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Sericin A Boon to Medical and Dental doctors – A Review

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Silk sericin is a natural polymer produced by the silkworm, Bombyx mori, which surrounds and keeps together two fibroin filaments in silk thread used in the cocoon. The recovery and reuse of sericin usually discarded by the textile industry not only minimizes environmental issues but also has a high scientific and commercial value. The physicochemical properties of the molecule are responsible for numerous applications in biomedicine and are influenced by the extraction method and silkworm lineage, which can lead to variations in molecular weight and amino acid concentration of sericin. The presence of highly hydrophobic amino acids and their antioxidant potential make it possible for sericin to be applied in the food and cosmetic industry. The moisturizing power allows indications as a therapeutic agent for wound healing, stimulating cell proliferation, protection against ultraviolet radiation, and formulating creams and shampoos. The antioxidant activity associated with the low digestibility of sericin expands the application in the medical field, such as antitumour, antimicrobial and anti-inflammatory agent, and anticoagulant, acts in colon health, improving constipation and protecting the body from obesity through improved plasma lipid profile. In addition, the properties of sericin allow its application as a culture medium and cryopreservation, in tissue engineering and for drug delivery, demonstrating its effective use, as an important biomaterial. The present review on sericin describes its properties and application in various fields.

Keywords: Silk, sericin, biomedical, dental, biomaterial, biodegradable, biocompatible.

Introduction

Silk is one of the oldest materials known to man, having been used as medical sutures as early as 131-211 AD by the Greek physician Aelius Galenus [1]. Silkworm silk protein biopolymer is made of two components—silk fibroin (SF) and silk sericin (SS) [2]. Silk fibroin forms the central core imparting toughness and load-bearing properties in silk, while Silk sericin is a gumming agent. Silk sericin, a group of water-soluble glycoproteins accounts for 25–30% (w/w) of total silkworm cocoons [3].

Silkworm, Bombyx mori, a holometabolous insect belonging to the order Lepidoptera and family Bombycidae, produces an amorphous glycoprotein, silk sericin, in the middle silk gland. B. mori produces a large amount of sericin by the end of the fifth larval instar and together with the fibroin forms the silk thread that leads to cocoon formation, a structure that provides ideal conditions for survival from larval metamorphosis to the adult stage [4].

In the textile industry, the cocoon is processed and sericin is largely removed through a process called degumming. Extracted fibroin is converted into raw silk and used in the manufacture of many types of yarn, silk fabric and other biomedical applications [5, 6]. Commercial silk farming is

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believed to be one of mankind's oldest agricultural explorations [7]. Historical data comes from northern China and goes back 5000 years. [8] where it has spread to other areas in the east and west.

In addition to its economic importance through applications in the agricultural industry, B. mori is the most important butterfly used in scientific research, gene and tissue engineering, a resource capable of elucidating a wide range of biological problems and diseases. Recently, the cocoon of B. mori and its silk proteins, fibroin and sericin, have been the subject of research showing potential uses in the field of polymers, biomaterials, cosmetics and the food industry [5, 9]. Sericin has long been neglected in silkworm breeding. It is estimated that 400,000 tons of dry cocoons worldwide produce 50,000 tons of sericin [10]; Sericin was discharged into wastewater, resulting in high chemical and biological oxygen demand and water contamination [11]. Therefore, the extraction and use of sericin could have strong economic, social, and environmental impacts, especially in countries where silkworm farming is practiced, such as China, India, and Brazil.

Sericin is a natural polymer that acts as an adhesive, binding two strands of fibroin to form silk yarn. The molecule is very hydrophilic with a molecular weight of 20 to 400 kDa and consists of 18 essential amino acids. The polar groups (carboxyl, hydroxyl and amino groups) of amino acid side chains and their organic composition and properties such as solubility, and structural organization allow for easy crosslinking, copolymerization and combination with other polymers, giving sericin unique properties of Antioxidant, Moisturizer, Wound Dressing, Wound Dressing, healing bandages, antibacterial, antimicrobial, protection against UV radiation and antitumor [12 - 14].

