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SILK SERICIN; A PROMISING SUSTAINABLE BIOMATERIAL FOR BIOMEDICAL, PHARMACEUTICAL AND COSMETICS APPLICATION

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ABSRACT

Silk sericin is a natural polymer which are obtain by silkworm, *Bombyx mori*. Silk consists of two types of proteins, silk fibroin and sericin and Sericin contributes about 20-30 percent of total cocoon weight acids. Silk filament is a double strand of fibroin, which is held together by a gummy substance called silk sericin or silk gum. Silk fibroin is the protein that forms the filament of silkworm and gives its unique physical and chemical propertie Silk filament is a double strand of fibroin, which is held together by a gummy substance called silk sericin or silk gum. Silk fibroin is the protein that forms the filament of silkworm and gives its unique physical and chemical propertie There are different methods of isolation of sericin from silk thread and its solubility, molecular weight, and gelling properties depend on the method of isolation. It has wide applications in pharmaceuticals and cosmetics such as, wound healing, bioadhesive ` Silk filament is a double strand of fibroin, which is held together by a gummy substance called silk sericin or silk gum. Silk fibroin is the protein that forms the filament of silkworm and gives its unique physical and chemical propertie Silk filament is a double strand of fibroin, which is held together by a gummy substance called silk sericin or silk gum. Silk fibroin is the protein that forms the filament of silkworm and gives its unique physical and chemical propertie Silk filament is a double strand of fibroin, which is held together by a gummy substance called silk sericin or silk gum. Silk fibroin is the protein that forms the filament of silkworm and gives its unique physical and chemical propertie Silk filament is a double strand of fibroin, which is held together by a gummy substance called silk sericin or silk gum. Silk fibroin is the protein that forms the filament of silkworm and gives its unique physical and chemical propertie Silk filament is a double strand of fibroin, which is held together by a gummy substance called silk sericin or silk gum. Silk fibroin is the protein that forms the filament of silkworm and gives its unique physical and chemical propertie Silk filament is a double strand of fibroin, which is held together by a gummy substance called silk sericin or silk gum. Silk fibroin is the protein that forms the filament of silkworm and gives its unique physical and chemical propertie Silk filament is a double strand of fibroin, which is held together by a gummy substance called silk sericin or silk gum. Silk fibroin is the protein that forms the filament of silkworm and gives its unique physical and chemical propertie Comparison of isolation methods, isolation with steam using autoclave method is more suitable. Sericin with join properties such a gelling property, sol-gel change, isoelectric pH, dissolvability of sericin, and sun–nuclear weight. Sericin inhibits the growth of microorganisms such as S.aureus as gram-positive microorganisms and E.coli as gram-negative microorganisms.

KEYWORD: Silk, silk protein, silk seicin.

1. INTRODUCTION

Sericin is a protein produced by the silkworm, *Bombyx mori*, a holometabolous insect belonging to the Bombycidae family. Silk is a natural fiber produced by different types of arthropods, such as spiders and scorpions, in addition to insects like bees and silkworm families, such as Bombycidae, Saturniidae, and Lasiocampida. Among these types, Mulberry silk produced by *Bombyx mori* L. (*B. mori*), is generally preferred because of its commercial feasibility compared to other silk types, which are restricted by various limitations due to their complex extraction conditions. Mulberry silk is named for being secreted by domesticated silkworms that only feed on mulberry leaves which namely *B. mori*.[1]

Two main proteins are the essential constituents of natural silk obtained from *B. mori*, namely fibroin (65–85 %) and sericin (SER, 15–35 %). These proteins are stored in the glands of arthropods, and upon secretion, they are converted into fibers when being spun.

Sericin, a water-soluble globular glycoprotein, is derived from the silkworm Bombyx mori. It is rich in serine, aspartic acid, and glycine. Sericin is localized around the fibroin fibers with successive sticky layers, to form the cocoon. It constitutes 20%-30% of the total cocoon mass. Sericin is composed of 18 types of amino acids of which most of them contain strong polar (hydroxyl, carboxyl, and amino) side groups.

