

## SERICIN AND ITS APPLICATIONS IN BIOMEDICAL SECTORS: AN OVERVIEW

### Abstract

The economic use of silk, a proteinous fibre made up of sericin and fibroin, allows for the production of superb silk clothing. Approximately 20–30% of a silk cocoon's sericin content dissolves during the silk reeling process and is regarded as a waste. Silk glue protein sericin, a naturally occurring polypeptide obtained from cocoons of silkworms, has received a great deal of attention due to its good biochemical activities and predictable physical-chemical features. It is employed in the biomedical field. Sericin is naturally cell adhesive and biocompatible, enabling cells to unite, multiply, and differentiate in materials containing sericin. In addition, sericin's many functional groups, which it derives from its diverse amino acid makeup, enable it to be biochemically altered and combined to produce flexible structures which might be utilized as substitute biological matrixes. Sericin has lately been added to a wide range of biological materials used in tissue construction and regenerative therapies, including films, scaffolding, conduits, micro-nano formulations, and devices. In this chapter, we provide a thorough examination of the biochemistry, and types of silk sericin protein, explain its many forms, and highlight recently established and potential biological uses.

**Keywords:** Sericulture, Silk sericin, properties, applications, biomedical sectors

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## I. INTRODUCTION

Silk is an old substance that is gaining popularity in biological applications. Silk resources are plentiful and have a short production cycle since it is a natural protein polymer generated in the glands of lepidopteran insects. Silk has been used for thousands of years in nations such as India and China, especially in textile industries. Silk has been taken into account as a promising natural material for biomedical applications, particularly in tissue engineering, drug/gene transportation, and emerging smart wearable electronics since its initial scenarios such as silk-based sutures in medical practice, and excellent biological properties of silk are gradually revealed. Silk filament is mainly composed of two proteins called fibrous protein fibroin and nonfibrous protein sericin, with very less amount of coloring agent, waxy substance, mineral salts, etc. The crystalline fibrous protein fibroin is present at about 70-80%, whereas the amorphous globular protein sericin is present at about 20-30%. The silk coats and attaches two fibroin filaments together in the cocoons. Sericin is a non-fibrous, glue-like protein with 18 amino acids, rich in L-serine. At the end of the fifth larval stage, lepidopteran holometabolous insect silkworm produces sericin protein for the formation of cocoons, which gives proper conditions for their further metamorphosis. When cocoons are further proceeds in the textile industry, a large amount of sericin is washed out and the fibroin is converted into raw silk. Furthermore, non-filamentous silk protein sericin protects the cocoon against UV radiation, low temperature, rain, wind, etc. According to Ki Yun *et al*, sericin has been discarded as a byproduct waste during silk production. Globally, over 400,000 tonnes of dried cocoons can create 50,000 tonnes of sericin. [6]. Much research has been done on the various biotechnological and biomedical applications of fibroin protein. Though sericin has been regarded as waste, still this hydrophilic globular protein now has a diverse variety of uses in the cosmetic industry, food industry, and also in the pharmaceutical industry. Various useful properties of sericin including, antioxidant, anti-tyrosinase, UV absorbing, moisture absorbing, etc, have been used for biomedical polymeric applications. By using its antioxidant biological properties, sericin protein shows a defensive effect on UVB-induced severe damage as well as 1,2-dimethylhydrazine-induced tumors in mice. As per reports, sericin powder may act as a potential antioxidant drug that can reduce blood sugar levels. Several elements like polyphenols and flavonoids have been isolated from sericin protein by Japanese scientists, which have a protective role against gastric mucosal damage. Having the anti-tyrosinase activity, sericin can protect cells against UV radiation. This chapter will discuss the biomedical uses of sericin protein, as well as how its qualities are exploited in biomedical disciplines.