Though sericin is considered a by-product and discarded as waste in the sericulture industry, it has attracted immense interest in the field of cosmetics, biomedical, and pharmaceutical applications owing to its antibacterial, antioxidant, anti-cancer, anti–inflammatory, anticoagulant and wound healing properties. Thus, the increasing demand for biocompatible and biodegradable materials reflects the growing interest in non-textile applications of silk protein across a wide range of science and medicine and justifies the present review describing the properties, biomedical and dental applications of sericin polymer extracted from cocoons of B Mori.

Sericin [15]

Sericin, an insoluble protein in cold water, boasts of high hydrophilicity and adhesive properties similar to that of gelatin. Its spherical structure permits the attachment of silk filaments, thereby maintaining the structural integrity of the cocoon during its formation. Apart from its adhesive property, sericin contains 18 amino acids, with the significant compounds being serine (32%), aspartic acid (18%), and glycine (16%). It is noteworthy that this protein is made up of 45.8% hydroxy amino acids (serine and threonine), 42.3% polar amino acids, and 12.2% non-polar amino acids. This protein can be copolymerized and mixed with other polymers to produce biodegradable materials due to its strong polar side chains such as hydroxyl, carboxyl, and amino that allow for easy cross-linking.

The molecular weight of sericin is dependent on the method of extraction. When obtained from cocoons, the molecular weight ranges from 40-400 kDa, while it ranges from 80-310 kDa when extracted directly from the glandular worm. This range varies depending on several factors such as the type of reactive agent used, whether acidic, alkaline, or enzymatic. Additionally, factors such as temperature, pressure, pH, and processing time can also affect the molecular weight of the extracted sericin.

Forms of Silk Sericin

Sericin can be classified into three fractions, depending on their solubility sericin A, sericin B, and sericin C. Sericin A is the outermost layer and is insoluble in hot water. It contains about 17.2% of nitrogen and amino acids like serine, threonine, glycine, and aspartic acid. Sericin B is the middle layer and on acid hydrolysis, it yields the amino acid of sericin A, in addition to tryptophan. It contains 16.8% of nitrogen. Sericin C is the innermost layer, which is adjacent to fibroin and is insoluble in hot water and can be removed from fibroin by treatment with hot dilute acid or alkali. On acid hydrolysis, it yields proline in addition to amino acids of sericin B. It also contains sulfur and 16.6% of nitrogen.

Sericin has been divided into various species based on relative solubilities. Various fractions of sericin are also designated by other researchers depending on their dissolution behaviour as sericin A and B, or sericin I, II, III, and IV, or S1, S2, S3, S4, and S5, and as α, β, and γ modification [16, 17]. The major molecular conformation of easily soluble sericin is a random coil, whereas the β-sheet structure is more difficult to dissolve. The repeated moisture absorption makes the molecular aggregation structure denser and forms a more crystalline structure, which is having reduced solubility.

The γ-ray study shows the three layers in the sericin structure. The outer layer contained some fibre direction filaments, the middle layer exhibits cross-fiber direction filaments, and the inner layer shows longitudinal filaments. The structure of sericin also depends on the casting temperature. Lower the casting temperature more the sericin molecules assume β-sheet structure rather than random coil [18, 19].

Properties

Sericin's unique properties allow it to form a gel when its random coil structure is transformed into a β-sheet structure. The random coil structure is soluble in hot water, but as the temperature decreases, it undergoes a conformational change to a β-sheet structure, leading to gel formation [20-21]. The solubility of sericin in water reduces when it is converted to a β-sheet structure.

The gelation of sericin happens more rapidly at low temperatures (10°C) and pH levels around 6-7. When the protein's random coil structure is transformed into β-sheet structure, an aqueous solution of sericin forms a gel. This process can be reversed by heating the sample in water to 50-60°C and cooled to room temperature, leading to the formation of gel again. According to Kweon et al. (2000), the gel strength of sericin increases when surface tension decreases, and the gelation time reduces with the addition of high concentrations of poloxamer gel. The hydrophilic part of the latter gel absorbs the water that surrounds sericin, resulting in this effect [15].

Sol-Gel Transition: Sericin has sol-gel properties as it easily dissolves into the water at 50-60^{o}C and again returns to gel on cooling [22].

