis (3-ethylbenzothiazoline-6-sulfonic acid); FRAP, Fluorescence Recovery After Photobleaching.

fibers during the silkworm's metamorphosis.[67] However, sericin can also cause the fibers to become stiffer and less flexible, leading to lower-quality silk fabrics. Therefore, removing sericin is an essential step in silk production to enhance the overall texture and appearance of silk fabrics.[68]

Silk degumming, also called silk sericin extraction, entails the elimination of the sericin layer from the silk filaments. Figure 2 demonstrates various methods for degumming silk, which include physical, enzymatic, and chemical processes. Physical degumming involves mechanically or chemically removing the sericin coating through boiling or ultrasonic treatment. Enzymatic degumming utilizes natural enzymes, such as proteases, to break down the sericin coating without damaging the silk fibers.[69] Chemical degumming, the most widely used method, involves treating the silk fibers with an alkaline solution to dissolve the sericin coating. On the other hand, with the development of fibroin-deficient mutant silkworms (e.g., *B. mori*, 185 Nd-s, and 140 Nd-s), perfect sericin could be obtained under mild conditions. Some important study showed intact sericin with different molecular weights isolated from fibroin-deficient silkworm cocoons. This was accomplished by treating cocoons with LiBr at 35 °C, yielding >90% silk sericin.[70] The selection of a degumming technique is contingent upon multiple factors such as the desired silk quality, production magnitude, and resource availability, each method presenting its own set of benefits and drawbacks. Physical degumming is suitable for small-scale production, while enzymatic and chemical methods are more efficient for large-scale production. Enzymatic degumming is an eco-friendly option, as it uses natural enzymes that are less harmful to the environment.[71]

Physical methods involve the use of mechanical or thermal treatments to break down the sericin protein. One such method is the water boiling method, which involves boiling silk fibers in water to loosen and remove the sericin.[72] Another physical method is the autoclave method, where silk fibers are placed in an autoclave and subjected to high-pressure steam to remove the sericin,[73] the Infrared (IR) method, which uses infrared radiation to heat the silk fibers, and the ultrasound method, which involves the use of high-frequency sound waves to break down the sericin protein.[74] Below are some physical degumming processes that have been described in various reference papers.

4.1. Physical Extraction

4.1.1. Hot Water/Boiling Extraction

It is the most conventional method for silk degumming and sericin extraction. Silva et al.[75] documented or recorded. The process of obtaining silk sericin involved immersing cocoon fragments cleaned and cut to about 1 cm in size, in deionized water at a ratio of 1:100 (w/v). This was carried out at a temperature of 100 °C for a duration of 60 min. After this time, the sericin solution underwent a process of controlled evaporation to attain the intended concentration. The concentration of the sericin solution that was extracted was determined through the dry weight method, which involved subjecting it to a temperature of 105 °C for a period of 24 h. The sericin solution in stock was stored at a temperature of 4 °C in preparation for subsequent experiments.

Chirila et al.,[76] Sothornvit et al.,[77] and Wang et al.[78] all these techniques relied on using hot water to remove sericin from silk cocoons, though at varying temperatures and for varying amounts of time. The optimal conditions for boiling silk cocoons to extract sericin are between 82 and 120 °C for 10 to 60 min. The method developed by Sothornvit et al. extracted 26.81 ± 1.11% of sericin at 115 °C for 37 min, representing 77.14% of the entire sericin.

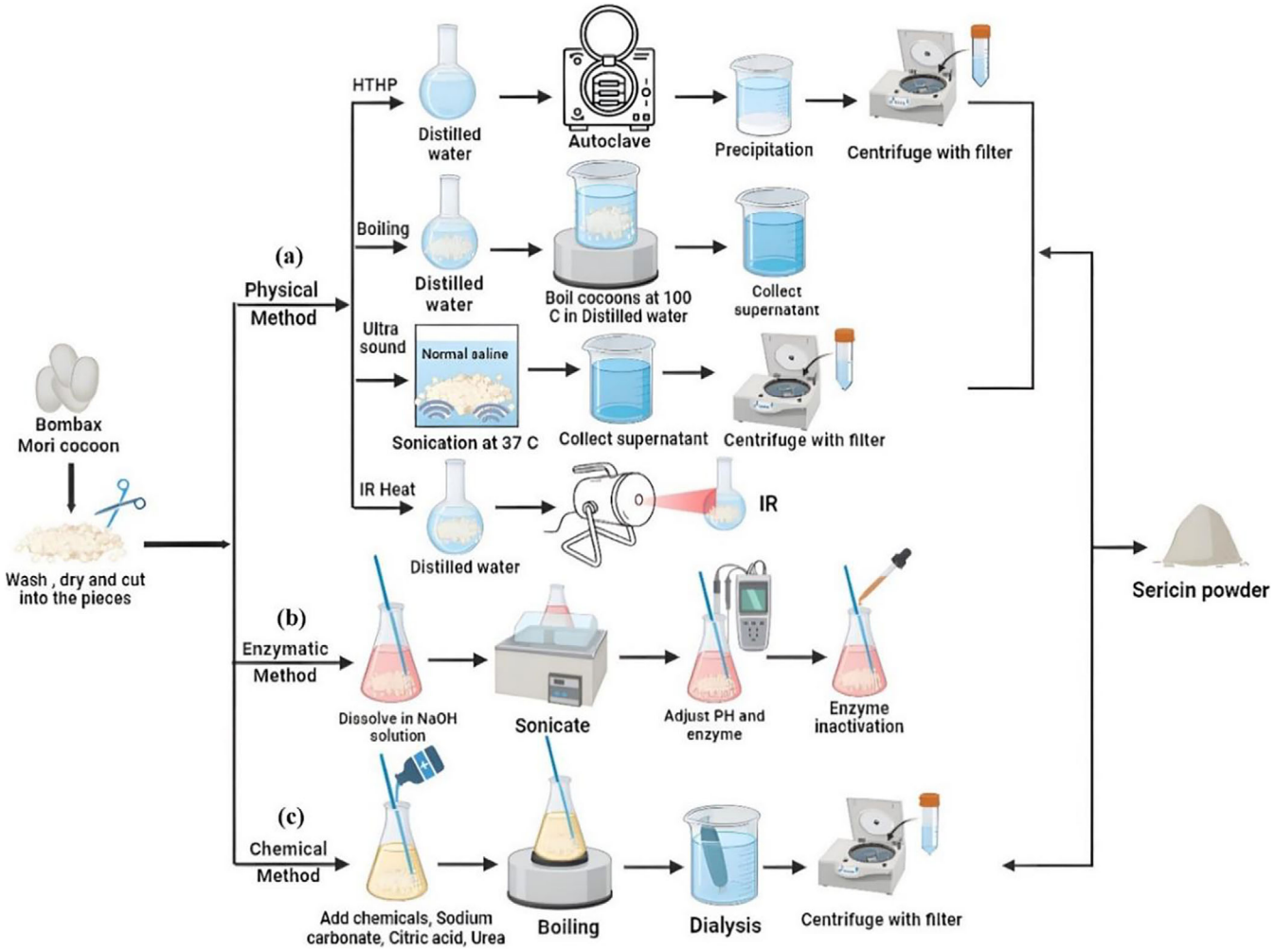


Figure 2. A schematic showing the several methods for extracting sericin. Reproduced with permission from Ref. [34]. Copyright 2022 Elsevier.

4.1.2. High Temperature High Pressure Method

The high temperature high pressure (HTHP) method is a well-established technique utilized in the processing of silk sericin; a protein extracted from silk fibers. This method involves subjecting the sericin to elevated temperatures and pressures, typically above 100 °C and 1 atmosphere, to achieve specific modifications or functional properties. The square sections of cocoons from Bombyx mori silkworms were obtained by Aramwit et al.,[79] with an approximate size of 5 mm^2. The colored cocoons of silkworms were subjected to a triple extraction process using 70% ethanol solution (1 g of silk cocoon and 30 mL of ethanol) for 24 h at ambient temperature (25 °C) to effectively eliminate all flavonoids and carotenoids. The residual cocoon shells, comprising approximately 97% of the initial cocoon weight, were subjected to an extraction process using purified water (30 mL) and 1 g of dry silk cocoon. The extraction was carried out through autoclaving at 120 °C and 15 lbf in^{-2} (1 lbf in^{-2} = 6.9 kPa) for 60 min. The aqueous solution from autoclaving silk cocoons yielded heat-degraded SS. The liquid solution, including water, was filtered to remove insoluble particles, such as fibroin. For SS powder, the filtrate was frozen and freeze-dried.

Many researchers used this method[74,80] for extracting sericin from silk cocoons, including modifying temperature and pressure, as well as centrifugation, and lyophilization. Overall, the methods used for sericin extraction from silk cocoons have shown varying yields of the protein. Gupta et al. achieved the maximum yield of sericin at 28%, while Rocha et al. obtained yields of 15% (w/w) with the freezing/thawing method and 18% (w/w) with the lyophilization method. The hot temperatures and pressures are a promising, environmentally friendly technology for sericin extraction,[77,81] offering economic, social, and environmental benefits without the need for harmful solvents.

4.1.3. Infrared (IR) Heating

The Infrared (IR) Heating method has emerged as a promising approach for processing silk sericin, harnessing the power of infrared radiation to induce controlled heating and modification of the protein's structure and properties. Raw silk was successfully and completely removed from its sericin by heating it to 110 °C in a water bath with infrared dyeing equipment described by Lamboni et al.[82] and Gupta et al.[83] There was a greater concentration of high-quality protein extracted using

this approach than with autoclaving silk sericin (SS) at 120 °C. Infrared heating's improved output can be attributed in large part to radiation heating, in which energy is sent to the substance in the form of electromagnetic waves. The water acted as an abrasive due to radiation, which aided in the separation of SS from silk and increased its solubility in water. This could also explain why this method is said to result in less protein degradation. Compared to the standard high-pressure, high-temperature autoclave extraction method, infrared extraction causes significantly reduced denaturation and degradation of SS molecules, as measured by fluorescence spectroscopy. The IR dyeing equipment was used to extract the color at temperatures of 90, 100, 110, and 120 °C for 15, 30, 60, 90, 120, and 150 min. The method for extracting SS from cocoons of *B. mori* seems to be well-established, while the method for extracting SS from cocoons of wild silkworms (*A. mylitta*) has not yet been fully optimized.

According to their report, it can be concluded that, infrared extraction of sericin is a gentle and sustainable method that can help preserve the bioactivity of sericin, although it may yield higher amounts of sericin compared to traditional extraction methods. Gupta et al. reported an output maximum of 26% w/w of sericin using IR extraction after 120 min of extraction at 110 °C.

4.1.4. Vaporizing Water Under Steam Heating

The Vaporizing Water under Steam Heating method is a novel technique in the processing of silk sericin, leveraging steam as a medium to apply heat and facilitate controlled transformations in the protein's composition and functionality. Degumming wastewater was concentrated at around 40 °C by vaporizing water under steam heating and recycling the condensate three times, as described by Padamwar et al.[26] and Wu et al.[84] Spray drying was used to turn the concentrate into flour. The flours were then mixed into a 1:10 (w/v) solution of distilled water, and the resulting mixture was refrigerated to around 4 °C. To achieve a final ethanol concentration of 75% (v/v), pure ethanol chilled at 18 °C was added gently to the sericin solution while swirling continuously. The resulting concoction was stored at 18 °C for a full day. The sericin powder was made by centrifuging the sericin solution at 3500 rpm for 20 min, then evaporating the alcohol at reduced pressure (reaching 0.1 MPa) while keeping the temperature at 40 °C, and finally freeze-drying the resulting lyophilized powder. Recovery via evaporation of degumming wastewater was first modified by Shelton, E. M., and Johnson. The sericin can be effectively recovered from wastewater generated by the silk industry, and the resulting sericin has high thermal stability and prospective uses in the food sector.

4.1.5. Ultrasonic Silk Degumming

Ultrasonic silk degumming is a process that uses high-frequency sound waves to remove sericin, a protein-based gum, from silk fibers. Studies conducted by Wang et al.,[85] Vyas et al.,[71] and Wei et al.[86] have demonstrated that sericin from silk cocoons can be prepared using ultrasonic silk degumming. A suitable quantity of cocoon shells was measured and mixed with 90 times its volume of distilled water (w/v). The mixture was subjected to ultrasonic treatment at an ultrasonic power of 600 W and a temperature of 100 °C for 2 h. The treatment was repeated after replacing distilled water. The degumming liquid was collected and concentrated under negative pressure. The liquid underwent centrifugation at a rate of 10,000 revolutions per minute for 30 min to eliminate insoluble impurities. The resulting supernatant was gathered and subjected to further concentration. The concentrated solution, which constituted 3 out of 12 parts, was subsequently subjected to drying via a spray dryer to produce a powdered sample with an elevated molecular weight of sericin (HS).

In their study, Wei et al. reported a degumming rate of 28.6% using the ultrasonic method. The authors and laboratory researchers, like Wang et al.'s study, a degumming rate of 22% was attained via ultrasonic irradiation at a temperature of 60 °C and a frequency of 40 kHz. The study analyzed and investigated the physical and chemical properties and in vitro biological activity of the low molecular weight sericin peptide and its hydrolysate. Sericin presents certain benefits, including increased degumming rates and the maintenance of sericin molecular weight. However, it may also pose certain drawbacks to energy consumption and equipment expenses.