## II. SILK PROTEIN SERICIN AND ITS BIOCHEMISTRY

Sericin belongs to a group of "gluelike" proteins that surround and bind the protein core of fibroin filaments. When sericin is present, fibre silk is hard and inflexible; when it is absent, it is soft and glossy. A globular protein with random coil and  $\beta$ -sheet structures, sericin. The random coil topology of the  $\beta$ -sheet is easily changed by the temperature at which the sol-gel transition occurs. In water that has been heated (to 50-60 °C or more), protein sericin takes on its soluble form. Lowering the temperature leads to a reduction in solubility and a shift in the random coil structure into  $\beta$ -sheets, which results in the formation of a gel. Sericin is a hydrophilic macromolecule made up of 18 amino acids, each of which has a strong polar group, such as an amino, carboxyl, or hydroxyl group. These groups can combine with polymers, form co-polymerizations, and form crosslinks. Sericin is composed

of 46.5% carbon, 31% oxygen, 16.5% nitrogen, and 6% hydrogen [8]. Its chemical structure confers significant biological properties on it, including biological compatibility, antibacterial activity, antioxidant capacity, and hydrating advantages

### Categories of sericin:

Sericin can be categorized based on its sources as well as its various properties. The basis of its solubility and molecular weight is one of its categorization parameters.

- 1. Based on Solubility:** Shaw and Smith [11] categorized it into three categories (sericin A, Sericin B, and sericin C) based on water solubility which is depicted in Table 1.
- 2. Based on the Site of Synthesis:** Based on their location of production in the site of the silk gland sericin was categorized as sericin A, M, and P by Takasu *et al.* [14]. The Ser1 gene encodes sericin P and M, which produce the first and second sericin layers that surround the fibroin, respectively. Sericin obtained from different sections of the silk gland was reported to show variations in amino acid as shown in Table 2. The details of all the amino acids present in the sericin protein have been listed in Table 3.

### III. APPLICATIONS OF SILK SERICIN IN BIOMEDICAL SECTORS

Studies on sericin's anti-inflammatory and biologically compatible capacity, conducted in vivo and in vitro, have shown that it is immune-suppressive, established its safety, and revealed an array of conceivable uses in biological medicine (table 4), including the food and beauty products industries, culture media supplementation, cryogenic preservation, wound repair, an antitumor effect, multiple metabolic effects in biological systems, and evidence of its use in the field of tissue engineering and as a means of delivering drugs.

- 1. Pharmacological Properties of Sericin Responsible for Anticancer Activity:** Sericin's antioxidant effect can result in broad fitness gains. According to research, this protein enables a decrease in oxidative stress inside human tissues including the colon, and a decrease in a variety of melanoma cells [15]. Furthermore, it has been shown that silk sericin limits the growth of replicate tumor cells and stimulates the apoptotic issue, resulting in cancer cell death in rats.
- 2. Pharmacological Properties of Sericin Responsible for Wound Healing:** Serine, the main amino acid of the distinctive moisturizing component in human skin, makes up around 30% of sericin. Less inflammatory symptoms and a faster reduction in wound size were seen in sericin-treated wounds compared to the control. The study discovered an elevated collagen content around the incision while the epidermis surface soon returned to normal thickness. Due to the presence of a few hydroxyl groups, sericin has stronger hydrophilic characteristics and hence has a better chance of healing wounds. Sericin was previously overlooked because of spurious responses to allergens, but a recent study found that it is biochemically compatible and might be utilized as a biological material.[2].