Isoelectric pH: As there are more acidic than basic amino acid residues the isoelectric point of sericin is about 4.0 [23]. The isoelectric point of a molecule is the pH at which it carries no net electrical charge. It is also defined as the reference concentration of hydrogen ions or other ions in which this condition can be observed. As such, the isoelectric point is typically defined in terms of the pH scale. The isoelectric point of sericin has been determined to be between 3.5 and 4.0. This is attributed to the presence of a higher amount of acidic amino acids compared to basic amino acids in sericin [15].

Solubility: Sericin is a partially soluble protein in hot water. The solubility of sericin increases with the addition of poly (Na acrylate) and decreases with the addition of polyacrylamide, formaldehyde, or resin finishing agents [24-26].

The solubility of sericin is also influenced by its amorphous and crystalline structure. The amorphous region is comprised of a random coil structure, which is the primary molecular conformation of the easily soluble sericin. In contrast, the crystalline region, known as the β-sheet, is more challenging to dissolve [15].

Molecular Weight Extracting sericin using 1% sodium deoxycholate solution followed by precipitation, using an equal volume of 10% trichloroacetic acid, shows molecular weight in the range of 17100 to 18460 [27]. Extraction of sericin by hot water shows a molecular weight of 24000 by gel electrophoresis, whereas the spray-drying method produced sericin of molecular weight 5000-50,000, with enzyme action 300-10,000 and 50,000 when it is extracted with aqueous urea at 100ºC [28].