4.1.6. Microwave Extraction

Microwave extraction is a method of extracting compounds or substances from a sample using microwave radiation. According to Bascou et al.,[78] Multiwave 5000 microwaves with a 20SVT50 rotor were used for the degumming process. Elevated temperatures and pressures have been maintained in closed vessels. The silk cocoons were heated to 120 °C for 30 min while being treated in a 1:100 material-to-liquor ratio. The maximum temperature and power were 130 °C, and1800 W, respectively. There were three stages to the degumming process: First, the solution is heated to the extraction temperature; second, the extraction time passes while the input temperature is maintained; and third, the solution is cooled. After the mixtures were degummed, the fibroin fibers were removed by ultra-sonicating them at 35 kHz for 5 min and then filtering them through a Whatman paper filter (grade 1, 11 m). Electric power for the microwave degumming was calculated by summing the area under the power curve. Microwave-assisted sericin extraction offers advantages such as shorter extraction times and higher yield percentages but may also have limitations in terms of equipment cost and potential degradation of the extracted sericin.

4.2. Enzyme Extraction

Enzymatic methods involve the use of enzymes to break down the sericin protein. This approach is favored due to its eco-friendliness and non-detrimental impact on the silk filaments. Enzymes such as proteases, lipases, and amylases[87,88] are used to selectively digest the sericin protein. The enzymatic method is gaining popularity in the silk industry due to its effectiveness and eco-friendliness.[89] Below are some enzymatic degumming processes that have been described in various reference papers.

Enzymatic hydrolysis has been investigated by Nakpathom et al.,[90] Padamwar et al.,[26] FAN et al.,[91] and Miguel et al.[92] the process involves the use of enzyme alkylase or 2–2.5g/L alkaline protease at 60 °C for 90 min, with a pH of 10. The process of extracting sericin involves hydrolysis with trypsin at varying concentrations, temperatures, and treatment durations. The hydrolysis of a 1% trypsin solution reaches near completion within 10 h and 32 h at temperatures of 37 and 20 °C, respectively. After a 4-h treatment, the quantities of sericin acquired with 1% and 8% trypsin solutions were 26.4% and 28.7%, respectively. Sericin extraction has been facilitated through the utilisation of proteolytic enzymes such as alcalase, savinase, degummase, papain, and trypsin.[93]

Miguel et al., an advanced approach involving ultrafiltration and nanofiltration has been investigated, demonstrated highly effective results. Utilizing this complex technique, it was possible to recover up to 86% of the sericin present in industrial degumming water while Nakpathom et al. found a similar reduction in percent weight loss (i.e., 20%–22%) of alkali/soap and papain enzyme used to degum Bombyx mori silk fibers. The advantage of enzymatic methods for sericin extraction is their ability to achieve high yield and purity, but a disadvantage is that they can be time-consuming, costly, and require specific conditions.

4.3. Chemical Extraction

Chemical methods involve dissolving the sericin protein with a variety of chemicals. Sodium carbonate is a commonly used alkali that dissolves the sericin at elevated temperatures, while ammonium sulfate is an acid that breaks down the sericin at lower temperatures.[94] Urea is a mild alkali that is effective at breaking down the sericin without causing damage to the silk fibers, making it a preferred method for delicate silks.[89] The process of acid degumming entails the utilization of acidic substances, such as hydrochloric acid or sulfuric acid, to yield a white silk fabric with a superior sheen. However, if executed improperly, this technique can be abrasive and result in harm to the silk fibers. Alkaline degumming, on the other hand, uses alkaline solutions, such as sodium hydroxide or potassium hydroxide, to dissolve the sericin protein, producing a softer silk with a lower luster.[95] The selection of a chemical technique is contingent upon the variety of silk and the intended result. It is imperative to meticulously contemplate the method and chemicals employed to guarantee the preservation of silk fibers and the attainment of quality benchmarks in the product.[96] Below are some chemical degumming processes that have been described in various reference papers.

4.3.1. Alkaline Degumming

Numerous researchers, including Aramwit et al.,[97] Nakpathom et al.,[90] Thitiwuthikiat et al.,[98] and Mandal et al.,[99] have used the alkaline degumming approach to isolate silk sericin protein from cocoons of the non-mulberry tropical tasar silkworm, *Antheraea mylitta*. The protein content of silk sericin can range from 10–20 mg per 1 g of cocoon.

Na_2CO_3 Extraction: The traditional technique for degumming silk was used, as described in a method by Choudhury et al.[100] The normal traditional method of boiling in a mixture of 0.3% sodium carbonate (Na_2CO_3) at 90° C for 30 min was used to degum Muga cocoons. The ratio of substance to liquid used was 1:40. Bascous et al. work[78] and Terada et al.,[101] Kumar et al.,[8] Kundu et al.,[28] FAN et al.,[29] and Tuwalska et al.[30] have all reported on different methods for degumming silk cocoons and extracting sericin, including the use of sodium carbonate at varying concentrations and temperatures, with varying material-to-liquor ratios and extraction times.

According to the findings reported by FAN et al., the maximum percentage of sericin obtained was 32.45% through the utilization of different enzymes at a temperature of 95 °C and a duration of 4 h. Tuwalska et al. reported an extraction yield of 30.04 ± 0.83% at a temperature of 120 °C, while Choudhury et al. obtained a yield of (22%–23) % for silk sericin. The utilization of the sodium carbonate method presents several benefits, including its straightforwardness, affordability, and safety. However, it may not result in the most optimal sericin yield and can potentially impact the physical and mechanical characteristics of the silk fibers.

NaCl Extraction: The NaCl extraction method is a widely used technique for isolating silk sericin from silk fibers, relying on the selective solubility of sericin in saline solutions to separate it from the fibroin component. The parameter for sericin extraction has been described by Ali et al.,[102] Dash et al.,[103] and Wei et al.[86] Bombyx mori cocoons were utilized to produce indigenous drugs, sourced from reputable commercial suppliers. The cocoons of silk were incised. The remnants of the silk moth were extracted. Subsequently, the cocoons were finely sliced. A quantity of 10 g of finely cut cocoon flakes were soaked in a 1% NaCl solution and subjected to agitation at 100 revolutions per minute for a duration of one night, as reported in reference.[104] On the subsequent day, the solution was transferred to centrifuge tubes and subjected to centrifugation at a speed of 3000 revolutions per minute. Subsequently, the supernatants were gathered.

The promising result reported by Ali et al. is a high yield percentage of 80% of total amount for sericin obtained from sodium chloride degraded silk sericin. The NaCl extraction method for sericin has advantages including high yield, simplicity, and low cost, but it may produce impure sericin and can be time-consuming and environmentally concerning.

Urea Solution Extraction: The urea solution extraction method is a sophisticated approach employed in the extraction of silk sericin. In the study conducted by Aramwit et al.,[79] cocoon shells that were recently cut (6 g) were immersed in 150 mL of aqueous 8 M urea for 30 min. Subsequently, the mixture was subjected to reflux at a temperature of 85 °C for 30 min. Insoluble residues were eliminated through the implementation of centrifugation and filtration techniques. The solution underwent a comprehensive dialysis process in distilled water, utilizing cellulose tubing (Cellusep T2; MWCO = 6000–8000; Sequin) for 72 h. Silk sericin's solution underwent freezing followed by freeze-

drying. The method for silk sericin extraction is discussed by Aramwit & P et al.,[97] Thitiwuthikiat et al.,[98] and Jo et al.[105] The papers cited suggest that the method of extracting silk sericin using urea solution is a widely used and efficacious technique. Aramwit et al. employed a technique that resulted in the production of sericin of superior quality, exhibited minimal cytotoxicity, was environmentally sustainable, and economically viable. The identical approach was deliberated in the works of Thitiwuthikiat et al. and Jo et al. Cao et al. employed a degumming technique with low efficiency in the presence of highly concentrated urea, which is solely appropriate for laboratory purposes.

Urea Mercaptoethanol Extraction: The Urea Mercaptoethanol extraction method is an advanced technique utilized in the extraction of silk sericin, combining urea as a denaturant and mercaptoethanol as a reducing agent to effectively solubilize and isolate sericin from silk fibers. The method employed by Yun et al.[106] and Takasu et al.[107] involved immersing cocoon pieces in an 8 M urea solution and heating them at 80 °C for a brief duration. Additionally, 5% (v/v) 2-mercaptoethanol was added to the 8 M urea solution. This method yielded high yields of sericin with minimum molecular weight degradation, and it was also time-efficient and cost-effective. Therefore, the urea-mercaptoethanol extraction method appears to be a promising option for obtaining high yields of sericin while maintaining its quality and minimizing cytotoxicity.

Conventional Soap-Alkaline Extraction: The conventional soap-alkaline extraction method is a traditional yet effective technique for extracting silk sericin, involving the use of alkaline solutions and soap to dissolve and separate sericin from silk fibers. In their study, Mandal et al.[99] utilized a conventional soap-alkaline method (Yun et al., 2013) to extract sericin from silk cocoons. Approximately 10 g of cocoons were immersed in a solution comprising 0.02% (w/v) sodium carbonate and 0.03% (w/v) natural organic soap. The mixture was subjected to heating for 15 min with intermittent stirring. Consequently, the sericin is extracted from the fibers, resulting in its presence in the solution. Subsequently, the solution underwent filtration via a Whatman filter and was subjected to dialysis towards distilled water for three days, to eliminate any residual impurities. The filtrate underwent freeze-drying to obtain sericin powder. Yun et al.[106] describe a process, Yang et al.[108] used sodium oleate and sodium carbonate for degumming at 100 °C for 1 h with a 28.1% rate, and Freddi et al.[109] performed alkaline degumming at 98 °C for 60 min with 7 g/L Marseilles soap. The papers cited suggest that the soap-alkaline method is a widely utilized and efficacious technique for the extraction of sericin from silk cocoons. Mandal et al. used this method with satisfactory results. The soap-alkaline method of sericin extraction has both advantages, including simplicity and effectiveness, and disadvantages, such as the use of harsh chemicals, potential harm to workers, and additional steps required for impurity removal.

Ammonium Sulfate Extraction: The ammonium sulfate extraction method is a strategic approach employed in the extraction of silk sericin, utilizing the differential solubility of sericin and fibroin in ammonium sulfate solutions to isolate sericin from silk fibers. In the study carried out by Gulrajani et al.,[40] the cocoon shells were subjected to a process of fragmentation prior to sericin extraction. The process of extracting sericin from cocoons was conducted using aqueous extraction. This involved boiling the cocoons in distilled water for 90 min, with a material-to-liquor ratio of 1:30. The addition of Ammonium sulfate (40 g) to each 100 mL of the extracted solution was performed to precipitate the sericin. The precipitated particles were subjected to filtration and drying processes, resulting in sericin powder. Padamwar and collagenous et al.[26] the addition of 15 g of solid ammonium sulfate to every 100 mL of sericin solution induces salting out, leading to the formation of a gelatinous precipitate that exhibits bacteriostatic properties. Based on the studies mentioned, there is a probability that the yield of sericin obtained by the ammonium sulfate extraction method would fall within the range of 17%–22%. Ammonium sulfate extraction for sericin has the advantages of high yield and selective extraction, but is time-consuming, can cause protein denaturation, and has environmental implications.

Sedimentation Method: The process of obtaining deposition through degumming soluble is detailed by Fatahian et al.[110] The authors suggest the addition of 40g of ammonium sulfate for every 100 mL solution, followed by filtration and drying of the resulting sedimentation to produce sericin powder at the ambient temperature.

4.3.2. Acidic Degumming

In the context of acid degumming, acids such as citric acid or tartaric acid, which contain a carboxylic acid group, can interact with the hydrogen ion (proton) on the surface of silk sericin to damage the amino acid structure of the sericin2. With the help of a surfactant, a hydrophilic site will be created. It was reported by Aramwit et al.,[97] Chopra et al.,[111] and Thitiwuthikiat et al.[98] that cocoons were sliced, and a citric acid solution (1.25%) was put into the cocoon shells, which was then heated in water for 30 min. The clean filtrate was then dialyzed for three days in distilled water via cellulose tubing (molecular-weight cut-off (MWCO): 6000–8000; Seguin, US) following filtration. The frozen and dried in the freezer filtrate solution was then discarded. Hydrolysis of sericin by acids (citric, tartaric, succinic, etc.) or depends (sodium carbonate, sodium phosphate, sodium silicate, sodium hydrosulfite, etc.) releases sericin into the alkaline or acidic solution, in which it is extremely soluble for subsequent extraction from silk.[7] The yield, physical, chemical, and mechanical qualities, and the biological properties of *B. mori* silk sericin are all affected by the extraction technique. Value of yield from extraction with citric acid (8.33–15.19%) and sodium carbonate (5.93%–12.69%) solutions. Additionally, additional purification processes are required to remove chemical contaminants from the sericin extracted using acids and bases. Aramwit et al.[112] modified their process for extracting SS powders that had been damaged by acids and alkalis. The

above-described high-temperature and high-pressure degumming procedures were used to cut cocoons and extract colors for acid-degraded SS powder formulations. The leftover cocoons were cooked for 30 min in a citric acid solution (1.25%; 1 g of dry silk cocoon and 18 mL of citric acid solution). The clean filtrate was subsequently dialyzed in distilled water using cellulose tubes [MWCO (molecular-mass cut-off) = 6000–8000] for 3 days to remove any remaining insoluble fibers. Freeze-drying was used on the SS solution after it had been frozen. Instead of citric acid, 0.5% sodium carbonate solution was used to make alkali-degraded SS powder.