In the textile industry, the cocoon is processed and sericin is largely removed in a process called degumming. The fibroin is converted into raw silk and used in the production of many types of yarns and silk fabrics.[1-3]

In addition to its economic importance arising from applications in agribusiness, *B. mori* is the main lepidopteran used in scientific research, a genetic resource capable of elucidating a wide range of biological problems.[2] Recently, the cocoon of the *B. mori* and its main proteins, fibroin and sericin , have been the subject of research that has shown the potential use in the field of polymers, biomaterials, cosmetics, and food industry.[3,4]

Figure No. 1.[35]

2. Sericin Synthesis

The sericin is synthesized in the labial gland of *B. mori*, commonly called silk glands, a pair tubular organ extending lateroventrally to the digestive tract, beginning in the labial segment to the caudal region. In *B. mori*, the gland is rudimentary from 1st to 4th instar producing small amount of silk, which is secreted at the end of each instar and is used to fix the tegument to be discarded after moulting to the substrate. At 5th instar, the gland hypertrophy occurs, an increase in cell volume, high silk biosynthesis, and secretion, and weight estimated to be between 20% and 40% of the total weight of insect.[5]

3. Silk sericin gland morphology

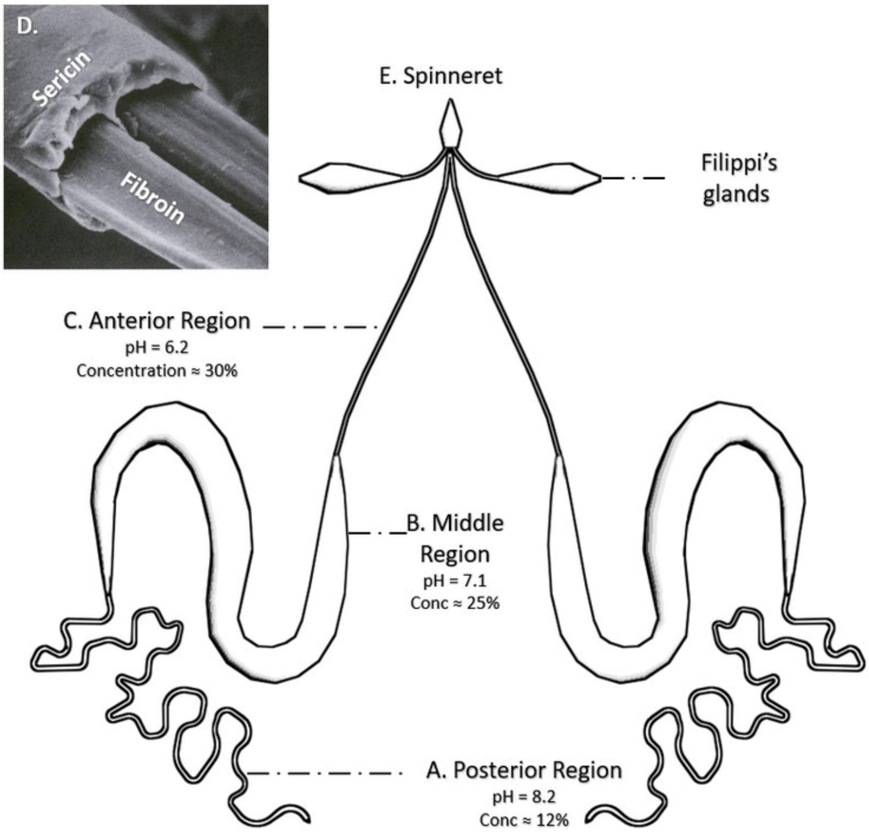

Figure No.-2.[36]

The silk gland is a typical exocrine gland, and, due to morphological and functional differences along the length, it is divided into three regions:

The anterior silk gland (ASG) that forms the excretory duct and has about 200 cells.

The middle silk gland (MSG) which secretes three types of sericin and is about 7 cm in length and approximately 300 cells.