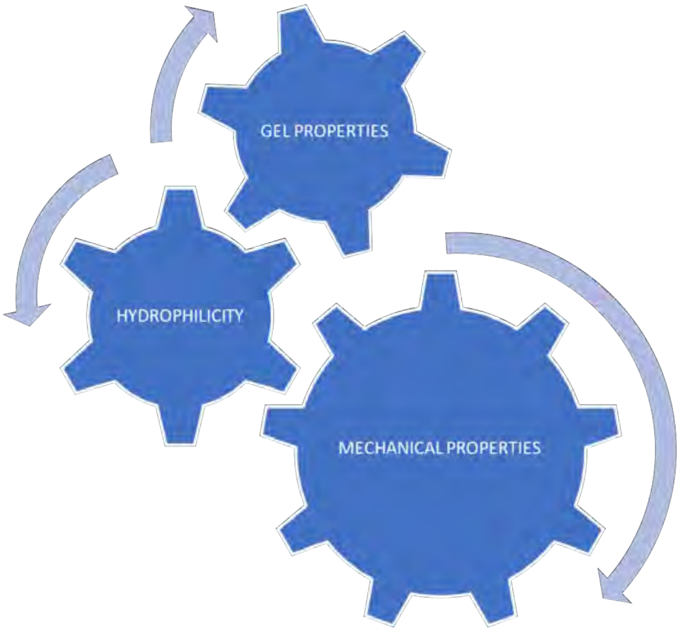

Figure 1. *Biochemical properties of sericin*

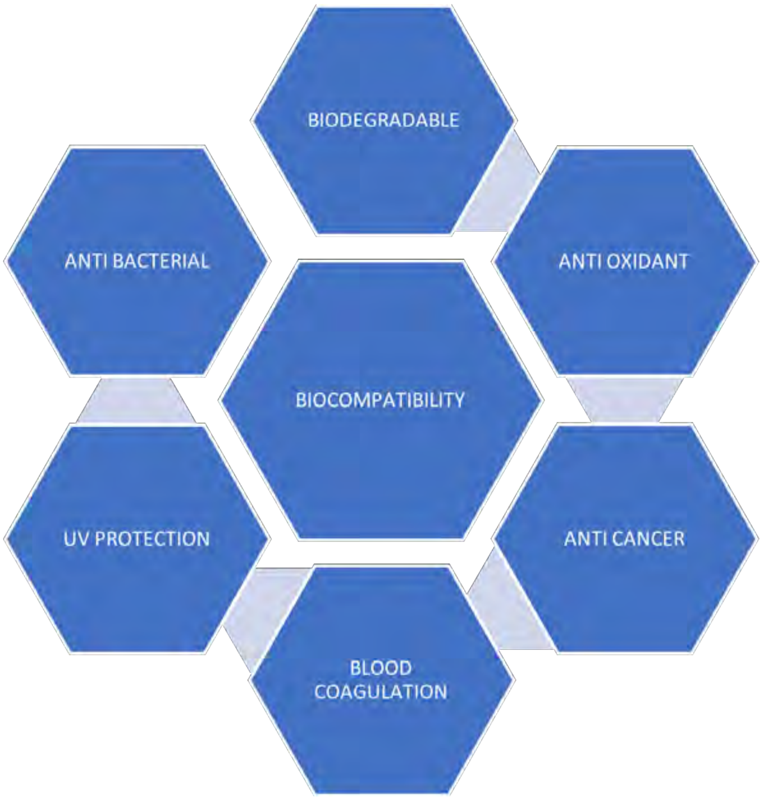

Figure 2. *Biological properties of sericin*

Recent research has highlighted the potential applications of sericin in various industries, including the biomedical, pharmaceutical, and food industries. Sericin has been utilized to develop products such as cancer drugs, blood thinners, and cell culture additives in the form of granules, gels, solutions, and films (Table 1). These developments have been reported in several countries, including Italy, the USA, China, Austria, Japan, and Romania [15].

Application of sericin in the Medical field [15]

Sericin exhibits both antioxidant and anticoagulant, Anticarcinogenic, and Healing properties, and used as Bandage.

Tissue engineering: Materials that can be used in drug delivery, grafts and immobilizing matrices such as matrices in 2D (films) and 3D (scaffold) are one of the main goals of biomedical research. Films and scaffolds have been successfully made using a mixture of gelatine and sericin extracted from the silkworm Antheraea mylitta. Fabricated supports have evenly distributed pores, good compressive strength and high swellability. In addition, they show high porosity, low immunogenicity, and improvement in both cell attachment and viability. These properties are critical for tissue engineering and biomedical applications, which reveals the potential use of sericin in the future development of bio-polymeric grafts [15].

Apart from its tissue engineering applications, sericin has been utilized for the regeneration of cartilage and nerves. In a study by Dinescu et al., they observed that a scaffold composed of collagen-sericin infused with hyaluronic acid and chondroitin sulfate may offer temporary physical support to human adipose-derived stem cells in cartilage tissue engineering. Hyaluronic acid and chondroitin sulfate are regarded as the most advantageous pro-chondrogenic factors in developing new biomaterials for cartilage tissue engineering, and adipose-derived stem cells have been proven to exhibit high chondrogenic potential. Meanwhile, Xie et al. have discovered that a pure sericin conduit may be utilized for peripheral nerve regeneration in a rat nerve injury model. This sericin/silicone nerve guidance conduit can act as a viable alternative to autologous nerve grafts in repairing damaged peripheral nerves, as it resulted in functional recovery that is similar to an autologous nerve graft [29].

As a wound dressing/wound care material: Over the past 25 years, wound dressing materials have undergone significant advancements. Sericin is a substance that possesses wound-healing properties and can be used as a covering material for wounds in the form of a film.

An ideal wound-healing material must be biocompatible, protective against secondary infections, and should prevent water loss while also controlling water vapor and oxygen permeabilities. Additionally, the wound dressing should possess mechanical properties, biocompatibility with the skin, and improve the healing process by actively attracting immune cells to the wound area. When sulphonated, both fibroin and sericin exhibit an antithrombotic effect. Sericin, in particular, is a novel wound coagulant material because of its flexible and biocompatible nature, as well as its ability to resist infections and absorb water. It promotes skin healing without causing any peeling of the skin during the regeneration process [30].

Sericin for Burn Dressing: Wound healing is a complex and dynamic process involving a highly organized and coordinated series of events. These complex events take place in four overlapping phases: hemostasis, inflammation, proliferation, and remodeling. Chronic wounds can be seen in burns, diabetic wounds, and ulcers due to tissue injury or disturbance in various factors that prolong one or more of the four normal healing phases, which becomes irreparable within a typical time period. A burn is a tissue lesion characterized by changes like local erythema to complete the destruction of the affected structure. Burns are associated with significant mortality, morbidity, multiple surgeries, high medical cost treatments, and longer period of hospitalization and rehabilitation. The purpose of managing and treating surface burns is to induce epithelialization, prevention of infection and reduction of functional and aesthetic sequelae. Burns often lead to sepsis; hence, topical antimicrobial agents are always prophylactically used to prevent the complications of infections [29].