- 3. Pharmacological Properties of Sericin Responsible for Skin Cells Regeneration:** Sericin protein can also be used as an 8% sericin-based cream, which improves wound healing with a significant decrease in the wound region as compared to cream base treated injuries. The injury recovery period is shorter with sericin cream (11 days) than with other cream base treated injuries (15 days). Microscopic study reveals that lesions treated with cream base had less epithelization, inflammation, and a greater amount of proliferating cells than lesions managed with sericin cream. [1].
- 4. Pharmacological Properties of Sericin on Metabolism:** The effect of the sericin protein on the digestive system has been studied in light of its antioxidant capacity and hydrophilic property. Sasaki *et al.* enriched the rats' food with 34% sericin for 12 days. Sericin increased the bioavailability of calcium ions (17%), magnesium (21%), zinc (41%), and iron (41%), by accelerating absorption. However, it did not affect urinary excretion and serum of those factors as quantified by an atomic absorption spectrophotometer [10].
- 5. Pharmacological Properties of Sericin on Immunity:** A mice weight loss program that included a diet containing sericin (4%), was utilized for 20 weeks. Feeding sericin decreased CD8a and CD80 cell percentages, but had no impact on body mass index, blood cell numbers, consciousness, or food intake, according to the study [5]. A sericin-derived oligopeptide was reported to boost NK activity against K562 target cells when peripheral blood mononuclear cells were exposed to it in vitro, with a dose-dependent impact. The authors found that while interleukin-2 (IL-2) and interferon-alpha (IFN-) are boosted, the effect on NK cells is indirect. Additionally, oral administration of sericin-derived oligopeptides to mice caused an increase in IL-2 levels and sustained NK cell activity.
- 6. Pharmacological Properties of Sericin on Anticoagulant Capabilities:** The researcher used chloro-sulfonic acid to sulfate the serine residue of the sericin protein that was extracted from the *B. mori* cocoon. They found that larger anticoagulant effects were seen at higher atomic fractions, which were calculated to be 1/10 to 1/20 of heparin. Sano *et al.* studied the interaction of the coagulation pathway with sulfated sericin to comprehend the anticoagulant mechanisms. The author claims that sulfated sericin inhibits fibrinolysis without slowing the underlying polymerization processes [9].
- 7. Pharmacological Properties of Sericin on Body Weight:** The impact of sericin on mice fed with a high-fat diet in terms of lipid and glucose metabolism. Body weight, nutrient uptake, or fat weight were unaffected by the addition of 4% sericin to the diet for 5 weeks, but serum concentrations of free unsaturated fats, triglycerides cholesterol, phospholipids, very low-density lipoproteins (VLDL), and low-density lipoproteins (LDL) were reduced. The limited digestibility of sericin protein, which can function as a dietary fibre and boost fecal lipid discharge while lowering plasmatic concentration, is to blame for the overall shift in plasma lipid profile and rise in cholesterol and triglyceride levels in stools, claims the study. Limpeanchob *et al.* discovered a decline in non-HDL (high-density lipoprotein) cholesterol and aggregate cholesterol in mice given an oral dosage of 10, 100, or 1000 mg/kg of sericin for 14 days, but no changes in triglyceride or HLD levels. The researcher discovered that sericin prevents cholesterol buildup in the digestive tract, resulting in a decrease in plasmatic cholesterol, in an in vitro experiment

utilizing isolated Caco-2 cells. This is most likely due to sericin's effects on cholesterol absorption and micelle formation [8].

- 8. Pharmacological Properties of Sericin related to Regeneration of Connective Tissue and Epithelium:** It can be shown that the sericin hydrogel is a natural biomaterial since it may be created by adding 10% alcohol to a sericin solution without the requirement for chemical or irradiation crosslinking. However, pure sericin produces brittle films and is difficult to utilize as a biomaterial in tissue engineering, sericin's physical properties have been enhanced in several ways. As per the research of Lamboni *et al.*, the inclusion of sericin into skin repair and wound healing materials creates a possible biomaterial that enhances fibroblast and keratinocyte migration, adhesion, and development as well as collagen formation and promotes re-epithelialization in skin wounds. [7]
- 9. Pharmacological Qualities of Sericin Related to Oxidative Stress:** The stable free radical DPPH (2, 2-diphenyl-1-picrylhydrazyl), which assimilates at 517 nm, is widely used to study the effect of radical rummaging. When an antioxidant gives protons to this radical, absorption diminishes. Sericin's antioxidant activity is assessed by estimating the decrease in absorption. According to another research [13], sericin inhibits lipid peroxidation, demonstrating its antioxidant abilities.
- 10. Pharmacological Properties of Sericin Related to Cardioprotective:** The protective characteristics of amino acids have only recently been accounted for as a fundamental improvement in heart protection, both silk proteins (fibroin and sericin) are abundant and reliable sources of amino acids, which can play a significant role in cardiac damage. The cardioprotective efficacy of *Bombyx mori* standard extract against doxorubicin-induced cardiotoxicity in the mouse model was attributed to its antioxidants, potential amino acids, and flavonoids. Flavonoids are more likely to behave as hunters of reactive oxygen species. Because of the abundance of free amino acids present. According to Srivastava *et al.*, an ethanolic extract of sericin exhibited cardioprotection in rats when used in an isoprenaline-induced myocardial infarction model on animals [12].
- 11. Pharmacological Properties of Sericin Related to Minerals:** The gastrointestinal absorption of some minerals including calcium, magnesium, iron, and zinc, has a synergistic effect with sericin. As of now, scientific findings have shown that sericin's addition to salad dressings has an emulsifying effect. These findings confirmed that high atomic weight protein improves the stability of the emulsion for up to two days. Bioactive peptides, which are particular segments of proteins, are present in significant concentrations in sericin. Its amino acid makeup is closely related to the advantages for body processes, particularly for immunological, cardiovascular, gastrointestinal, and brain systems. By showing that sericin reduces in vitro lipid peroxidation, Kato *et al.* provided the first evidence of the silk protein's ability to operate as a cancer-preventative agent.[4].