And the posterior silk gland (PSG), secretory of fibroin, that is about 15 cm long and about 500 secreting cells.[6]

In Figure, the pair of silk glands can be visualized, each with its distinct regions. The anterior region ends in a single structure near the head, the silk spinning organ, the spinnerets. The middle region may be subdivided into four areas: anterior, anterior-middle, posterior-middle, and posterior. These areas differ due to the density and morphology of the material contained in secretory vesicles, and each of them synthesizes a different type of sericin in the lumen.[7] The silk gland growth occurs during embryonic development and remains in the larval stage, during which cellular DNA replication occurs without mitosis process that is known as endomitosis. Thus, in the silk thread, the sericin forms three layers around two fibroin filaments coming from each of the silk glands. The fibroin is secreted into the glandular lumen in solution form with approximately 15% of protein, migrating to the middle region where it is surrounded by the sericin. Gradually, water is absorbed by the cells of the glandular epithelium, forming a solution similar to a gel with 30% of protein, which exhibits the property of nematic liquid crystal. While spinning, the proteins flow through the anterior silk gland duct, where excess water and ions are absorbed, and the crystalline liquid solution solidifies gradually converting into a solid filament. Furthermore, a specific and continuous movement of *B. mori* head during spinning also acts on the orientation of protein molecules in the silk thread, and as the silk proteins aggregate and crystallize, they become more hydrophobic, inducing the loss of water on the surface of the thread.[8]

The production of cocoon lasts about three days and occurs from outside in and where silk threads are "glued" using the glue property of the sericin. Cocoon is formed by a long silk thread, whose size ranges from 900 to 1500 meters and its evolution over millions of years provides optimum protection during metamorphosis to silk moth against adverse environmental conditions and attacks of biological agents such as birds, insects, and bacteria.

Its main proteins, fibroin and sericin, make up 98% of the structure, besides the presence of the p25 protein and seroin which are probably responsible for the resistance to predators, fungi, and microorganisms, which are also secreted by the silk glands. Other substances such as fats and waxes (0.4 to 0.8%), inorganic salts (0.7%), and pigment (0.2%) are also present in the cocoon.[9]

Silk gland undergoes morphological and functional changes resulting from insect metamorphosis, degenerating completely 48 hours after the beginning of the pupal stage.[10]

4. Biology and life-cycle

The life-cycle of silkworm has four stages

egg, larva, pupa or chrysalid encased in a cocoon and moth or adult. A complete life-cycle lasts about 44 days in. summer and about 85 days in winter.

Egg

The eggs are oval in shape with a hard chitinous chorion of candid white colour with colorless glue and devoid of any markings. The egg colour generally changed from candid white to bluish just before hatching. The pattern of follicular imprints is very distinct. Cells are polygonal and inter-cellular space are small and the respiratory spines present in between the cells (Jolly et al., 1979 and Sarmah, 1992).

Larva: The larva hatch outgrow from the eggs generally in morning hours after 9 to 10 days in summer and 14 to 15 days in winter at normal temperature. The larva is generally eruciform and has a hypognathus head with biting and chewing type mouth parts. The newly hatched larva is greenish yellow in colour, elongated and cylindrical in shape measuring about 5.0 × 10.0 mm and weighs about 1.5 mg and body colour changes gradually to pure yellow by the end of the third day. From the third instar onward the body colour segregates into yellow, cream, green or blue depending upon races. The fully mature larva which measures about 7.0 × 1.5 cm is translucent and covered with white powdery substances. Both spotted and unspotted larva are found. The spots are of various types; single, double, zebra and semi-zebra (Jolly et al., 1979 and Chowdhury, 1982). The tiny larvae tend to remain together and do not easily move about. The larvae feed ceaselessly and continue growing only stopping to shed their skins during the larval period. The larvae moult or shed off their skins four times and this complete the larval period in five different instars. During the moulting period they do not feed. Unlike the other non-mulberry silkworm, eri silkworm does not eat the empty egg shell on hatching nor the cast off skin after moulting (Jolly et al., 1979) and they have a very poor gripping power.

Silk gland: Larvae are prepared for productions of silk. Silk is a secretion of a pair of large silk gland which correspond to salivary glands of insects. The single gland is a long, tubular structure folded in characteristic manner. The silk gland is the largest organ of the body and occupies almost the whole body of the mature larva. There are large secretary cells and spinning apparatus with press and tube (Chowdhury, 1982).