Silk sericin has been used in regenerative medicine for the proliferation of keratinocytes and fibroblasts during the wound-healing process. It can induce fibroblast proliferation and collagen synthesis without the activation of pro-inflammatory cytokines. Thus, sericin can be formulated and used as a wound dressing or cream to control and prevent wound infection and treat burns and reduce scarring. The antioxidant activity of silk sericin helps in the scavenging of ROS generated in chronic wounds. hence, sericin-containing formulations may prevent prolonged inflammation and infection of chronic wounds helping in rapid healing. Both sericin cream and a combination of sericin with silver sulfadiazine have been shown to facilitate the healing of full-thickness burn wounds in rats. Clinical studies have also indicated that a cream containing silk sericin in conjunction with silver sulfadiazine is both safe and effective for treating burns. Furthermore, in animal models, chitosan-sericin-silver nanocomposite films have been found to accelerate the process of burn wound healing through fibroblast differentiation, angiogenesis, and collagen reorganization, as reported in a recent study [29].

Sericin As a raw material for making contact lenses: Silk sericin has biological beneficial properties helpful in the development of contact lenses. The biocompatible graft polymers were prepared with methyl methacrylate or styrene along with sericin to develop a raw material for contact lenses. Oxygen-permeable membranes made of fibroin and sericin with 10-16 percent water are used for contact lenses and as artificial skin [30].

Sericin as a medicine for improving digestion and curing digestive diseases: Food containing sericin has been found to alleviate constipation, inhibit the progression of bowel cancer, and enhance the absorption of minerals. When consumed orally, sericin induces a dose-dependent reduction in the development of colonic aberrant crypt foci. It has also been shown to decrease the incidence and number of colon tumors due to its potent anti-cancer activity, according to a study [30].

Antimicrobial use: Rajendran et al [31] have developed a straightforward and efficient method for extracting sericin from the cocoons of B. mori silkworms using the chilled ethanol precipitation technique. Their study aimed to investigate the antimicrobial properties of cotton fabric coated with sericin extracted through this method. The sericin-coated fabric exhibited a high level of bactericidal activity against the test organisms E. coli and S. aureus utilized in their study..

Antioxidant: Recently Intake of dietary antioxidants has been of great interest, especially due to the findings on the effect of free radicals in the body, which can have serious consequences if their products are not neutralized by an efficient antioxidant system or antioxidant medicine. studies have shown the antioxidant properties of sericin B. mori. Cocoons of B. mori has natural pigments typically flavonoids and carotenoids accumulated in sericin layers and which are known for their biological properties as antioxidants and antityrosinase. The antioxidant properties of sericin could be related to high serine and threonine content [42].

Application of sericin in the dental field

Sericin as implant coated bio active material [32]

Numerous techniques have been developed over the years to coat or chemically modify titanium implantable surfaces for dental applications in order to improve the implant response to oral microbe microbiota to reduce the risk of implant failure. The coating of dental implants with bioactive molecules is a recent approach to modify pristine Titanium biochemical properties and hinder bacterial colonization of implant surface. A natural biomolecule that has been shown to possess interesting biological characteristics is silk sericin. An in vitro study was done to evaluate the effectiveness of different experimental protocols to obtain a sericin-based coating on medical grade Titanium able to reduce microbial adhesion and biofilm formation on the dental implant surface.

Apart from its use in tissue engineering applications, sericin has recently been investigated for its potential in cartilage or nerve regeneration. Dinescu et al. reported that a collagen-sericin scaffold combined with hyaluronic acid and chondroitin sulfate can serve as temporary physical support for human adipose-derived stem cells for cartilage tissue engineering. Hyaluronic acid and chondroitin sulfate are known to be the most beneficial pro chondrogenic factors used in the development of new biomaterials for cartilage tissue engineering, with adipose-derived stem cells exhibiting high chondrogenic potential. Xie et al. reported the first use of a pure sericin conduit for peripheral nerve regeneration in a rat nerve injury model. This sericin/silicone nerve guidance conduit can be utilized as an alternative to autologous nerve grafts to repair damaged peripheral nerves, as it induces functional recovery comparable to that of an autologous nerve graft [29].

Figure 3. *Commercially available oral gargle containing silk proteins*

Sericin for Drug Delivery: Drug delivery systems can improve the effectiveness of therapeutic medicines by efficiently targeting, modulating release, or stabilizing the molecular state of drugs.