In their study, Kurioka et al.[113] employed an acid degumming technique utilizing citric acid. On the other hand, Kumar et al.[114] made modifications to the said protocol by fragmenting cocoons into smaller pieces and subjecting them to boiling in either citric acid or Na_2CO_3. Meanwhile, Jo et al.[105] utilized a 1.25% citric acid solution at 100°C for 30 min, followed by dialysis, for extracting sericin from silk cocoons. Kurioka et al. reported a high yield percentage of 94.12% of total amount for sericin obtained from citric acid-degraded silk fibroin, which is a promising result. As for the best extraction method, it depends on the specific application and desired properties of the sericin. The disadvantage of silk sericin degumming by citric acid is that it requires a longer degumming time, which may result in a lower yield and lower quality of sericin. Additionally, the use of citric acid may cause environmental issues due to its potential to generate wastewater with COD and a low PH.

4.3.3. I-SPs (Isolate Sericin Peptides of Interest) Extraction by Ice Affinity Absorption

The I-SPs (isolate sericin peptides of interest) extraction by ice affinity absorption method is an innovative technique designed for precise extraction of specific sericin peptides from silk, capitalizing on their differential affinities to ice crystals for targeted isolation and purification. Wu et al.[115] employed a novel ice extraction technique to I-SPs from a solution. The equipment included a 1,000 mL low-temperature-resistant sandwich glass reactor with insulating foam covering and plastic tubes with a 1 cm inner diameter for transport. The temperature of the solution was controlled by a configurable water bath, while 95% cold ethanol was pumped by a low temperature circulating pump in the interlayer of the glass container to chill the reactor. 500 mL of SPs solution was added to the glass reactors, and the extraction process began with slow stirring using an electric agitator. The undercooling condition was disrupted by the addition of a small particle of ice crystal seed, and the resulting ice steadily grew around the inner glass wall, forming a hemisphere, as the SPs bonded to it. The I-SPs were persistently coupled to the expanding ice, while other solutes were kept out. The remaining unfrozen sample was released at the end of the run, and the ice fraction containing the adsorbed SPs was slowly washed twice with deionized water at 4 °C. The "ice fraction," the portion that had been frozen, was thawed and analyzed in further depth with techniques including a second round of ice affinity extraction (IAE). Lyophilization was used to extract the absorbed I-SPs from the ice fraction.

In their 2013 study, Wu et al. utilized an alkali degumming technique to isolate and characterize ice-binding sericin peptides from *Bombyx mori* silk. The authors obtained a yield of about 30.59% for the isolated ice-binding sericin peptides; these peptides have potential applications in the food business. Various methods for extracting silk sericin have been developed, each with their own specific degumming conditions, yield, molecular weight, benefits, and drawbacks detailed in the literature. Among the different methods, heat extraction is the most used due to its ability to obtain sericin without impurities, but it can also cause some degradation of sericin. Enzymatic methods have also been developed, which offer a more selective and controlled extraction of sericin, with lower degradation effects. However, these methods are currently limited by their excessive cost and the need for specific enzymes. Chemical methods, such as alkali, urea, ammonia, and acid extraction, have also been developed for sericin extraction. Serin extracted with acids and bases, on the other hand, needs to go through further purification stages to get rid of chemical contaminants that might drastically degrade the protein. The degrading effect of urea on sericin is reduced, but the extraction process is laborious and time-consuming, and the resulting sericin can be very hazardous to cells. Recent advances in extraction technologies have focused on developing more sustainable and effective methods for sericin extraction. These include the use of infrared heat, ultrasound, and carbon dioxide supercritical fluid. Infrared heat and ultrasound have shown promise in achieving efficient and selective extraction of sericin, while also reducing the degradation of the protein. Carbon dioxide supercritical fluid has also been shown to be effective in extracting sericin with high purity, but it requires specialized equipment.

Various methods for extracting silk sericin have been developed, each with their own specific degumming conditions, yield, molecular weight, advantages, and disadvantages, as outlined in Table 4. Among the different methods, heat extraction is the most commonly used due to its ability to obtain sericin without impurities, but it can also cause some degradation of sericin. In conclusion, while traditional heat extraction and enzymatic methods remain the most used techniques for sericin extraction, there is a growing need for more sustainable and effective methods that can overcome the limitations of current methods. New extraction technologies such as infrared heat, ultrasound, and carbon dioxide supercritical fluid show promise in achieving this goal. Chemical methods such as alkali, urea, ammonia, and acid extraction should be used with caution due to their potential degradation effects and the need for additional purification steps.

4.4. Amino Acid Analysis

Amino acid analysis (AAA) of silk sericin involves determining the composition and concentration of amino acids present in sericin, the proteinaceous component of silk fibers. This analysis is crucial for understanding the biochemical properties of sericin and its potential applications in various fields.[147] The process typically includes hydrolyzing sericin into its constituent amino acids,

Table 4. A review of different techniques for sericin extraction from cocoons.

Degumming Methods	Name of Methods	Degumming Conditions	Yields (%)	Molecular Weight	Advantages	Limitations	Ref.
Physical	Electrolyzed H_2O	≥pH 11.50; 100 °C; 1:40 (w/v); 20 min	~27	>30 kDa	Recycle sericin	Commercial viability needs to be assessed	[116]
–	Infrared heating H_2O	120 °C; pH 6.80; 1:20 (w/v); 60 min	~26	100kDa to 250kDa	High yield and quality of silk sericin (SS)	Extra equipment	[83, 117]
–	Ultrasound wave	pH 8.0–9.0; 60 °C; 1:30 (w/v); 90 min	~21	200 kDa to 100 kDa	Cleaner and eco-friendly	Expensive, degrade sericin. Extensively low efficiency	[118]
–	Gel Electrophoresis	Fluid at the anterior and the middle silk gland	–	20–400 kDa	Improves efficiency, water and energy conservation	Introduce chemicals, not well established in industry	[94, 119, 120]
–	Hot water	Boiling at 80○ C and 120○ C	21.99 ± 0.96	20–400 kDa	Ecofriendly; no chemical effluents generation; lecithin recovery	Only applicable for removal of HPLs removal; less efficient	[121, 122]
–	–	Autoclave at 120○ C for 30 min Heated at 100○ C for 10 min	~15.33	12–66 kDa	Simple; low-cost; high efficiency; no contamination	Affects fiber whiteness and absorbency. Affects fiber whiteness and absorbency; Removes only the outer layer of sericin. Sericin is degraded (when used at high temperatures).	[85, 123–126]
–	–	Autoclave at 120○ C for 30 min Heated at 95○ C for 120 min	17.00–21.27	5 to 100 kDa	–	–	–
–	–	Autoclave at 121○ C for 60 min	–	–	–	–	–
–	–	~120 °C; 1:25 (w/v); 60 min	~15	20 to 400 kDa	–	–	–
Conventional	Na_2CO_3	0.5% Na_2CO_3 aqueous solution at 80○ C and 120○ C	~30	20kDa to 100kDa	Effective	Sericin is highly degraded. Sericin recovery is difficult. It is not environment-friendly/effluent problems	[79, 85, 101, 108, 118]
–	–	0,2% Na_2CO_3 solution heated at 95○ C for 120 min	6–12	6 and 67 kDa	–	–	–
–	–	–	–	–	–	–	–

Table 4. (Continued)

Degumming Methods	Name of Methods	Degumming Conditions	Yields (%)	Molecular Weight	Advantages	Limitations	Ref.
Chemical	LiSCN solution	LiSCN saturated solution Silk gland fluid, shaken gently for 30 min	~23	20–400 kDa	Low degree of degradation; suitable for structural studies and fabricating pure sericin-based bulk materials	Inefficient; complex; purification process; short storage period	[107, 117, 127]
–	pH-adjusted LiBr	9 M LiBr; pH 5.0–7.0	–	20kDa to 260kDa	–	–	–
–	Bromelain solution	Distilled water and bromelain solution heated at 55○ C for 60 min	–	10–250 kDa	Low deweighting rate; Brings silk bright whiteness	Hard to apply to industry; Smells awful	[74, 128]
–	Urea buffer	8 M, pH 7.0; 80–90 °C; 120 min, >2 times	~27	350 to 25 kDa	Effective; time-consuming; sericin is poorly degraded	Purification steps are needed to remove the chemical; impurities, toxic to cells	[79, 82, 85, 129]
–	–	8 M urea for 30 min followed by heating at 85 °C for 30 min	18–20	10 to > 225	–	–	–
–	Alkaline	Electrolytic alkaline water at 95○ C for 7 or 13 hs	~34	5–18 kDa	Better efficiency; Shorter time and low cost; Strong action	Use of chemicals; possible damage to fibroin; decrease in fiber strength; purification steps are needed; it is not environment-friendly/effluent problems	[122, 130–132]
–	Neutral soaps	25%, pH 7.0.; 93 °C; 1:30 (w/v); 30 min	~20	–	Brings silk bright whiteness. Excellent strength and elasticity. Increased dye uptake.	Degumming bath cannot be repeatedly used; effluent problems	[111, 133, 134]
–	Acidic solution	pH 2.0.; 100 °C; 1:18 (w/v); 30 min	~27	35 to 150 kDa	Sericin is less degraded than when using alkaline solutions. Tensile strength improved	Dye uptake slightly decreased. Sericin is degraded not efficiency. Purification steps are needed. It is not environment-friendly/effluent problems.	[79, 85, 113, 135–137]
–	–	Calcium hydroxide (0.025%) for 40 min and neutralization with acids	85% recovery	< 20 kDa	–	–	–

Table 4. (Continued)

Degumming Methods	Name of Methods	Degumming Conditions	Yields (%)	Molecular Weight	Advantages	Limitations	Ref.
–	–	Novel surfactant based on silk amino acids and lauryl chloride (0.2%) for 30 min	–	–	–	–	–
–	Citric acid solution	Autoclave at 120○ C for 60 min 1.25% citric acid solution heated for 30 min 0.2% Na_2CO_3 solution	21.27 ± 3.83	20–220 kDa	–	–	–
Bio	Microbial	pH 7.0.; 28 °C; 1:30 (w/v); 30 min	~24	–	Better efficiency	Expensive; Time consuming; use of organic solvents membrane fouling	[138, 139]
Enzymatic digestion	Enzyme degumming	Commercial proteolytic enzymes for 5–240 min. at 50–65 °C	–	5 to 20 kDa	Effective; Environment-friendly/no effluent problems; Improved dye affinity (particularly with reactive dyes)	Easy to deactivate; high cost; possible overreaction to fibers; sericin is degraded; time-consuming; not applicable for high gum amount	[82, 93, 116, 140–146]
–	–	Novel protease isolated from Bacillus sp	20.7 ± 0.8	–	–	–	–
–	–	Protease enzymes using pH 10.0.; 37 °C; 1:30 (w/v); 180 min	~20	–	–	–	–
–	–	hydrolysis by protease 110○ C for 300 min	~30.4	65 kDa	–	–	–
–	–	Alcalase and Savinase at 55 °C, 30 min	21.52	–	–	–	–
–	–	Alcalase and Savinase at 55 °C, 60 min	20.08	–	–	–	–
–	–	Alcalase/Savinase and for soap in 120 min	22.58	–	–	–	–

Table 5. Silk sericin isolated from *B. mori* contains an amino acid profile that varies depending on how it was prepared (mol%).

Amino Acid	Heat[112]	Boiling[148]	Conventional (Na_2CO_3)[101]	Enzymatic[79]	Urea-Degradation[112]	Acid-Degradation[112]	Alkali-Degradation[112]
Serine	33.63	28.004	32.2	25.55	31.27	31.86	30.01
Aspartic acid	15.64	17.970	18.0	17.33	18.31	15.93	19.88
Glutamic acid	4.61	6.249	4.6	5.04	5.27	5.75	5.93
Glycine	15.03	16.289	15.7	8.23	11.23	10.49	11.01
Histidine	1.06	1.316	1.3	1.40	3.26	2.47	1.72
Cystine	0.54	0.691	>0.05	1.19	0.39	0.53	0.23
Arginine	2.87	3.516	1.8	3.48	5.41	4.92	4.92
Threonine	8.16	7.777	8.4	5.79	8.36	8.51	6.49
Proline	0.54	0	0.6	0.87	1.46	0.78	1.24
Valine	2.88	3.767	3.6	2.57	2.96	2.95	2.94
Methionie	3.39	0	<0.05	0.01	0.12	0.06	0.15
Tysine	3.45	2.870	3.7	2.93	0.36	5.56	5.24
Lysine	2.35	3.722	2.5	3.14	3.14	3.48	2.89
Isoleucine	0.56	0	0.7	0.69	0.96	0.87	0.75
Leucine	1.00	1.211	1.1	0.92	1.58	1.43	1.56
Phenylalanine	0.28	0.644	0.4	0.48	0.60	0.71	0.81
Alanine	4.10	5.200	5.3	2.80	4.33	3.72	4.21

followed by separation and quantification using techniques SS extracted from various methods is shown in Table 4. There were slight variations in the amino acid percentage in SS extracted by different methods; however, the main amino acid component in SS was still the same. In Table 5 we can see the amino acid makeup of silk sericin (SS) produced by different methods of extraction. Although diverse techniques of SS extraction resulted in varying amino acid percentages, the primary contents remained consistent.[79] Serine was the most abundant amino acid, making up around 30% of the SS. About 10%–20% of the SS was made up of aspartic acid and glycine, respectively. Heat-degraded SS had a greater methionine content than SS prepared by other means. However, urea-recovered SS had noticeably less tyrosine than SS extracted using other methods. Consistent with our previous report, these results show that the production of collagen is most strongly stimulated by heat-extracted SS due to its high concentrations of sericin, methionine, and cysteine (all sulfur-containing amino acids that can promote double-helical structures).[112] These findings are important because they show that the amino acid composition of SS significantly affects collagen synthesis. The possible application of SS as a biomaterial in tissue engineering and regenerative healthcare could be illuminated by additional studies in this field.