Cocoon: The larva attains maturity at the end of fifth instar. At this stage the larva stops feeding and empties its alimentary canal by passing out the last excreta. The mature larvae search a suitable cocooning place on the Chandraki (mountage) to spin cocoon. The spinning starts with to and fro movement of the head. First the base of the cocoon is formed followed by the formation of sides and finally the upper part, but during these operations the head movement is irregular. The cocooning is completed in three to five days and the larva gets deeply embedded in the thick layers of silk. Eri cocoons are elongated, soft, flossy, peduncle less, open mouthed and exhibit colour polymorphism being creamy white and brick red. The shape and size of cocoons vary according to host plant and type of cocoonage (mountage) used.

Pupa

The larva metamorphoses inside the cocoon into pupa or chrysalid. The pupae are of obtect adectious type and brown in colour. The pupa is a prelude to moth stage with all the appendages of future moth such as compound eyes, wings, antennae, legs, genitalia etc. which can be seen in bold relief. The female pupae are heavier than the male. The colour of pupae turns black before emergence of moth and there is harp movement of posterior portion of the abdomen.

Moth or Adult

The eri silkmoths are stout, brownish or blackish in colour and covered with white scales. The male moth is smaller than the female. Wings two pairs, buff coloured with white coloured strips in the marginal portion. Wings covered with scales of different colours and shape. Forewings longer and narrower than hind wings. The forewings of both sexes are more or less similar in structure and colour pattern. The characteristics anti-median line is bright chocolate coloured with a white border on either side and almost runs through the centre. The post median line is black with a single dull grey border on either side. A conspicuous black spot, the plerostigma with a whitish tinger is present at the top of the wing apex. In additional the wing has a few white oblique lines. The ocellus in both sexes is crescent-shaped and is characteristic of the insect. The hyaline area is almost invisible and located in the most anterior region of the ocellus. The space between the ocellus and post median line is darker. The remaining colouration of both fore and hind wings is identical except the yellow strips of ocellus which is broader and prominent in hind wings (Jolly et al., 1979 and Sarmah, 1992). The emergence of moth takes place after about two weeks of pupal stage. The moth bores its way out through the open end of the cocoon in the morning hours and continues till mid-day. Soon after emergence they emit a creamy opaque liquid and within an hour they become fully active and prepare for mating. The freshly emerged earlier healthy female moths are collected and tied on „Khariks"s" - a straw stick with a hooking arrangement at the proximal end for convenient egg deposition and are hung on strands of wire stretched across the grainage room. Either the male moths are positioned by hand or they themselves approach the virgin female moths for coupling.