Sericin has the potential as a drug delivery carrier due to its biocompatibility, adjustable morphology, chemical activity, and pH responsiveness [29]. Wang et al. developed a covalently crosslinked 3D pure sericin hydrogel that is injectable and has physical and chemical properties that promote sustained drug release [38]. This hydrogel could potentially serve as an efficient drug delivery system. Nishida et al. evaluated the release and biodegradation of a charged protein, fluorescein isothiocyanate-albumin, using sericin of different molecular sizes, concentrations, and forms [39]. Higher concentrations of sericin resulted in a longer release of the charged protein. In a rat model, the sericin preparation gradually decreased in size and weight, while the charged drug-protein remained for 3 to 6 weeks or longer [39]. These studies suggest that sericin can be used as a biomaterial for drug delivery.

Sericin for bone regeneration

Sericin extracted from silk cocoons is used for soft tissue engineering, such as for repairing epithelial and connective tissues. While the mechanical properties of sericin are suitable for soft tissue repair, its lack of mechanical strength makes it challenging for bone regeneration. However, with modifications to improve its mechanical and bone-inducing properties, sericin can potentially be used as an artificial bone substitute for severe bone defects.

Pure sericin is not typically used as a scaffold for bone tissue engineering due to its poor mechanical properties, as previously mentioned. However, the addition of other bioactive ingredients can improve the nucleation of hydroxyapatite (HA) crystals, which are formed by the binding of $Ca2+$ to the anionic side chains in sericin. The nucleation of hydroxyapatite crystals can be influenced by the amount of acidic amino acids present in sericin [40]. A study by Zhang et al. demonstrated that composite films made of hydroxyapatite and sericin were able to maintain the differentiation of mesenchymal stem cells, leading to structural and functional repair within a 12-week period [40, 41]. These findings suggest that sericin-based biomaterials have the potential for use in bone tissue engineering.

Conclusion

Silk sericin, which is extracted from silkworm cocoons of B.mori, has been the subject of extensive study and research in the biomedical field due to its remarkable biological, and biochemical activities, and controlled physical-chemical properties. It is biocompatible, and biodegradable, and naturally enables cell adhesiveness, attachment, proliferation, and differentiation, making it an ideal therapeutic material for biomedical applications. Furthermore, its variable amino acid composition and abundant functional groups allow sericin to be chemically modified and cross-linked to form versatile constructs that serve as alternative matrixes for various biomedical applications. Sericin has been used to develop a wide range of biomaterials, including films, hydrogels, scaffolds, conduits, devices, and micro-nano formulations, for tissue engineering and regenerative medicine purposes. This review systematically summarizes the properties of silk sericin, describes its different forms, and highlights their uses in the medical and dental fields.

Looking forward, with the ongoing advances in the medical and dental fields, new materials are being researched and developed to provide the best possible treatment and services to patients. The recent advancements in sericin-based biomaterials for tissue engineering and regenerative medicine have opened up a new era of silk proteins and their applications. Sericin, as a by-product of the silk industry, has tremendous potential in biomedical research and applications due to its biochemical and biological properties. Further developments and advanced studies in this field may change the current status of the silk industry and promote the transformation and modernization of traditional industries, as well as tissue engineering, regenerative medicine, and biomedical applications.