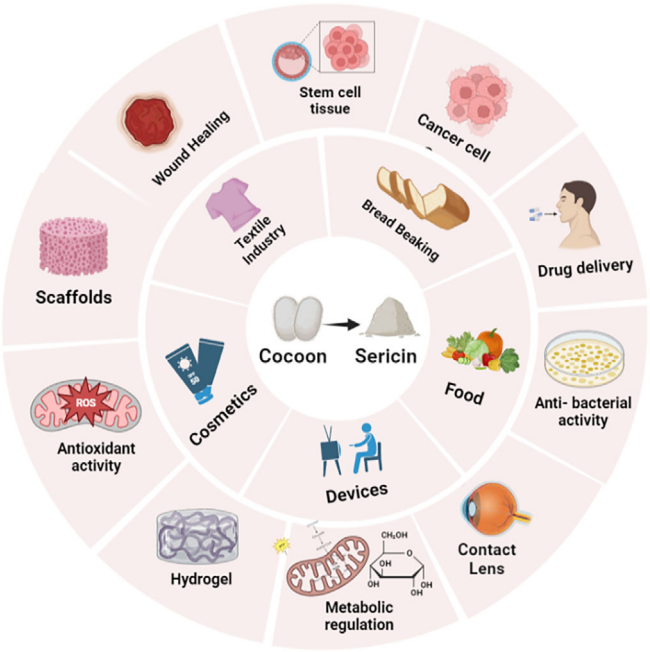


Figure 3. Prospects of exploration and applications of silk sericin.

5. Applications of Silk Sericin

Recent studies have shown promise for sericin's use in a variety of fields, including healthcare, nutrition, cosmetics, textiles, and more shown in Figure 3. Since silk's native protein sericin offers broad potential commercial applications.[149] Surgical sutures, gloves, pads, bandages, aprons, and sheets are just a few examples of the many medical textiles that might benefit from sericin's antibacterial qualities in the medical business.

Sericin is also used in drug delivery systems and tissue engineering.[82] In the pharmaceutical industry, sericin has been used as a stabilizing agent for drugs and investigated as a treatment for diseases such as cancer and diabetes.[32] Sericin has been used as an emulsifier, stabilizer, and thickener in the food industry and studied as a potential functional food ingredient. In the cosmetic industry, sericin has been used in skincare and hair

care products for its moisturizing and antiaging properties.[150] In the textile industry, sericin has been used to produce UV-protective fabrics, as a natural dye, and to improve textile durability and water-repellent properties. The potential applications of sericin are diverse and promising, making it an exciting area of research with numerous practical uses.[149] More and better uses for sericin in different fields are sure to emerge as research into the substance progresses. The various applications of silk sericin are summed up in Table 6.

5.1. Tissue Engineering

Stem tissue cells are a form of immature cells that can change into a variety of specialized cell types in the body. They are essential to tissue engineering because they can be manipulated to differentiate into kinds of cells and used to regenerate damaged or diseased tissues. Stem cells can be extracted from various locations within the body, such as bone marrow, adipose tissue, and umbilical cord blood.[180] From Figure 4, three major applications presented, where (a) bone tissue engineering, harvesting silk cocoons and degumming the sericin protein for use in tissue engineering. To build a composite material, the extracted sericin is utilized to prepare a biomaterial scaffold, which is then mixed with mesenchymal stem cells. The stem cells are seeded into the composite material, which is subsequently applied to the injured cartilage to stimulate the growth of new bone tissue, (b) a silk sericin scaffold is used for skin tissue engineering in mice by first constructing the scaffold, then growing stem cells on the scaffold, and finally adding growth factors into the composite scaffold. Enhanced cell proliferation and tissue regeneration, better wound healing, and less scar formation are some of the potential outcomes of evaluating the wound for evidence of healing and tissue regeneration after a period of 0 to 14 days,[181] and (c) 3D bioprinting with silk sericin involves cultivating stem cells in a bioink, printing them onto a scaffold, and then implanting the resulting tissue into a patient with a bone or cartilage lesion. The resulting tissue construct has therapeutic potential for wound healing by stimulating tissue regeneration and repair via many stem cell types.

5.1.1. Bone Tissue Engineering

In bone tissue engineering, bone marrow specimens were subjected to isolation and culturing procedures as per established protocols, involving density gradient centrifugation and short-term adherence to plastic culture plates, as reported in literature[182] and Figure 4a. Due to its inadequate mechanical properties, sericin is not employed as a scaffold in its pure form. The nucleation of hydroxyapatite crystals is influenced by the quantity of acidic amino acids present in sericin. In their study, Qi, and colleagues[183] developed a hydrogel composed of sericin methacryloyl and graphene oxide. This hydrogel was designed to possess adjustable mechanical strength and osteoinductive properties and was utilized as a scaffold for the purpose of repairing bone tissue in a functional manner. The scaffold exhibited favorable biocompatibility, cell adhesion characteristics, cell proliferation and migration capabilities, and osteogenic induction potential. Following implantation into a rat model with a calvarial defect, the scaffold demonstrated significant efficacy in promoting new bone regeneration and inducing differentiation of autologous bone marrow-derived mesenchymal stem cells. This resulted in successful structural and functional repair within 12 weeks period. Hence, biomaterials based on sericin possess the potential to be employed in the field of bone tissue engineering. According to Zhang et al.[184] study, sericin composite films were found to be capable of preserving the viability of human osteosarcoma MG-63 cells. This was attributed to the deposition of sericin and its three-dimensional structure. As a result, these films have potential applications in bone tissue engineering. According to Veiga et al.,[185] sericin nanocomposites were found to be nontoxic and were observed to enhance cell viability.

5.1.2. Skin Tissue Engineering

Skin tissue engineering has successfully engineered skin tissue in the laboratory and is in high demand for the treatment of burns and wounds. Although biomaterials, stem cells, and connective tissues have demonstrated remarkable potential in generating skin substitutes, their ability to fully restore damaged skin remains limited, resulting in scar formation. Hence, the domain of skin tissue engineering continues to pose difficulties.[186] Numerous investigations have been carried out regarding the utilization of sericin in stem skin tissue engineering, and the outcomes have exhibited exciting potential as shown in Figure 4b. Hafeman et al.[187] conducted a study to examine the utilization of sericin as a scaffold for skin tissue engineering. The study revealed that the utilization of sericin-based scaffolds facilitated cellular attachment, proliferation, and differentiation, resulting in the generation of novel skin tissue. The study's authors concluded that sericin exhibits significant potential as a scaffold material in the field of skin tissue engineering. Mandal et al.[188] conducted a study investigating the utilization of sericin in conjunction with chitosan for skin tissue engineering. The study revealed that the co-application of sericin and chitosan resulted in an augmentation of cellular proliferation and differentiation. Furthermore, the resultant tissue exhibited an improved capacity for wound regeneration and healing. The proposition put forth by the authors posits that sericin has the potential as a viable natural biomaterial for skin tissue engineering. Kundu et al.[28] conducted a review paper that provided an overview of the potential applications of sericin in tissue engineering, which encompasses skin tissue engineering. The authors proposed the utilization of sericin-based scaffolds to repair and regenerate injured skin tissue. Additionally, these scaffolds could be employed for the administration of growth factors and other bioactive molecules to facilitate tissue regeneration.

5.1.3. Tissue Engineering by 3D Bioprinting

The use of sericin as a biomaterial in stem cell-based tissue engineering and 3D bioprinting has shown great promise. Because of its biocompatibility, biodegradability, and capacity to pro-

Table 6. Application of silk sericin in different industries.

Industry	Segments	Applications	Ref.
Biomedical, pharmaceutical	Tissue	This study explores the possible uses of sericin composite materials in bone tissue engineering, specifically as bone substitutes and scaffolds. Skin tissue engineering. Sericin/bacterial cellulose wound healing. Sericin/agarose-glycerol chronic wound treatment.	[117, 151, 152]
–	Metabolic effects	On lipid metabolism and obesity. Within the gastrointestinal system. Within the cardiovascular and immune systems.	[7, 153]
–	Drug	Drug delivery, coating and stabilizing agents, sericin-drug coupling pure sericin nanocarrier sericin polymer nanocarrier	[7, 154, 155]
–	Cell	The mechanism for cell multiplication implantable matrix, vaccine stabilizer culture, media, and cryopreservation supplement.	[7, 156]
–	Cancer	It inhibits the development of colon cancer and colon tumors and possesses antitumor properties. Consumption of sericin reduces the number of cancer cells in the bowel and prevents oxidative stress in the colon.	[82, 157]
–	Immune structures	Sericin did not affect body mass, food intake, or blood cell count, but it lowered CD8a and CD80 cell percentages. Sericin oligopeptides increase NK cell activity and IL-2 levels, making them useful in the treatment of tumors and infectious diseases.	[158, 159]
–	Scaffolds	Cartilage regeneration, osteogenic differentiation, bone biomineralization, ischemic stroke damage treatment, full thickness wound healing	[82, 117, 160, 161]
–	Hydrogels	Cell culture and drug delivery. Skin tissue regeneration. Antibacterial wound dressing. Hypertrophic lesions develop at the donor's site of split-thickness skin grafts. Dermal reconstruction.	[117]
–	Wound healing	Human skin's characteristic moisturizing factor. Promoting collagen synthesis. Promotes collagen association and re-epithelialization.	[113, 149, 162]
–	Bandage	Sericin bandage outcomes demonstrated enhanced wound healing and decreased patient suffering.	[163]
–	Others	Development of contact lenses. Tonics rich in amino acids. Treating industrial wastewater with adsorptive pollutants. Peripheral nerve regeneration. Biomaterial to contradict cold.	[164, 165]
Cosmetic	Skincare	Antiaging and anti-wrinkle effect. Fights melanin and lightens the skin. UV protection. Protects the skin and enhances its elasticity. Antioxidant component of cosmetics.	[7, 151, 166]
–	Nailcare	Prevents cracking and brittleness and increases the inherent brilliance.	[166, 167]
–	Haircare	Conditioner and damage prevention for hair. Shampoo containing sericin and polaritonic acid of pH 3.5 or higher to repair. Shampoo containing sericin and polaritonic acid of pH 3.5 or higher to prevent.	[164, 167]
–	Gel	It helps skin retain its natural moisture and can be found in products like foundation and eyeliner.	[168]
–	Powder	Capacity to absorb moisture and protect against dermatitis. Cosmetics additive used to extend the validity of guarantees.	[7]
Food	Analytical test	To improve the flavor and texture of oatmeal. Supplement as a nutrient.	[164]

Table 6. (Continued)

Industry	Segments	Applications	Ref.
–	Antioxidant activity	Edible antioxidants utilized in fatty foods. Prevents discoloration of various foods. Antioxidants added to dairy items. Antioxidant and gastrointestinal cancer suppressant. Fight constipation and weight gain.	[164, 168]
–	Minerals	Minerals are absorbed more quickly; nutritional supplement. Beverage rich in amino acids.	[7]
Textile	Fabric	In fabrics for moisture absorption. Fabrics for cleaning. Nanofibers. Fabricated nanofiber. Nanofiber manufactured for use in dyeing to replace salt. Sericin can be utilized to enhance coating of materials. Sericin is copolymerized to produce a synthetic polymer film. Sericin can strengthen bio-polymeric grafts in the future.	[7, 169–172]
–	Medi-textile	Textiles with enhanced antibacterial action. UV protection of textiles. medical applications developing a long-lasting. Curative garments. bioactive coating on polyester for application in medical and athletic apparel; garments that heal.	[164, 173]
Devices	Sensor	Human motion and skin temperature detection. Human health and activity monitoring. Sweat loss monitoring. An electromagnetically shielded textile strain sensor.	[174–177]
–	Battery	Li-S full-capacity, flexible battery Toggle switch with resistance	[178, 179]
Others	–	Pollutant adsorption therapy for wastewater treatment. Products that filter the air. Antifreeze for highways and rooftops. A dialysis paper. Artificial leather products. Coated film on roads and roofs. Art pigments.	[151, 164]

mote cell proliferation and distinction, it is a promising candidate for use in tissue engineering. Kim et al.[189] found that printing stem cells into sophisticated 3D structures requires the use of bio-inks as illustrated in Figure 4c. Hydrogels are widely employed as bioinks, with a wide variety of applications due to their diverse characteristics. Bioinks with the right chemical and physical qualities have been produced, and these include both natural and manufactured materials such as alginate, gelatin, collagen I, fibrin, polyethylene glycol, and pluronic gels. These substances act as scaffolding that is like the extracellular matrix (ECM) seen in living organisms. To improve the ECM's replication, de-cellularized extracellular matrix (DECM) scaffolds have recently been produced. DECM is made by extracting cellular components from primary tissues through chemical or enzymatic processing. For instance, Huang et al.[190] showed that human adipose-derived stem cells cultured in a 3D bio-printed scaffold on a sericin-based hydrogel could expand and differentiate. Markstedt et al.[191] demonstrated the utilization of nano-fibrillated cellulose and alginate as scaffolds for 3D-printed ear prostheses, with a subsequent 73%–86% chondrocyte survival rate upon transplantation. The integration of stem cells with 3D bioprinting technology and biomaterials like sericin is expected to revolutionize the field of tissue engineering, allowing to produce functional tissues and organs for transplantation and regenerative medicine, as discussed in Khan et al.'s paper.[192]