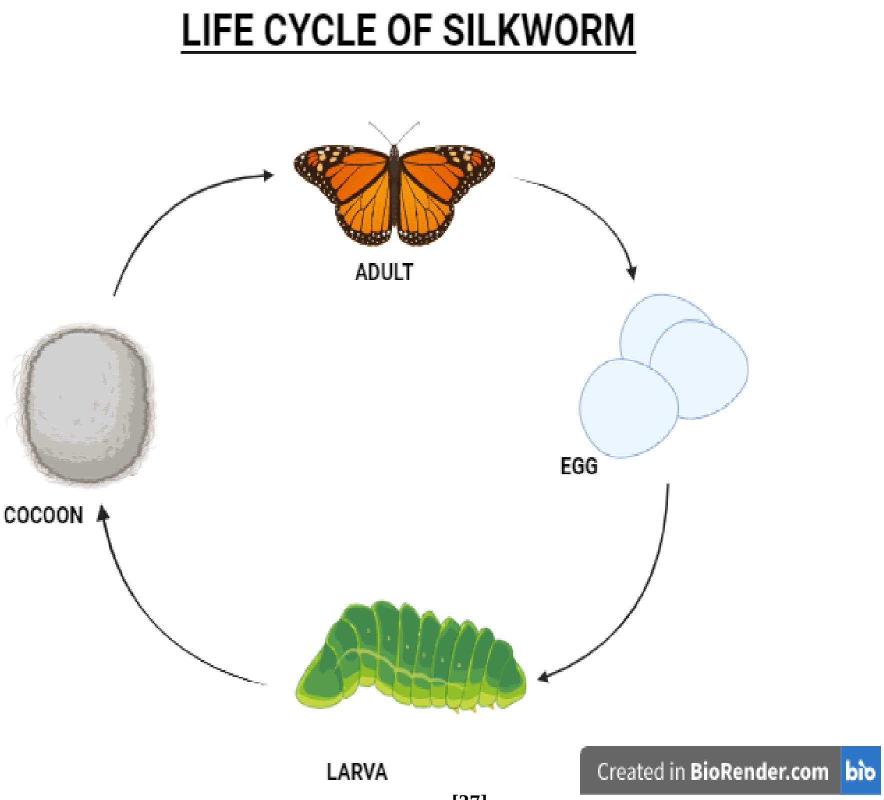

Figure No.-3.[37]

5. Sericin biochemistry

Structurally, sericin is a globular protein consisting of random coil and β-sheets. Changes in random coil structure for β-sheet easily occur in response to mechanical stretching properties, moisture absorption, and temperature, where the sol-gel transition occurs.

In hot water, 50–60°C or higher, protein adopts its soluble form. At lower temperatures, the solubility is reduced and the random coil structure is converted into β-sheets, resulting in the formation of a gel.

Macromolecule of hydrophilic character is composed of 18 amino acids with strong polar groups such as hydroxyl, carboxyl, and amino groups which is capable of forming crosslinks, copolymerizations, and combinations with other polymers. Its organic composition is given by 46.5% carbon, 31% oxygen, 16.5% nitrogen, and 6% hydrogen.

The biochemical characteristics give in which sericin have important biological properties such as biocompatibility, antibacterial activity, antioxidant, and moisturizing, among others.[11,16]

6. Forms of sericin

A: There are three forms of sericin according to their solubility in water

Sericin A, which are more soluble fraction in warm watee and is found in the outermost layer of the cocoon and contains approximately 17.2% nitrogen, with serine, threonine, glycine, and aspartic acid as major amino acids.

In the intermediate layer is found sericin B, which contains 16.8% nitrogen and an addition of tryptophan; it is composed of the same amino acids as sericin A.

The last fraction, sericin C which is adjacent to fibroin and it is found in the innermost layer and it is insoluble in hot water and contains a lower proportion of nitrogen, 16.6%.

B:-Classified sericin on the basis of molecular weight

Sericin classifiction based in place of synthesis in the middle region of the silk gland, as sericins A, M, and P, that comprises the three largest polypeptides that make up the protein.

Sericins P and M are encoded by *Ser1* gene and form the first and second sericin layers that involve the fibroin, respectively. Your transcripts are expressed in the posterior and middle areas of MSG until day 6 from the 5th instar and are not expressed in the anterior area.

Ser2 gene expression is detected in the anterior area; it is rare in the middle area and not expressed in the posterior area. Your expression is detected until day 4 and disappeared after day 6 from fifth instar.

Ser3 gene encodes sericin A that occurs mainly in the floss and outer layer of the cocoon and is mostly detected in the anterior area and rare in the middle subpart. The signal of *Ser3* transcript initiates on day 5 and increases in intensity until day 7 from 5th instar.

While products of *Ser1* and *Ser3* genes compose the sericin layers in *B. mori* cocoon, the proteins encoded by *Ser2* gene are classified as noncocoon and are related with larval silk.

A small amount of silk is spun by silkworm before each instar changes and previous to the cocoon production, which fixes the cocoon to a suitable substrate.[17-19]

7. Properties of Silk Sericin

Gelling Property

Sericin contains random coil and beta sheet structure. Random coil structure is soluble in and as the temperature lowers the random coil structure convert to beta sheet structure, which result in gel formation.

Sol –gel transition

It has sol-gel property as it easily dissolves into water at 50-60 degree celcius and again return to gel on cooling.