References

1. Goel A (2015) Surgical sutures—a review. Off Sci J Delhi Ophthalmol Soc 26:159–162.
2. Kundu S et al (2012) Nonmulberry silk biopolymers. Biopolymers 97:455–467
3. Rockwood DN et al (2011) Materials fabrication from Bombyx mori silk fibroin. Nat Protocols 6:1612
4. S. C. Kundu, B. C. Dash, R. Dash, and D. L. Kaplan, “Natural protective glue protein, sericin bioengineered by silkworms: potential for biomedical and biotechnological applications,” Progress in Polymer Science, vol. 33, no. 10, pp. 998–1012, 2008.
5. M. Mondal, K. Trivedy, and S. N. Kumar, “The silk proteins, sericin and fibroin in silkworm, Bombyx mori Linn.,—a review,” Caspian Journal of Environmental Sciences, vol. 5, no. 2, pp. 63– 76, 2007.
6. A. R. Padol, K. Jayakumar, K. Mohan, and S. Manochaya, “Natural biomaterial silk and silk proteins: applications in tissue repair,” International Journal of Materials and Biomaterials Applications, vol. 2, no. 4, pp. 19–24, 2012.
7. G. H. Altman, F. Diaz, C. Jakuba et al., “Silk-based biomaterials,” Biomaterials, vol. 24, no. 3, pp. 401–416, 2003.
8. J. Nagaraju and M. R. Goldsmith, “Silkworm genomics-progress and prospects,” Current Science, vol. 83, no. 4, pp. 415–425, 2002.
9. B. Joseph and S. J. Raj, “Therapeutic applications and properties of silk proteins from Bombyx mori,” Frontiers in Life Science, vol. 6, no. 3-4, pp. 55–60, 2012.
10. M. L. Gulrajani, “Sericin: a bio-molecule of value,” in Proceedings of the Souvenir 20th Congress of the International Sericulture Commission, pp. 21–29, Bangalore, India, 2005.
11. C. Fabiani, M. Pizzichini, M. Spadoni, and G. Zeddita, “Treatment of waste water from silk degumming processes for protein recovery and water reuse,” Desalination, vol. 105, no. 1-2, pp. 1–9, 1996.
12. P. Aramwit, S. Kanokpanont, W. De-Eknamkul, and T. Srichana, “Monitoring of inflammatory mediators induced by silk sericin,” Journal of Bioscience and Bioengineering, vol. 107, no. 5, pp. 556–561, 2009.
13. N. Kato, S. Sato, A. Yamanaka, H. Yamada, N. Fuwa, and M. Nomura, “Silk protein, sericin, inhibits lipid peroxidation and tyrosinase activity,” Bioscience, Biotechnology, and Biochemistry, vol. 62, no. 1, pp. 145–147, 1998.
14. J.-H. Wu, Z. Wang, and S.-Y. Xu, “Preparation and characterization of sericin powder extracted from silk industry wastewater,” Food Chemistry, vol. 103, no. 4, pp. 1255–1262, 2007.
15. Jaime A. Barajas-Gamboa, Angélica M. Serpa-Guerra, Adriana Restrepo-Osorio, Catalina Álvarez-López. Sericin applications: a globular silk protein. Ingeniería y Competitividad, Volumen 18, No. 2, p. 193 - 206 (2016).
16. Komatsu K, Silk (its formation, structure, character, and utilization), the polymeric materials encyclopedia, (CRC Press) 1996.
17. Voegeli R, Meier J & Blust R, Sericin silk protein: unique structure and properties, Cosmet Toilet, 108 (1993) 101-108.
18. Tsukada M, J Polym Sci: Polym Lett Ed, 18 (1980) 133-134.
19. Ayub Z H, Arai M & Hirabayashi K, Biosci Biotechnol Biochem, 57 (11) (1993) 1910-1912.
20. Zhu L J, Yao J & Youlu L, Structural transformation of sericin dissolved from cocoon layer in hot water, Zhejiang Nongye Daxue Xuebao, 24(3) (1998) 268-272.
21. Huddar P H, A study of natural and synthetic compound with reference to chemistry of formation of silk in silkworm, Ph D Thesis, Submitted to University of Pune, India, 1985, 23-75.
22. Zhu L J, Arai M & Hirabayashi K, Sol-gel transition of sericin, (Fac Technol, Tokyo Univ Agirc, Japan) Nippon Sanshigaku Zasshi, 65(4) (1996) 270-274.
23. Voegeli R, Meier J & Blust R, Sericin silk protein: unique structure and properties, Cosmet Toilet, 108 (1993) 101-108.
24. Kataoka K, The solubility of sericin in water (Seric Exp Stu, Minist Agric For, Tokyo, Japan), Nippon Sanshigaku Zasshi, 46(3) (1977) 227-230.
25. Ishizaka H & Kakinoki H, Solubility of sericin from cocoons of poor reliability. II Effect of addition of water soluble high polymers and resin finishing agents to cocoon cooking feed water on sericin solubility, Nippon Sanshigaku Zasshi, 49(1) (1980) 18-22.