5.1.4. Corneal Tissue and Contact Lens Engineering

Human corneal endothelial cells can be cultured using silk sericin as a substratum. The cornea is the front transparent viewport of the eye. It must allow all visible light to pass freely and perform primary focusing without aberration. The *B. mori* sericin-based materials are not as robust as the *B. mori* fibroin-based materials, and they may need to be improved in this regard before they can be used as surgical implants.[193]

According to the findings of Parekh et al.,[195] human corneal endothelial cells (HCECs) cultured on a denuded Amniotic membrane (AM) retained their endothelial phenotype both in vitro and in vivo described in Figure 5. Transplanted HCECs on denuded AM had an ultrastructure and density that were highly consistent with those of regular CECs grown in vitro. Flat polygonal endothelial cells of uniform size and the presence of tight connections were seen in HCECs grafted on denuded AM in an in vivo rabbit model. Contamination and transfer of infectious illnesses, biological diversity between donor tissues, sub-optimal transparency, and unexpected degradation rates are some of

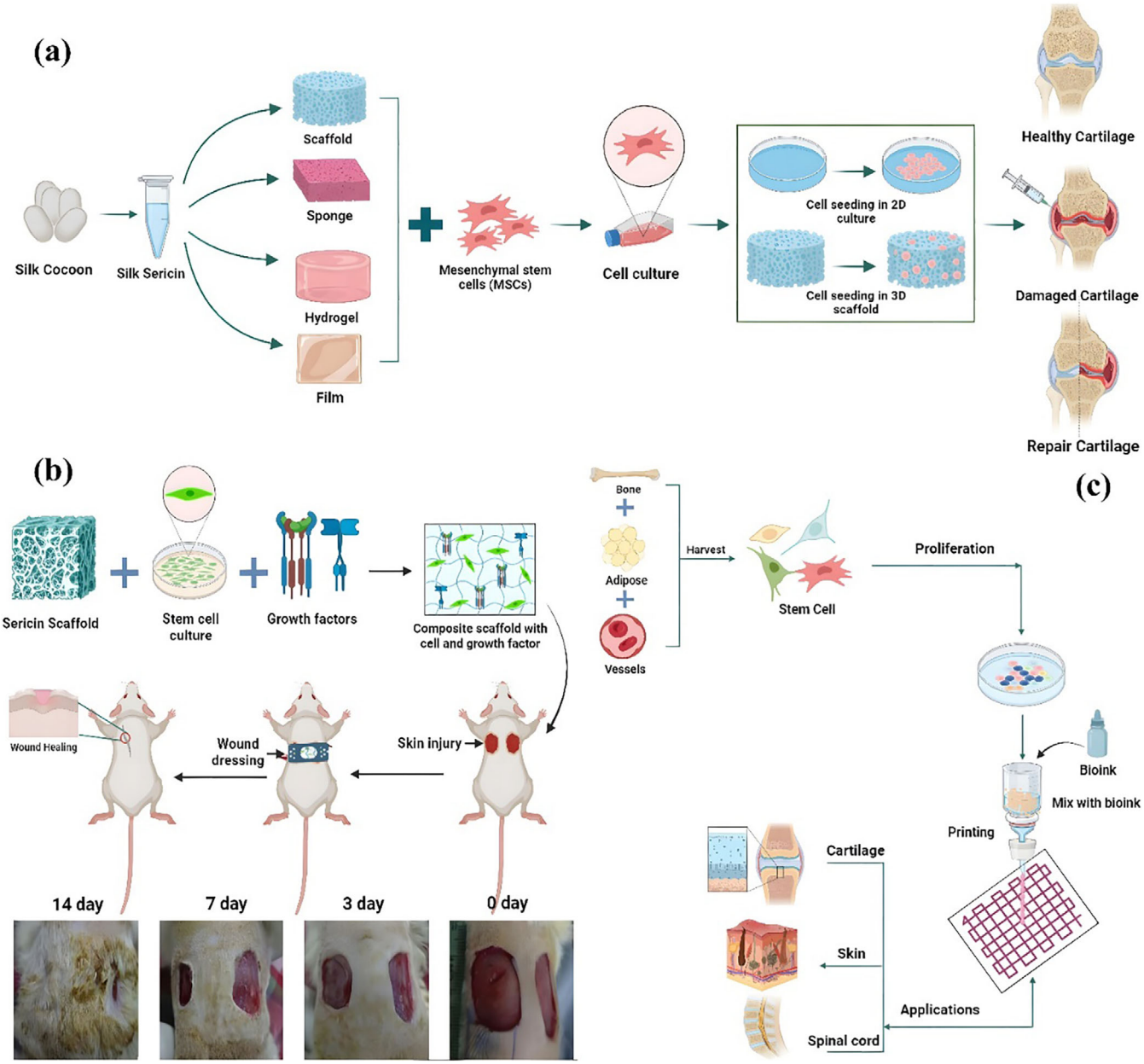


Figure 4. Schematic illustration of (a) bone tissue engineering and (b) silk sericin scaffold for skin tissue engineering in mice. Reproduced with permission from Ref. [181]. Copyright 2012, Elsevier B.V. (c) 3D bioprinting with silk sericin.

the challenges that prevent AM from being widely used as a scaffold for HCECs. The process of making silk film by designing artificial corneas with the same physiological features as a natural cornea, as Madden et al.[196] did, the risk of significant problems following implantation can be minimized. The mechanical characteristics of the normal cornea, like microporosity and optical clarity, are required for the long-term stability and accessibility of the artificial cornea; the capacity to support cornea cells constantly is also critical to prevent the destruction of collagenase and promote corneal tissue repair. With just 20,000 reported donors annually to cover the needs of 3.5 million people, Guérin et al.[197] found that the shortage of corneas for transplants is particularly severe in undeveloped nations, where 90% of corneas are recorded. Keratoprosthesis is one solution being developed as an alternative to using corneas from deceased donors. However, biocompatibility with plastic materials, long-term integration within living tissues, and exposure to air are all obstacles that must be overcome to develop effective keratoprosthetics.

Hydrogels, based on poly-2-hydroxyethyl methacrylate (PHEMA), were initially described by Wichterle and Lim in 1960[198] as a synthetic biocompatible material useful for contact lens applications. Silicone-based hydrogels represent the greatest significant improvement to contact lenses. When worn at night, these reduce the effects of "induced hypoxia on corneal physiology"][199] and are hence beneficial to contact lens wearers. New generation soft contact lenses with increased oxygen permeability, prosthetic corneas, skin grafts, and epileptic

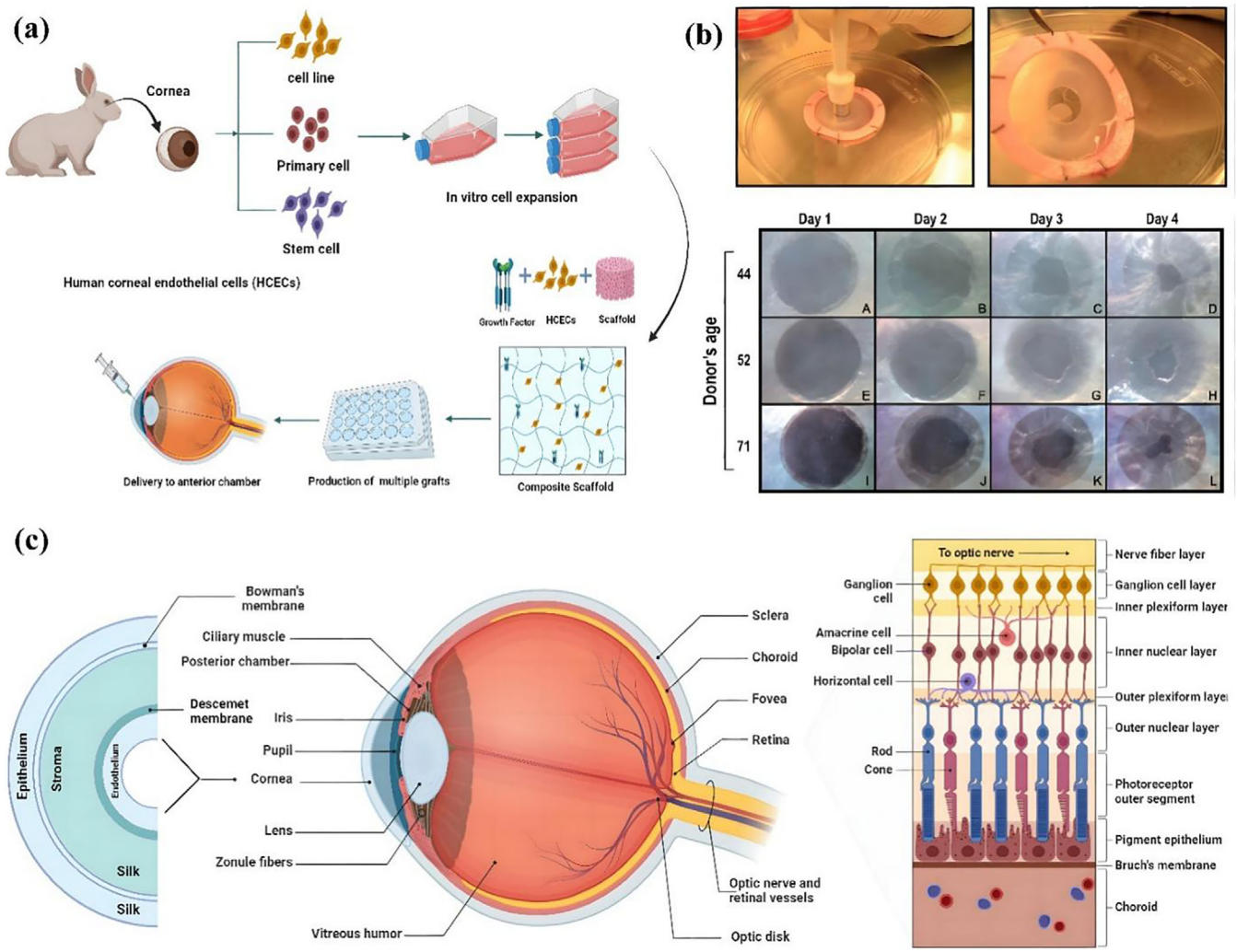


Figure 5. The generation of injuries on tissue-engineered human corneas. Reproduced with permission from Ref. [194]. Copyright 2015, Elsevier.

medication permeable devices are only some of the potential future uses of silk biomaterials described by Wenk et al. The biodegradable sericin composites can be used to make bioengineering components including functioning membranes and ligaments.

5.2. Wound Healing

Healing a wound is a dynamic, intricate process that requires a well-coordinated set of steps. The four stages of these complex processes are hemostasis, inflammation, proliferation, and remodelling, and they all occur simultaneously. Tissue damage from chronic wounds including burns, diabetic wounds, and ulcers cannot be repaired in the usual time limit because of disruption by numerous causes that lengthen one or more of the four normal healing phases.[200] Local and systemic wounds can be treated with a wide variety of scaffolds, films, hydrogels, fibres, foams, and spheres as shown in Figure 6.[201] To show the versatility of sericin, Pornanong et al.[163] created a sericin/PVA hybrid scaffold that accelerated wound healing in rats more effectively than a PVA scaffold devoid of sericin. A clinical trial including the treatment of a split-thickness skin graft (STSG) donor site corroborated these findings. When compared to the commercially available Bactigras dressing, the sericin/PVA scaffold significantly accelerated the time it took for the patient's wound skin to heal. Wound dressings made on pure SS gel films were developed by Teramoto et al.[202] These films' morphology was not affected by chemical treatment, and they were resistant to swelling. They absorbed up to 80% of their weight in water without changing their handling characteristics, even while wet. Also, the films were found to be elastically deformable in the wet state up to a strain of 25%, making them a suitable candidate for usage in joints and other movable parts. The low cell adherence and lack of cytotoxicity observed with SS gel films also aid in wound healing. These characteristics favor using SS gel films as wound dressings. Aramwit et al.[11] conducted a clinical trial on the treatment of second-degree burn wounds in which the effectiveness of sericin in combination with a conventional antibacterial cream (silver zinc sulfadiazine) for open wound care was examined in a total of 29 patients with 65 burn wounds. No infections or serious reactions were found in any wounds treated