Isoelectric pH

As there are more acidic than basic amino acid residues the isoelectric point of sericin is about 4.0.

Solubility of sericin

Solubility of sericin in water decrease when the sericin molecules are transformed from random coil into the beta sheet structure.

The solubility of sericin increase by addition of poly(Na acrylate).

8. Extraction of silk sericin

Sericin can be obtain by different methods;

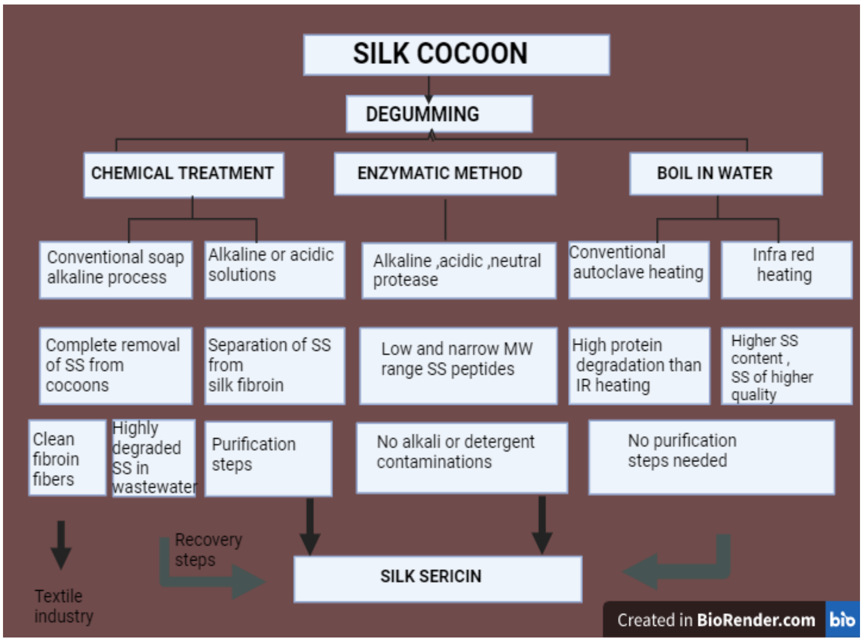

Figure No.-4.[38]

9. Sericin properties and Biomedical Application

The physicochemical properties and molecular proerties of sericin based on functionality and these characteristics are directly influenced by extraction methods.

Studies of biocompatibility and antioxidant potential, both *in vitro* and *in vivo*, have demonstrated that sericin is immunologically inert and have proven the safety and open wide possibility of applications of sericin in biomedicine, such as the food and cosmetic industries, supplement in the culture media, cryopreservation, wound healing, antitumour effect, various metabolic effects in organic systems, and indicate your use in tissue engineering and as a vehicle for drug delivery.[20]

9.1. Immunological Response

Silk fibres have been used in the biomedical field as sutures, since their biocompatible characteristics make them a promising biomaterial. A few studies show the immune system activation front the silk proteins and, historically, the hypersensitivity reactions were attributed to the sericin.[21]

However, the subsequent studies have shown a differential immunological role for sericin. An interesting finding regarding the immunological responses to silk has been presented by Panilaitis et al. they examined the inflammatory potential of intact silk fibres and their *in vitro* extracts. The authors found that silk fibres and soluble sericin are immunologically inert in culture of murine macrophage cells, while insoluble fibroin particles can induce significant release of TNF-α (tumour necrosis factor-α). Even though sericin does not activate the immune system itself, it was found that when it covers the fibroin fibres, there is a strong macrophage in response to bacterial lipopolysaccharide. Thus, the authors confirm that the low inflammatory potential of silk fibres, making them promising candidates for biomedical applications.

In a study involving cocoons of different lines of silkworms, Chlapanidas et al. found that sericin has antiproliferative activities in peripheral blood mononuclear cells stimulated *in vitro*, as well as reducing the release of interferon gamma (IFN-γ), without having effects on the release of interleukin 10 (IL-10) and TNF-α, thus highlighting the applicability of sericin dermatologically, showing its anti-inflammatory role, related positively your biocompatibility, as well as protection against endogenous cells aggressions.[22]

Aramwit et al. investigated the inflammatory mediators induced by sericin *in vitro* and *in vivo*. When the sericin was added to the culture media of mouse monocyte and alveolar macrophage cell lines, there was an increase in cell proliferation and the generation of TNF-α and interleukin-1 beta (IL-1β); however, this increase in cytokines does not activate other inflammatory cascades.