**Table 1: Categories of sericin based on its solubility.**

Sericin category	Water solubility	Position in cocoon	Major Amino acids	Nitrogen Present (%)
Sericin A	Soluble in warm water	The outermost surface of the cocoon	serine, threonine, glycine, & aspartic acid	17.2% nitrogen
Sericin B	Soluble in hot water	The intermediate layer	serine, threonine, glycine, aspartic acid, & tryptophan	16.8% nitrogen
Sericin C	Insoluble in hot water	Adjacent to fibroin	serine, threonine, glycine, aspartic acid, tryptophan, & proline	16.6% nitrogen

**Table 2: Sericin obtained from Various Sections of the Silk Gland.**

Sericin Fraction	Abundant Amino Acids in Sericin	Content (Mol%)
Sericin A	Glutamic acid	13%
Sericin M	Threonine	11%
Sericin P	Threonine	11%

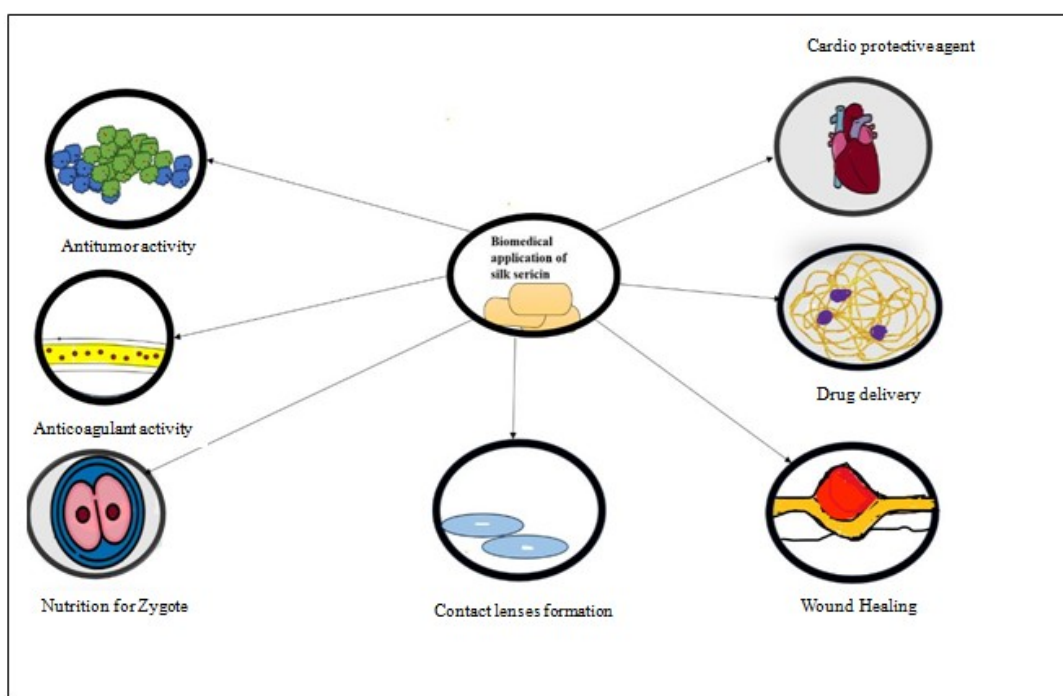
**Table 3: The Amino acid composition of Sericin protein.**

Amino acid residues (mol%)	Content in Mulberry Sericin
Serine	32.16
Threonine	8.04
Tyrosine	3.14
Phenylalanine	0.64
Tryptophan	0.2
Glycine	16.43
Alanine	4.35
Leucine	0.80
Isoleucine	0.66
Valine	2.56
Asparagine	18.71
Glutamine	3.83
Arginine	3.74
Lysine	1.79
Histidine	1.46
Methionine	0.64
cysteine	0.13
Proline	0.97