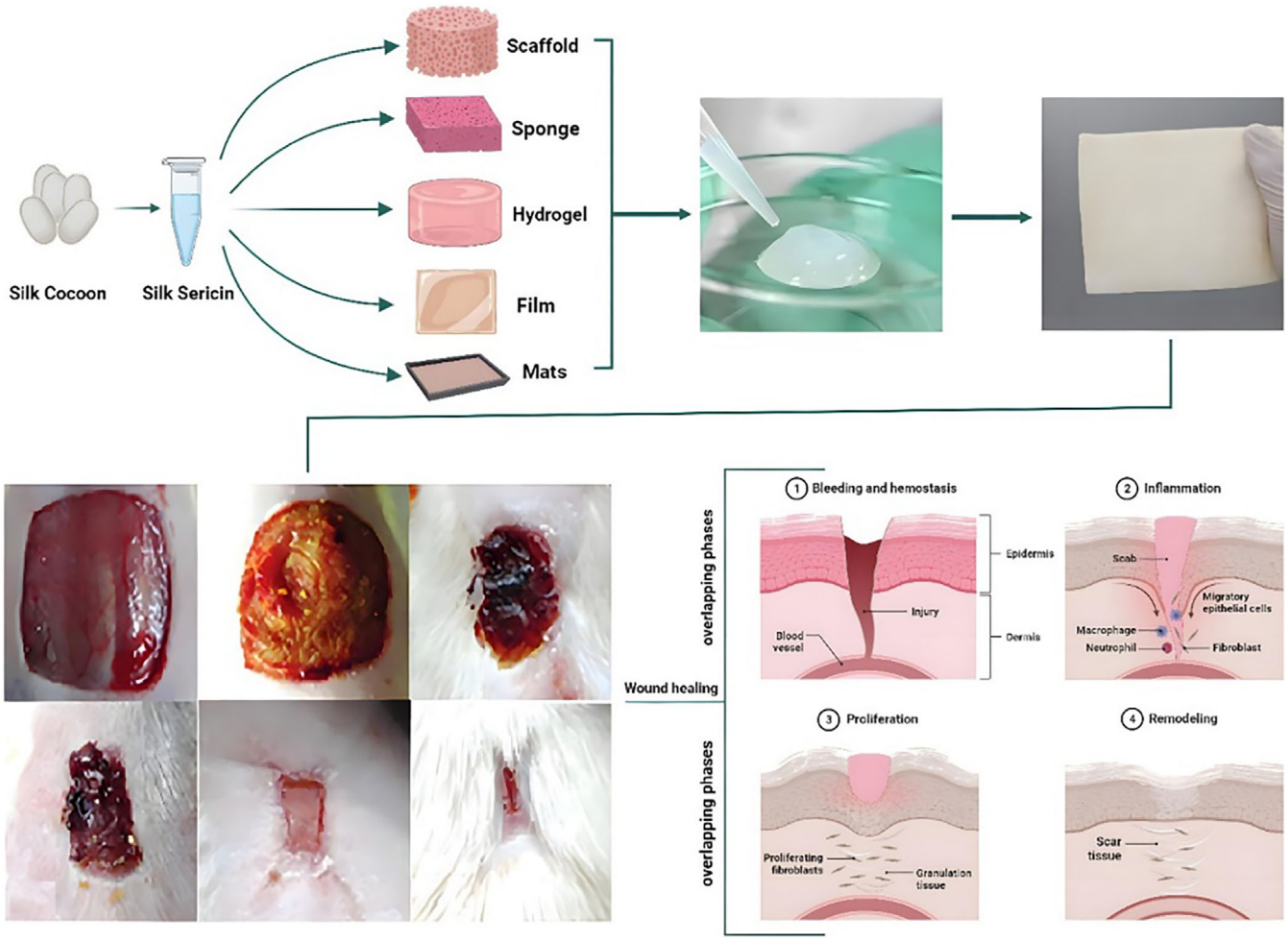


Figure 6. Wound healing biomaterials. Wound dressing preparation (a) wound healing process and (b) wound closure and healing. Reproduced with permission from Ref. [203]. Copyright 2019, Elsevier B.V.

with sericin, proving its safety. In addition, sericin helped speed up the healing process; while it took the control group (wounds treated with silver zinc sulfadiazine cream only) 29.28 ± 9.27 days to fully recover, the sericin group only needed 22.42 ± 6.33 days.

A wound is the outcome of any injury that breaks the skin's surface and extends deeper than the outermost layer.[204] Surgeons and emergency room doctors may encounter significant challenges when treating wounds resulting from mechanical trauma, acute and chronic burn injuries, and pressure and foot ulcers.[205,206] Sericin wound-healing qualities make it an interesting therapeutic target for future research. More research is needed to determine the exact processes by which sericin promotes healing and to create safe and effective sericin-based therapeutics for use in wound care.[207]

5.3. Matrix for Implants

The collagen and sericin biomatrix is composed of two natural compounds in a ratio that permits biodegradability rate control and assures sufficient time for novel in situ tissue formation from Figure 7. According to the study conducted by Dinescu et al.,[208] the matrix is typically made by combining sericin and collagen with a scaffold or hydrogel. To boost tissue regeneration, the matrix may also contain growth factors or other bioactive molecules. The matrix is then seeded with human adipose-derived stem cells (hADSCs) and permitted to proliferate and differentiate. Following this, the hADSC-seeded matrix is implanted into the animal's incision. A piece of skin or tissue may be removed to produce the wound. Monitoring the incision over time to assess the performance of the matrix. This may involve evaluating the rate of wound closure, the formation of new tissue, and the fusion of the matrix with the surrounding tissue. Once the wound has completely recovered, the newly developed tissue is analyzed to determine its quality and composition. This may involve histological, immunohistochemical, and gene expression analysis. In another applicable study, sericin and collagen were combined to create a scaffold for tissue engineering by Dai et al.[209] The scaffold was then inoculated with adipose-derived stem cells and cultured, resulting in the formation of new tissue. Due to its biocompatibility and capacity to support cell growth and differentiation, the authors determined that the sericin/collagen scaffold showed promise for use in tissue engineering applications.

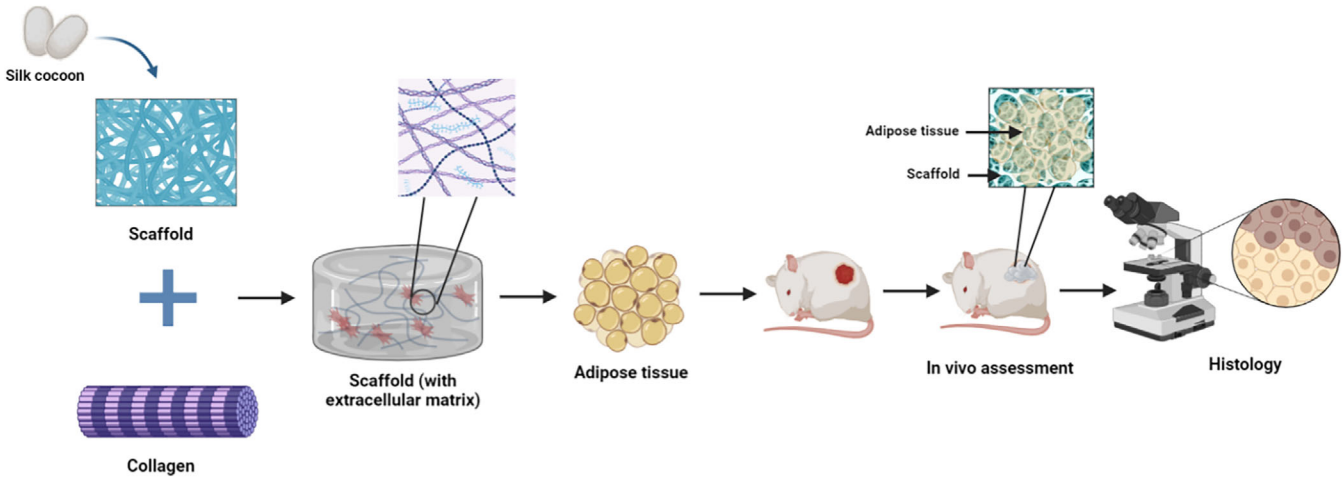


Figure 7. Extracellular matrix scaffolds in wound healing: harnessing the potential of human adipose-derived stem cells (hADSCs).

Due to its biocompatibility and its capacity to improve the performance of collagen-based scaffolds, sericin has great promise as a biomaterial for use in tissue engineering applications. Sericin has been shown to enhance collagen synthesis and organization and promote cellular adhesion, proliferation, and migration.

5.4. Anticancer or Antitumor Activity

Inhibiting the development and spread of cancer cells or tumors is what is meant by the term "anticancer" or "antitumor" activity. This can include various mechanisms such as inducing cell death (apoptosis), suppressing cell proliferation, preventing angiogenesis (formation of blood vessels that supply nutrients to tumors), and modulating the immune system to attack cancer cells.[210]

A proposed procedure for targeted antitumor activity is illustrated in Figure 8. Mesenchymal Stem Cells (MSCs) are collected from bone, adipose, or cartilage tissue and cultured before being mixed with silk nanoparticles loaded with anticancer drugs prepared by electrospinning or other methods. The MSCs and nanoparticles are incubated to allow for proper uptake of the nanoparticles before being transferred to the tumor site by injection, where the MSCs deliver the drug-loaded nanoparticles. The response to treatment is monitored using imaging techniques, and the treatment's effectiveness and safety are assessed. By increasing the treatment's specificity and decreasing the risk of adverse effects, this strategy holds enormous promise for the discovery of effective and safe cancer treatments. According to Mandal et al.[211] research, Ceresin, which is the primary protein found in Silk, is associated with flavonoids and polyphenols, and exhibits anticancer characteristics. The findings indicate that sericin cells experience a 50% decrease in survival upon exposure to sericin. This occurs in the elevation of intracellular ROS by sericin, leading to cell cycle arrest in the G1 phase and subsequent apoptosis. Thus, sericin exhibits anticancer properties by suppressing cancer growth through its pro-oxidative effect. Another study Ali et al. and Pongcharoen et al.[212,213] have reported on the anticancer properties of sericin, specifically its antitumor activity against colon cancer. Sericin has been applied to decrease the longevity of SW480 cancer cells. The protein's mode of operation involves the induction of apoptosis in SW480 cells through the upregulation of caspase-3 activity and the downregulation of B-cell lymphoma 2 (Bcl-2) expression by serine. The antiproliferative impact of sericin is achieved through the arrest of the cell cycle during the S phase. Based on the findings, it can be concluded that sericin can safeguard colon cancer cells and may serve as a beneficial dietary component in preventing them. Studies have shown that sericin, a protein in silk, can fight cancer and is especially effective against colon cancer. Increased intracellular reactive oxygen species (ROS), cell cycle arrest, and reduced Bcl-2 expression are all mechanisms by which sericin promotes apoptosis in cancer cells. Therefore, sericin could be a promising new drug for treating cancer, particularly colon cancer. The treatment's potential and safety as a cancer remedy, however, require additional research.

5.5. Platelet Lysate

Platelet lysate (PL) is an alternative to fetal bovine serum (FBS) for cell growth and tissue regeneration. The PRP technique entails collecting whole, uncoagulated blood from donors and centrifuging it to isolate the red blood cells and platelet concentrate.[214]

Centrifugation separates three layers, with the middle one (called the "buffy coat") being collected and combined with plasma to make platelet concentrate using the buffy coat method. To make PL, platelet concentrate is frozen and thawed several times, and then filtered to remove any remaining cells. The resulting PL has been used in both cell culture media and regenerative medicine. The combination of PL and serum supplement (SS) is an effective strategy for tissue regeneration that can be utilized in place of fetal bovine serum (FBS) in cell expansion and tissue repair procedures. Human bone marrow mesenchymal stem cells were studied by Bari et al.,[215] who found that the combination of silk sericin and platelet lysate dramatically increased cell proliferation and differentiation into

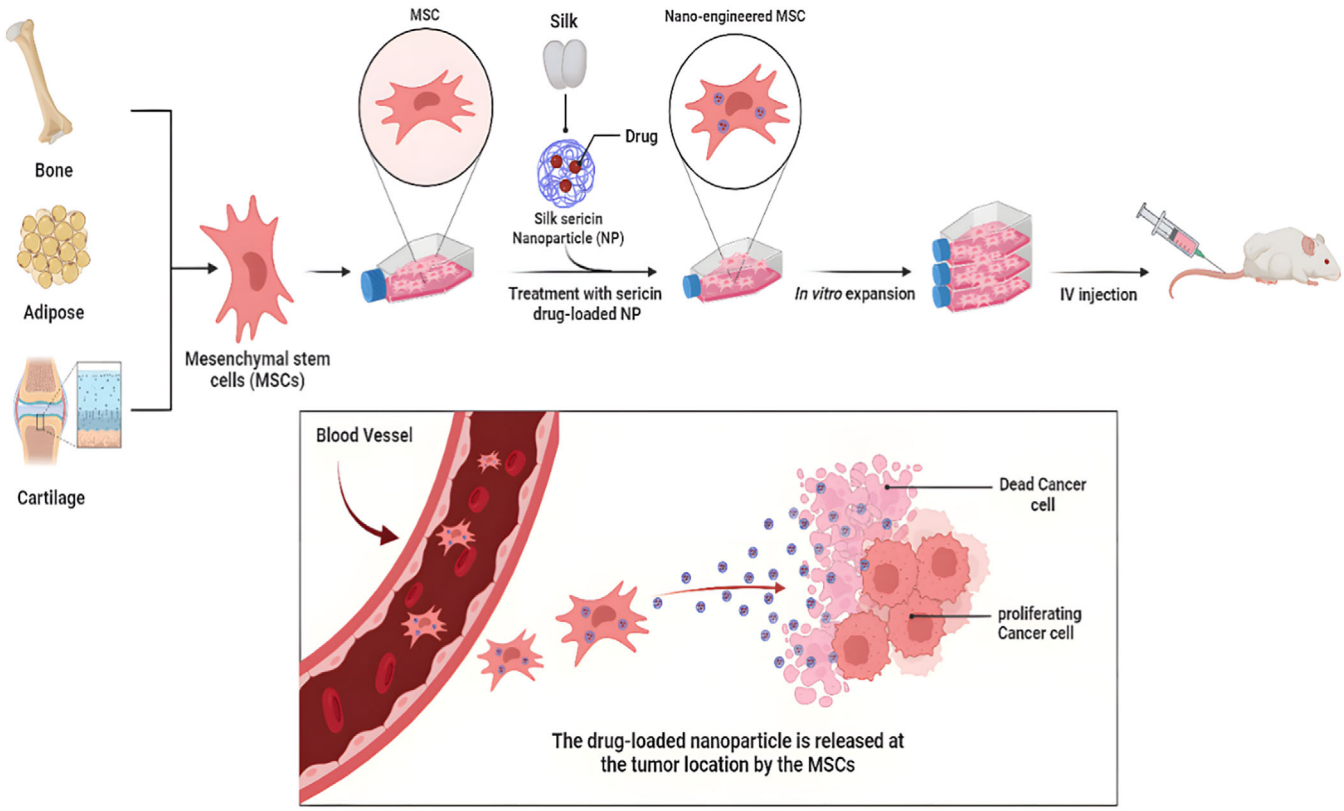


Figure 8. Schematic illustration of the fundamental concept underlying active and passive drug delivery systems in the tumor niche.

bone-forming cells. Mori et al.[200] investigated coating titanium implants with silk sericin and platelet lysate and found that this combination significantly enhanced the adhesion, proliferation, and differentiation of osteoblasts on the titanium surface. Together, silk sericin and platelet lysate have demonstrated considerable promise for use in tissue engineering and regenerative medicine, with benefits seen in promoting cell proliferation, differentiation, and extracellular matrix synthesis (see Figure 9).