In their *in vivo* assay, the authors used an 8% sericin cream, which was applied topically on wounds on the back of rats. After 7 days of treatment, there was a reduction of the expression of TNF-α and IL-1β in tissue and the overall wound healing was accelerated in treated animals. In this way, sericin promoted wound healing without exacerbating the inflammatory process.

Considering that a protein or new substance can be used as a biomaterial or a biomedical product, the immunological response is normally cytokines, especially IL-1β and TNF-α, both *in vitro* and *in vivo*.[23] Therefore, sericin can be considered as a biocompatible protein, since it presents very low immunogenicity, and it can be utilized in various biomedical areasthat evaluated as an inflammatory reaction.

9.2. Antioxidant

Dietary antioxidants have 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.[24] In this sense, studies have shown the antioxidant properties of sericin *B. mori*. Kato et al. showed, for the first time in *in vitro* study, that sericin inhibits lipid peroxidation in rat brain homogenate.

The lipid peroxides that derived from polyunsaturated fatty acids, are unstable and may decompose into malondialdehyde; whose levels are associated with cardiovascular risk factors, hypertension, diabetes, and hyperlipidaemia.[25]

Similarly, sericin was effective in inhibiting tyrosinase, the enzyme responsible for browning reactions of various foods and the synthesis of melanin, in addition to its role in cancer and neurodegenerative diseases.[26]

Cocoons of *B. mori* can provide natural pigments typically flavonoids and carotenoids that accumulate in sericin layers.[27] These pigments are known for their biological properties as antioxidants and antityrosinase. Aramwit et al. demonstrated that the antityrosinase activity of sericin was greater when obtained from cocoons with pigments, but the potential was also present in cocoons submitted to the pigment extraction process, showing that sericin itself has a significant antityrosinase activity.

Thus, the sericin and pigment are responsible for antioxidant properties. Furthermore, the authors point out that the lineage of *B. mori* and the method of extraction of sericin affect their physical and chemical properties, influencing the antioxidant activity. Sericin extracted by urea solution, with molecular weight ranging from 10 to 225 kDa, has had the highest degree of antityrosinase activity, whereas alkali-degraded sericin showed no inhibition of tyrosinase.

The high amount of arginine and valine amino acids, which can be observed in extraction by urea solution it is perhaps responsible for the antityrosinase activity, since arginine-containing peptides are the most tyrosinase-binding in shorter peptides and valine-containing peptides are the highest tyrosinase-inhibitor. Chlapanidas et al. working with cocoons of 20 lineages of *B. mori* also demonstrated its influence on the antioxidant properties (antityrosinase, antielastase, and elimination of reactive oxygen species) of sericin.

Dash et al. analysed the antioxidant and photo protector potential of sericin from *Antheraea mylitta*, against ultraviolet light B (UVB) in irradiated human keratinocytes. The analysis in flow cytometry revealed that previous treatment with sericin inhibited apoptosis induced by UVB, by inhibiting the expression of proapoptotic protein bax and upregulation of bcl-2, and it prevents the activation of caspase-3.

There was also the inhibition of hydrogen peroxide formation in keratinocytes treated with UVB, indicating a role of sericin in preventing mitochondrial damage.

In addition to these effects, intracellular reactive oxygen species (ROS) and activation of poly-ADP-ribose polymerase enzyme (PARP) were also decreased, directly involved in DNA cleavage processes, their own apoptotic process.

The authors conclude that sericin that are for these purposes, is a potent antioxidant and antiapoptotic agent. Likewise, the sericin antioxidant potential, extracted from *A. mylitta* cocoon, was demonstrated in skin fibroblasts (cell line AH927) exposed to hydrogen peroxide for 24 hours, using catalase, lactate dehydrogenase, and malondialdehyde as indicators.