26. Zhu L J, Arai M & Hirabayashi K, Relationship between adhesive properties and structure of sericin in cocoon filament, J Sericult Sci Jap, 64(5) (1995) 420-426.
27. Rassent J, The molecular weight of sericin, Biochem Biophys Acta, 147 (1967) 595-597.
28. Tsubouchi K, Yamada H & Yoko T, Manufacture of high molecular weight sericin by extraction, Jpn Kokai Tokkyo Koho Jap 11092564 A2 (to Norin Suisansho Sanshi Konchu Nogyo Gijutsu Kenkyusho, Japan) 06 April 1999, Heisei, pp 6; Chem Abstr,130(22) (1999) 301746.
29. You-Young Jo , HaeYong Kweon and Ji-Hyeon Oh. Sericin for Tissue Engineering. Appl. Sci. 2020, 10,1-17 8457: 2 -17; doi:10.3390/app10238457.
30. S. K. Rajput and Mukesh Kumar. Singh. Sericin – A Unique Biomaterial. IOSR Journal of Polymer and Textile Engineering (IOSR-JPTE). Volume 2, Issue 3 (May -Jun. 2015), PP 29-35.
31. Rajendran, R., Balakumar, C., Sivakumar, R., Amruta, T., and Devaki, N., ‘Extraction and application of natural silk protein sericin from Bombyxmori as antimicrobial finish for cotton fabrics’, The Journal of The Textile Institute, Vol. 103, No. 4, April 2012, 458-462.
32. Paolo Ghensi , Elia Bettio , Devid Maniglio , Emiliana Bonomi , Federico Piccoli, Silvia Gross, Patrizio Caciagli , Nicola Segata , Giandomenico Nollo and Francesco Tessarolo. Dental Implants with Anti-Biofilm Properties: A Pilot Study for Developing a New Sericin-Based Coating. Materials 2019, 12, 2429;1-15.
33. Kurioka, A.; Kurioka, F.; Yamazaki, M. Characterization of sericin powder prepared from citric acid-degraded sericin polypeptides of the silkworm, Bombyx Mori. Biosci. Biotechnol. Biochem. 2004, 68, 774–780.
34. Padamwar, M.; Pawar, A. Silk sericin and its applications: A review. J. Sci. Ind. Res. 2004, 63, 323–329.
35. Padamwar, M.N.; Pawar, A.P.; Daithankar, A.V.; Mahadik, K. Silk sericin as a moisturizer: An in vivo study. J. Cosmet. Dermatol. 2005, 4, 250–257.
36. Kumar, H.A.; Muralidhar, T.; Acharya, S.; Das, M.J. EMS induced morphometric biomass and phytochemical variations in Morus species (Genotype RFS135). J. Exp. Agric. Int. 2013, 3, 43–55.
37. Kang, Y.-J.; Ahn, S.-H.; Kim, Y.-W.; Jo, Y.-Y.; Kweon, H.; Kim, S.-G. Non-randomized, one way cross-over, open label preliminary clinical trial for silk protein based oral gargling. Int. J. Ind. Entomol. 2019, 38, 14–17.
38. Wang, Z.; Zhang, Y.; Zhang, J.; Huang, L.; Liu, J.; Li, Y.; Zhang, G.; Kundu, S.C.; Wang, L. Exploring natural silk protein sericin for regenerative medicine: An injectable, photoluminescent, cell-adhesive 3D hydrogel. Sci. Rep. 2014, 4, 7064.
39. Nishida, A.; Yamada, M.; Kanazawa, T.; Takashima, Y.; Ouchi, K.; Okada, H. Sustained-release of protein from biodegradable sericin film, gel and sponge. Int. J. Pharm. 2011, 407, 44–52.
40. Yang, M.; Shuai, Y.; Zhang, C.; Chen, Y.; Zhu, L.; Mao, C.; OuYang, H. Biomimetic nucleation of hydroxyapatite crystals mediated by Antheraea pernyi silk sericin promotes osteogenic differentiation of human bone marrow derived mesenchymal stem cells. Biomacromolecules 2014, 15, 1185–1193.
41. Qi, C.; Deng, Y.; Xu, L.; Yang, C.; Zhu, Y.; Wang, G.; Wang, Z.; Wang, L. A sericin/graphene oxide composite scaffold as a biomimetic extracellular matrix for structuraland functional repair of calvarial bone. Theranostics 2020, 10, 741–756.