Together, silk sericin and platelet lysate have demonstrated considerable promise for use in tissue engineering and transplantation, with benefits seen in the promotion of cell proliferation, differentiation, and extracellular matrix synthesis.

5.6. Biomineralization

The term "biomineralization" refers to the process through which minerals are synthesized and incorporated into the tissues of living organisms. Biomineralization of sericin can take place either through the organic mineralization process or by employing biomimetic strategies.[216] Natural biomineralization mimics the effects of sericin by encouraging hydroxyapatite (HAp) crystal formation along the c-axis, as observed by Veiga et al.[156] In the absence of sericin, HAp particles with properties like mineral bone can be obtained, but only at very particular temperatures and pH values. However, Veiga et al.[217] discovered that nucleation of HAp in sericin films is easily induced by changes in the protein structure of sericin in response to various triggers. The arrangement of carboxyl groups on the protein and the attachment of HAp crystals to the sericin molecular chains can be understood in terms of the orientation of functional groups in sheet sericin. Nucleation sites for sericin/HAp particles are provided by chelated calcium ions in the precipitation medium. The processes that lead to the development of sericin/CaP composites. It emphasizes that HAp is more likely to assemble in a homogenous fashion when sericin is present and that the induction sites for HAp nucleation in sericin films are governed by changes in the protein shape and the arrangement of carboxyl groups on the protein. Research on sericin/CaP composites has shed light on the processes that lead to their formation.

5.7. Metabolic Effects

Metabolic effects refer to the changes that occur in the body's metabolism, which incorporates cellular activities like tissue repair and energy production. These changes can have a significant impact on overall health, including conditions related to gastritis, obesity, metabolism, and the immune system.[218]

5.7.1. Gastrointestinal Tract

The digestive system, often known as the gastrointestinal tract (GI tract), is a muscular tube that extends from the mouth to the anus. Its main purpose is to break down food and draw out

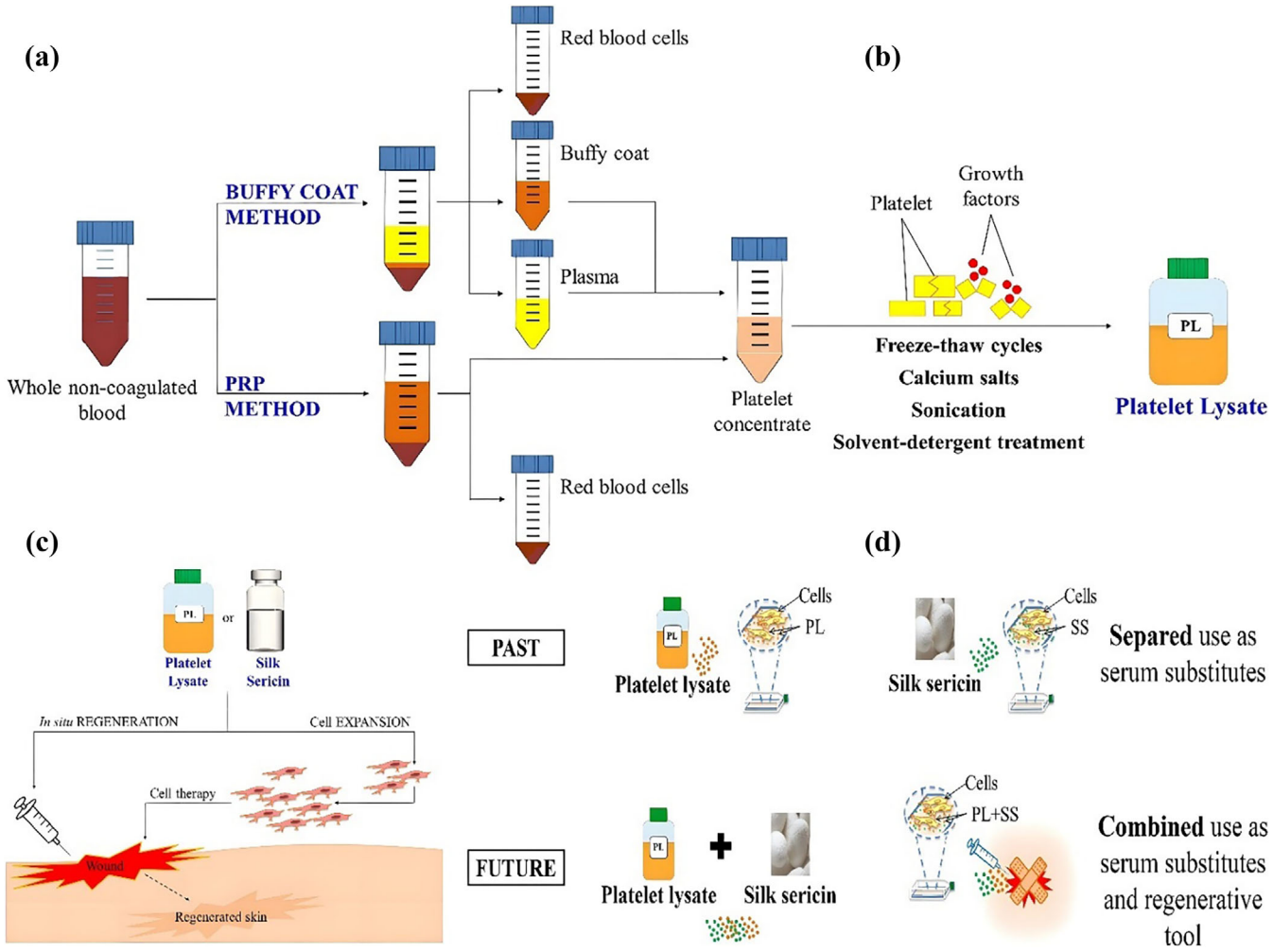


Figure 9. Generating platelet lysate. (a) Platelet Rich Plasma (PRP) technique; (b) buffy coat method; (c) platelet lysate (PL) and serum substitute (SS) used independently in regenerative medicine, and (d) integrating PL and SS holds promise for tissue regeneration. Combination can replace FBS for cell growth or support tissue repair and regeneration directly. Reproduced with permission from Ref. [200]. Copyright 2018, Elsevier B.V.

useful substances including nutrients, electrolytes, and water.[219] The gastrointestinal (GI) application of sericin has been the subject of multiple research efforts. Rats fed a meal containing 3% sericin for 12 days absorbed more zinc, iron, magnesium, and calcium ions, according to research by Sangsawad et al.[220] For 14 days, Keawkorn et al.[221] fed animal model food supplemented with 4% sericin to avoid atropine-induced constipation. In addition, Xu et al.[158] showed that sericin benefited colon health by modifying the immune response and the intestinal barrier function and that it increased the quantity of immunoglobulin A (IgA) present in the colon, which is linked to a reduced risk of colon cancer and ulcerative colitis. These results indicate that sericin may have value as a gastrointestinal functional food.

5.7.2. On Lipid Metabolism and Obesity

Lipid metabolism refers to the biological processes by which lipids, including fats, oils, and cholesterol, are synthesized, broken down, and utilized by the body. Excessive fat storage to the point where it may compromise health is the hallmark of the medical disease known as obesity.[222] Sericin has been demonstrated to have powerful anti-obesity benefits in scientific studies detailed in Figure 10. Sericin, through activating AMP-activated protein kinase (AMPK), was found to decrease body weight growth, visceral fat formation, serum triglyceride levels, and increase glucose tolerance and insulin sensitivity in a 6-week study by Kunz et al.[223] Similarly, Seo et al.[224] observed that rats supplemented with sericin for 4 weeks had significantly reduced body weight gain, serum triglyceride levels, and liver lipid accumulation, and had improved insulin sensitivity and glucose tolerance. Sericin was reported to scavenge free radicals and reduce oxidative stress in rats fed a high-fat diet, resulting in significant decreases in serum lipid peroxidation and improvements in antioxidant enzyme activity.[225] Cumulatively, the research points to sericin's promise as a dietary supplement or functional food ingredient for the management of weight and related metabolic problems. Further research is warranted because of its antioxidant characteristics and its capacity to activate AMPK, control lipid metabolism, and prevent fat storage.

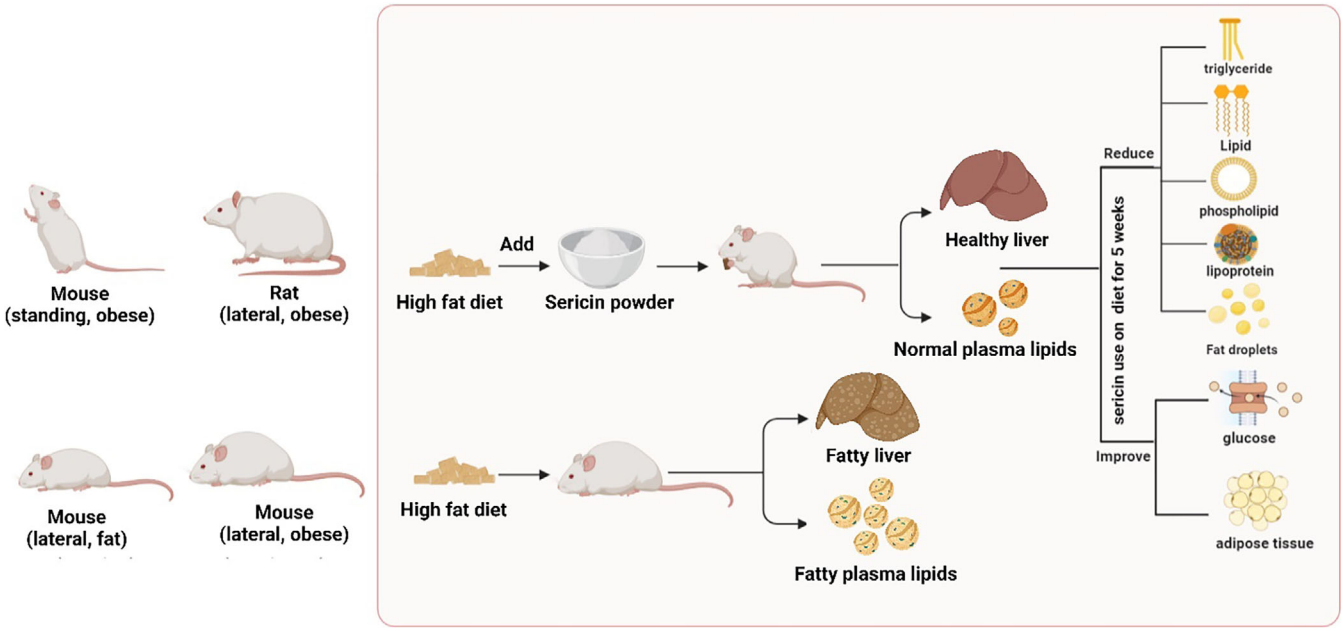


Figure 10. Potential beneficial effects of sericin on lipid metabolism and obesity.

5.8. Drug Delivery

A controlled and targeted method of providing medications or therapeutic agents to the body in order to achieve therapeutic impact while minimizing negative effects is referred to as drug delivery.[226] Figure 11 illustrates sericin drug delivery; it can be extracted from silk fibers using various methods such as degumming, dissolution, or enzyme hydrolysis. Then it proceeds for dialysis to remove impurities in silk sericin. Sericin nanoparticles can be loaded with drugs by dissolving both the drug and the modified sericin in a solvent, followed by the formation of nanoparticles through solvent evaporation or other techniques. The effectiveness, safety, and pharmacokinetics of the drug-loaded sericin nanoparticles can be assessed in in vitro and in vivo experiments.

Venous (Intravenous) Drug Delivery: In a review paper by Kumar and Abrahamse et al.,[43] the authors mentioned that sericin-based nanoparticles can be used for intravenous drug delivery. They stated that these nanoparticles have shown high biocompatibility, stability, and sustained drug release, making them suitable for targeted drug delivery through the bloodstream. Potential risks include thrombosis and infection at the injection site, along with variability in drug distribution, which may lead to inconsistent therapeutic outcomes.

Oral Drug Delivery: In a research paper, Kashyap et al.[227] discussed the use of lipid nanoparticles with sericin for oral drug delivery of curcumin. They found that these nanoparticles improved the bioavailability and absorption of curcumin while also protecting it from degradation in the gastrointestinal tract. Challenges include variability in gastrointestinal conditions affecting drug release and the risk of first-pass metabolism, which can significantly reduce bioavailability.

Ointment (Transdermal) Drug Delivery: In a review paper by Liu et al.,[228] the authors mentioned the use of sericin-loaded lipid nanoparticles in a gel for transdermal drug delivery. They stated that sericin can improve the skin's permeability while also providing a protective barrier for the drug-loaded nanoparticles. Transdermal delivery may be limited by skin barrier properties, and some drugs may cause localized toxicity or irritation if not formulated correctly.