**Table 4: Various applications of sericin in the biomedical sectors.**

<b>Applications in biomedical</b>	<b>Pharmacological properties of sericin responsible for the application</b>
<b>As an anticarcinogenic agent</b>	<ul style="list-style-type: none"> <li>Sericin contains good antioxidant properties which support the control of cancer cells.</li> </ul>
<b>As wound healer</b>	<ul style="list-style-type: none"> <li>Sericin has an excellent moisturizing capacity and also helps in collagen union and re-epithelialization.</li> </ul>
<b>As a healing agent for skin cells</b>	<ul style="list-style-type: none"> <li>Sericin-based creams show a good effect on skin wound as it possesses moisture absorbance and UV protective properties.</li> </ul>
<b>Help in mineral absorbance</b>	<ul style="list-style-type: none"> <li>Sericin consumption elevates intestinal absorption of zinc, iron, magnesium, and calcium in rats.</li> </ul>
<b>As an anticoagulant agent</b>	<ul style="list-style-type: none"> <li>Sulfated sericin inhibits fibril gathering without delaying the underlying polymerization process.</li> </ul>
<b>As an immunity-boosting agent</b>	<ul style="list-style-type: none"> <li>Sericin had no effect on body weight, meal intake, or blood cells, however, it did lower the proportion of CD8a and CD80 cells. Oligopeptides produced from sericin are used to treat tumors and infectious conditions by increasing NK cell activity and decreasing IL-2 concentrations.</li> </ul>
<b>As a cholesterol-level-maintaining agent</b>	<ul style="list-style-type: none"> <li>Sericin's low digestibility alters the plasma lipid profile and raises levels of cholesterol and triglycerides. In mice, sericin lowers total and non-HDL (high-density lipoprotein) cholesterol. Sericin decreased blood concentrations of cholesterol, triglycerides, free unsaturated fats, phospholipids, very low-density lipoproteins (VLDL), and low-density lipoproteins (LDL), but it had no effect on body weight, nutrient use, or fat weight.</li> </ul>
<b>As a Cardioprotective agent</b>	<ul style="list-style-type: none"> <li>In animal models, ethanol-extracted sericin from <i>B. mori</i> displayed cardioprotective effectiveness against doxorubicin-induced cardiotoxicity.</li> </ul>
<b>As an antioxidative agent</b>	<ul style="list-style-type: none"> <li>Sericin inhibits lipid peroxidation, indicating that it has antioxidant effects.</li> </ul>
<b>As bandages</b>	<ul style="list-style-type: none"> <li>The results of the sericin bandage revealed improved healing and decreased patient discomfort.</li> </ul>
<b>As a polymeric Graft agent</b>	<ul style="list-style-type: none"> <li>Sericin may be utilized to enhance bio-polymeric grafts in the future.</li> </ul>
<b>As a vehicle for drug delivery</b>	<ul style="list-style-type: none"> <li>Sericin, either pure or conjugated, can be utilized to create matrices, particles, and hydrogels that increase drug delivery</li> </ul>

	capability.
<b>In contact lenses preparation</b>	<ul style="list-style-type: none"> <li>• Sericin is a component utilized in the manufacture of contact lenses.</li> </ul>
<b>Protein source for Zygote</b>	<ul style="list-style-type: none"> <li>• In bovine oocytes and zygotes, sericin can be employed as an alternate protein complement for IVM and IVC.</li> </ul>
<b>As an epithelial and connective tissue-repairing agent</b>	<ul style="list-style-type: none"> <li>• Sericin has been used in skin restoration and improved collagen formation. When 10% alcohol is added to a sericin solution, a hydrogel is created without the requirement for cross-linking.</li> </ul>



**Figure 1:** Biomedical applications of silk sericin protein.

#### IV. CONCLUSION

Silk protein sericin is a distinctive polymer that is one of the major components responsible for the formation of silk cocoons. There are many methods for isolating sericin from silk thread. Silk is extremely flexible, has a biologically compatible structure, and degrades quickly. Sericin has become a valuable economic asset in a variety of industries thanks to its few significant features, including those that make food, medicine, cosmetics, and various useful biomaterials. Sericin, a silk protein, is thought of as a waste material from the silk industry. Nevertheless, several professionals are attempting to increase awareness of sericin, which might be employed in several medical and pharmaceutical investigations. Sericin's future is uncertain, but a study on the topic will benefit the silk and related sectors.