Bone (Intraarticular) Drug Delivery: In a research paper, Ahmad et al.[229] discussed the use of polymeric micelles with sericin for intraarticular drug delivery of docetaxel. They found that these micelles improved the drug's bioavailability and efficacy while also reducing the side effects associated with systemic administration. Intraarticular injections can lead to pain, inflammation, and infection at the site, and long-term effects of localized drug delivery need further investigation to ensure safety.

5.9. Cell Delivery or Cell Amplification

Cell delivery is the process of introducing cells into a specific location in the body for tissue repair and regeneration. Cell amplification involves expanding a small number of cells in vitro to generate a larger population for transplantation.[230] The possibility of sericin as a carrier for cell transport is discussed by Lamboni et al.[82] They mention how sericin can be utilized to create a capsule around cells, shielding them from damage during transplanting. Sericin can also be modified with other compounds to improve cell adherence and growth. Sapru et al.[231] explore the potential of sericin hydrogels for cell multiplication in a study publication. Researchers discovered that human embryonic stem cells may be expanded and kept in a pluripotent state for numerous passages when cultured in sericin hydrogels. The authors propose that sericin hydrogels may prove to be an effective medium for cultivating stem cells

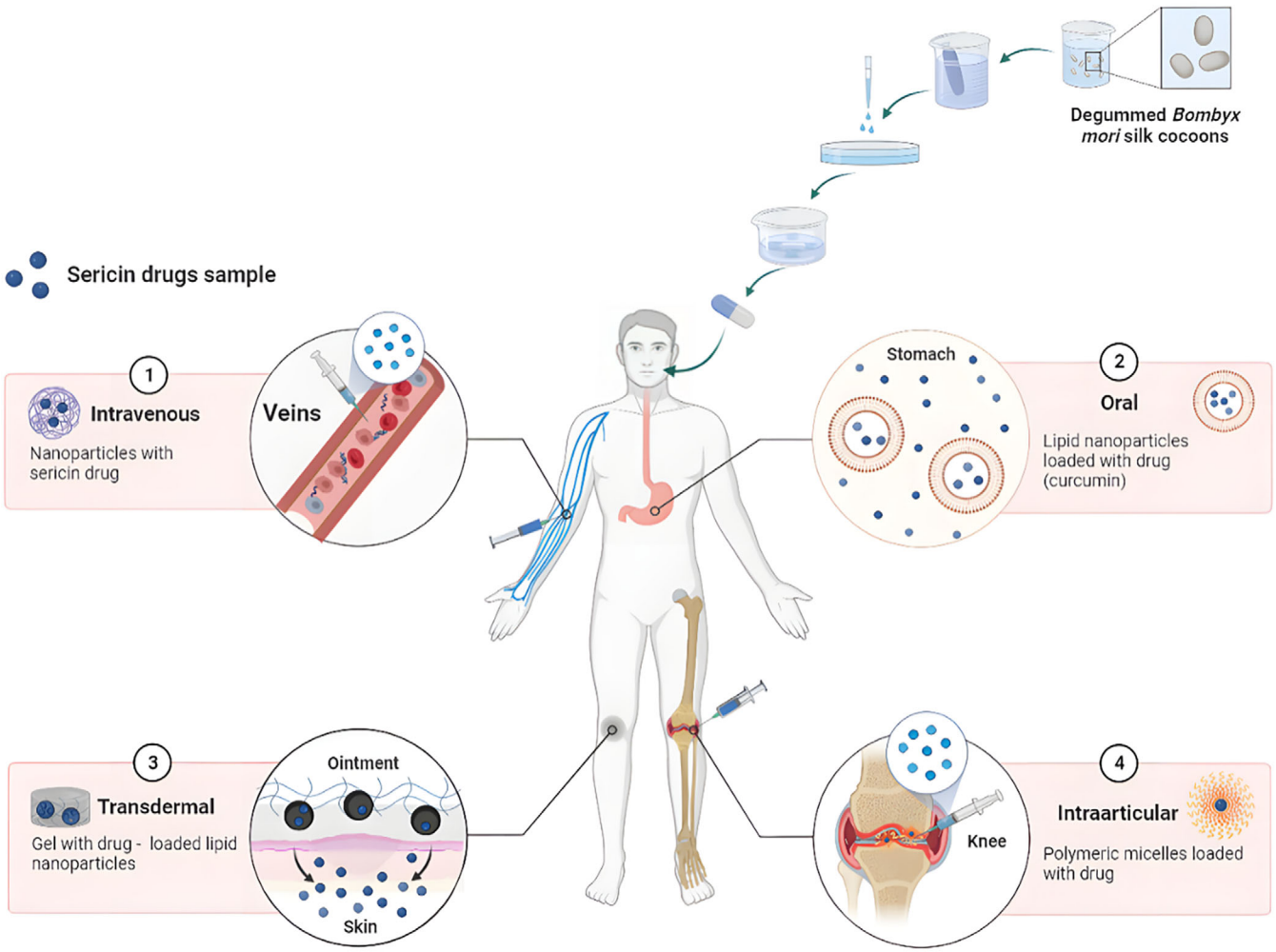


Figure 11. Potential applications of sericin-based drug delivery systems.

and constructing artificial tissues. The potential of sericin-based biomaterials for cell transport and tissue engineering is discussed in another review article by Lamboni et al.[82] They point out that sericin is an appealing alternative for cell transplantation due to its biocompatibility and low immunogenicity. In addition, the authors highlight sericin's potential for usage in tissue engineering scaffolds, which can provide a three-dimensional environment favorable to cell growth and differentiation. Das et al.[232] investigate sericin nanoparticles as a drug delivery mechanism for cancer treatment. While this paper primarily addresses the delivery of drugs, the authors do acknowledge that sericin nanoparticles may also be useful for transporting cells. They imply that sericin nanoparticles may be employed to selectively target cancer cells for therapeutic drug delivery, with little off-target effects on healthy tissues.

5.10. Cosmetics

The silkworm cocoon contains a protein called sericin, which is commonly used in cosmetics due to its moisturizing and anti-inflammatory effects. Lotions, creams, shampoos, and even nail polish contain it because of its positive effects on skin and hair. Sericin has been widely used in skincare products due to its excellent moisturizing properties. It can penetrate the skin's surface and form a protective barrier, preventing moisture loss and keeping the skin hydrated. Sericin also has anti-inflammatory properties, making it effective in reducing skin irritation and redness. It is often used in lotions, creams, and facial masks. According to a study by Akturk et al., sericin-containing cream showed significant improvement in skin hydration and elasticity compared to the control group.[205]

Sericin has been found to be beneficial for hair health due to its ability to coat and protect the hair shaft, making it smoother and shinier. It also helps to reduce hair breakage and split ends. Sericin is often used in hair conditioners, shampoos, and hair masks. A study by Gamboa et al. showed that sericin-containing shampoo improved hair strength, elasticity, and shine. Sericin has been found to be effective in strengthening and protecting nails.[233] It helps to prevent nail breakage and promotes healthy nail growth. Sericin is often used in nail care products such as nail polish and cuticle creams. A study by Giovannelli et al. showed that sericin-containing nail polish had better durability and glossiness compared to regular nail polish.[234]

Sericin is often used in creams due to its excellent moisturizing and anti-inflammatory properties. It is effective in reducing skin irritation and redness, making it suitable for sensitive skin. Sericin is often used in face creams, body lotions, and hand creams. According to a study by Aramwit et al.,[235] sericin-containing cream showed significant improvement in skin barrier function and moisture retention. Sericin is also used in gel-based skincare products such as facial masks and eye gels. It has a soothing effect on the skin and helps to reduce inflammation and redness. Sericin is also effective in improving skin elasticity and firmness. A study by Giovannelli et al.[234] showed that sericin-containing eye gel improved skin hydration and reduced the appearance of fine lines and wrinkles. Sericin is a valuable protein in the cosmetics industry, with numerous benefits for skin, hair, and nail health. Its moisturizing and anti-inflammatory properties make it an essential ingredient in various cosmetic products, and scientific studies have validated its effectiveness.

5.11. Other Applications

Sericin's ability to detoxify wastewater by eliminating metal ions and organic contaminants has been demonstrated. To remove lead and cadmium ions from wastewater, one study discovered that sericin-coated magnetic nanoparticles might be utilized as an effective adsorbent.[236] Sericin has been explored as a potential anti-frosting agent due to its ability to lower the freezing point of water. One study found that sericin could be used to create a superhydrophobic coating on surfaces, which could prevent frost formation.[237] Sericin has been used to create dialysis papers, used in treating kidney disease. One study found that sericin-based dialysis papers could effectively remove urea and creatinine from blood samples.[76] Sericin has been used to create artificial leather products that are eco-friendly and biodegradable. One study found that sericin-based leather products had good mechanical properties and were resistant to abrasion.[16,238] Sericin has been used to create a coated film that can be applied to roads and roofs to improve their durability and resistance to weathering. One study found that sericin-based coatings could improve the waterproofing and thermal insulation properties of roofing materials.[239] Sericin is used extensively in wastewater treatment, where it functions as an organic pollutant and heavy metal remover by acting as a natural coagulant. Its capacity to remove metal ions from wastewater, including cadmium and lead, is demonstrated by experiments that use magnetic nanoparticles coated with sericin as effective adsorbents.[34] Furthermore, when coupled with other polymers, sericin can aid in the manufacture of biodegradable, environmentally friendly plastics. This combination preserves the desired mechanical qualities while improving the sustainability of the material.[240] The antioxidative and antibacterial properties of sericin make it a valuable ingredient in the world of functional foods. Its inclusion in food items may increase their health benefits and promote greater food safety.[241] Furthermore, sericin has been explored as an anti-frosting agent, effectively lowering the freezing point of water and creating superhydrophobic coatings to prevent frost formation. It is also used in producing dialysis papers for kidney disease treatment, showing efficacy in removing urea and creatinine from blood samples. Sericin has been used as a binder for art pigments, as it is nontoxic and can help to improve the adhesion of pigments to surfaces. One study found that sericin-based art pigments had good color fastness and were resistant to fading.[242]

6. Future Prospects

In the future, it is imperative to explore new applications of silk sericin and promote its commercialization.

By converting waste materials like silk sericin into useful products, the biowaste to functional materials process helps to create a circular economy by lowering waste in the environment and increasing resource efficiency. This conversion reduces the requirement for fresh raw materials and lowers energy usage. The incorporation of materials obtained from biowaste into industries like cosmetics and medicine not only increases product sustainability but also opens up new markets. In the end, this strategy promotes growth in the economy and supports environmental objectives; it is consistent with the circular economy's core values. The potential of silk sericin in various fields, coupled with its cost-effective and sustainable extraction methods, makes it a promising biomaterial. Therefore, it is crucial to continue research on silk sericin to fully understand its properties and potential applications, leading to a more sustainable and innovative future.

7. Conclusions

Silk sericin's unique qualities and applications in a wide range of sectors have made it the topic of intense study. The extraction of sericin from waste material has garnered significant attention as a cost-effective and sustainable approach. The conversion of biowaste, such as silk sericin, into useful chemicals has important advantages for sustainability and green chemistry. We may lessen environmental waste and advance a circular economy by making use of silk sericin, which is frequently wasted during the silk production process. By opening up new markets for goods based on sericin, this strategy not only reduces the environmental impact of resource extraction but also improves the silk industry's financial sustainability. Green chemistry principles, which prioritize ecologically friendly techniques, are applied in the extraction of sericin and have the potential to reduce the use of hazardous chemicals and solvents that are often employed in conventional processes. However, the commercialization of silk sericin still presents a significant opportunity for future research and development. Wound healing, medication delivery, and tissue engineering are just a few of the medical applications where silk sericin has shown promise. Therefore, more research is required to properly understand the potential of silk sericin in the medical field. There has been some investigation on recycling for usage in areas like the food and beauty sectors.

The incorporation of silk sericin in these industries can enhance product quality and provide sustainable solutions. While several studies have been conducted on silk sericin, there are still gaps in research that require attention. For instance, the characterization of silk sericin and its structure-function relationship necessitates further investigation. While the fundamental structure of sericin has been elucidated, its functional properties and how they relate to its molecular structure require more comprehensive exploration. A deeper understanding of these relationships would enable the rational design of silk sericin-based materials with specific properties for diverse applications. Extraction and purification procedures for silk sericin also need to be refined, highlighting the need for greater study in this field. The utilization of silk sericin for diverse functional purposes poses both prospects and obstacles. Silk sericin possesses distinctive characteristics such as remarkable biocompatibility, biodegradability, and antimicrobial efficacy, rendering it a highly auspicious biomaterial for a wide range of applications. Furthermore, the sustainable retrieval of silk sericin from discarded materials presents a financially viable and ecologically conscious method. However, the development of silk sericin for functional applications also poses challenges. For instance, there is still much to learn about the structure-function relationship of silk sericin, which can limit its rational design for specific applications. Additionally, the optimization of extraction and purification methods for silk sericin remains a challenge, particularly for large-scale production. Furthermore, the safety and regulatory requirements for silk sericin-based products must be addressed to ensure their commercial viability. Despite these challenges, the development of silk sericin-based materials for different functional applications presents an exciting opportunity for researchers and industry professionals. The potential applications of silk sericin span across diverse fields, including medicine, food, and cosmetics. The incorporation of silk sericin in these fields can improve product quality, provide sustainable solutions, and contribute to the development of a circular economy.

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Conflict of Interests

The authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Keywords: Applications · Extraction · Properties · Silk sericin · Structure

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