The field of biomedical engineering is still developing in this area, which calls for extensive research as well as the translation of that research into beneficial consequences for people.

## REFERENCES

- [1] Aramwit, P., Keongamaroon, O., Siritientong, T., Bang, N., & Supasynhd, O. (2012). Sericin cream reduces pruritus in hemodialysis patients: a randomized, double-blind, placebo-controlled experimental study. *BMC nephrology*, 13(1), 1-11.
- [2] Chirila, T. V., Suzuki, S., & McKirdy, N. C. (2016). Further development of silk sericin as a biomaterial: comparative investigation of the procedures for its isolation from Bombyx mori silk cocoons. *Progress in biomaterials*, 5(2), 135-145.
- [3] Gupta, D., Agrawal, A., & Rangi, A. (2014). Extraction and characterization of silk sericin.
- [4] [4] Katoh, N. (2000). New physiological functions of sericin and its application for cosmetic and food. *Fragrance J.*, 4, 28-33.
- [5] Keawkorn, W., Limpeanchob, N., Tiyaboonchai, W., Pongcharoen, S., & Sutheerawattananonda, M. (2013). The effect of dietary sericin on rats. *Science Asia*, 39(3), 252-256.
- [6] Lamboni, L., Gauthier, M., Yang, G., & Wang, Q. (2015). Silk sericin: A versatile material for tissue engineering and drug delivery. *Biotechnology advances*, 33(8), 1855-1867.
- [7] Limpeanchob, N., Trisat, K., Duangjai, A., Tiyaboonchai, W., Pongcharoen, S., & Sutheerawattananonda, M. (2010). Sericin reduces serum cholesterol in rats and cholesterol uptake into Caco-2 cells. *Journal of Agricultural and Food Chemistry*, 58(23), 12519-12522.
- [8] Rajput, S. K., & Singh, M. K. (2015). Sericin-a unique biomaterial. *IOSR Journal of Polymer and Textile Engineering*, 2(3), 29-35.
- [9] Sano, M., Tamada, Y., Niwa, K., Morita, T., & Yoshino, G. (2009). Sulfated sericin is a novel anticoagulant influencing the blood coagulation cascade. *Journal of Biomaterials Science, Polymer Edition*, 20(5-6), 773-783.
- [10] Sasaki, M., Yamada, H., & Kato, N. (2000). Consumption of silk protein, sericin elevates intestinal absorption of zinc, iron, magnesium and calcium in rats. *Nutrition Research*, 20(10), 1505-1511.
- [11] [11] Shaw, J. T. B., & Smith, S. G. (1951). Amino-acids of silk sericin. *Nature*, 168(4278), 745-745.
- [12] Srivastav, R. K., Siddiqui, H. H., Mahmood, T., & Ahsan, F. (2013). Evaluation of cardioprotective effect of silk cocoon (Abresham) on isoprenaline-induced myocardial infarction in rats. *Avicenna journal of phytomedicine*, 3(3), 216.
- [13] Takechi, T., Wada, R., Fukuda, T., Harada, K., & Takamura, H. (2014). Antioxidant activities of two sericin proteins extracted from cocoon of silkworm (*Bombyx mori*) measured by DPPH, chemiluminescence, ORAC and ESR methods. *Biomedical Reports*, 2(3), 364-369.
- [14] Takasu, Y., Yamada, H., & Tsubouchi, K. (2002). Isolation of three main sericin components from the cocoon of the silkworm, *Bombyx mori*. *Bioscience, biotechnology, and biochemistry*, 66(12), 2715-2718.
- [15] Zhaorigetu, S., Sasaki, M., Watanabe, H., & KATO, N. (2001). Supplemental silk protein, sericin, suppresses colon tumorigenesis in 1, 2-dimethylhydrazine-treated mice by reducing oxidative stress and cell proliferation. *Bioscience, biotechnology, and biochemistry*, 65(10), 2181-2186.