In Takechi's et al. study, the methods of 1,1-diphenyl-2-picrylhydrazyl (DPPH), chemiluminescence, and the oxygen radical absorbance capacity (ORAC) proved a major antioxidant potential of sericin obtained from the yellow-green cocoon. According to the authors, the flavonoid pigment present in the sericin layers is responsible for this characteristic.

By contrast, the electron spin resonance (ESR) shows that white sericin is better probably because the antioxidant potential of flavonoids pigments may not be involved in the elimination of hydroxyl radicals, detected by this method. Therefore, the results confirmed that all sericins have high antioxidant property against various free radicals, and the antioxidant property of the bread was improved by the addition of sericin powder.

Li et al. observed a protective effect of sericin in hepatic and gastric injuries caused by alcohol in mice. The treated animals showed higher alcohol elimination in urine, and this lowers concentration in serum. The sericin restored the normal parameters of antioxidant enzymes, demonstrating its protective role against lipid peroxidation and generation of ROS in the liver.

The sericin significantly reduces intracellular ROS detected by fluorescence. Micheal and Subramanyam suggested that the main constituent amino acids of sericin protect the midgut epithelial cells of *B. mori* and haemocytes from oxidative damage, probably by the ability of sericin to eliminate ROS.

The antioxidant properties of sericin could be related to your high serine and threonine content, whose hydroxyl groups' act chelating trace elements such as copper and iron.[28]

Devi et al., in their study about sericin from *Antheraea assamensis,* and Prasong, that compared the silk of *Samia ricini* with *B. mori*, concluded that the presence of polyphenols and flavonoids in sericin is responsible for its antioxidant role. Therefore, the studies suggest the use of sericin as a natural and safe ingredient for food and cosmetics industries.

9.3. Cosmetology

The use of sericin in cosmetic formulation, such as creams and shampoos, leads to an increase in hydration, elasticity, cleaning with less irritation, and antiaging and antiwrinkle effects and also prevents nails from chapping and brittleness.

These applications are especially due to the presence of amino acids with hydrophilic side groups (80%), such as serine (30 to 33%), which has large capacity to absorb water. sericin may also form a soft and smooth film on the surface of the skin to preventing the loss of water.

Padamwar et al. studied in vivo moisturizing effect of sericin on human skin and found its action to decrease the impedance and increase in the level of hydroxyproline and hydration of the epidermal cells.

The increase in hydration was attributed to the occlusive effect of sericin, which prevented the transepidermal water loss, responsible for skin dryness. The moisturizing power remained flat epidermal topography. The authors still argue that sericin has similar amino acid structure to filaggrin, present in the stratum corneum of the skin and acts in the natural hydration of the skin; and, thus, sericin itself is an important moisturizing agent.

The dryness is characteristic of a number of skin diseases such as atopic dermatitis and ictiosis, which lead to a decrease in free amino acids in the stratum corneum.

Using silk proteins, fibroin and sericin, as treatment in an animal model of atopic dermatitis, Kim et al. observed that adding 1% of sericin to the diet for 10 weeks caused an improvement in epidermal hydration. To The consumption of sericin provided the increase of total filaggrin and free amino acids, as well increased of peroxisome proliferator-activated receptor (PPARγ), peptidylarginine deiminase-3 (PAD3), and caspase-14, molecules responsible for the increase in expression of profilaggrin and filaggrin degradation of free amino acids that recover dry skin conditions. And therefore, sericin is presented as a potential alternative therapy as an adjunct in the treatment of dry skin conditions such as atopic dermatitis.

9.4. Tissue Engineering

As already mentioned, sericin-based scaffolds can be used as drug delivery systems and as hydrogels, films, sponges and others for tissue engineering purposes.[29] In fact, up to now, sericin is a biomaterial that has been mostly investigated for the regeneration of skin and bone, but also cartilage and adipose tissues, among others.[30]

Sericin alone can be used for bone regeneration, which was already evaluated by Noosak et al.[31] where it was verified that sericin could increase the proliferation of osteoblast cells (MC3T3-E1) up to 135%, compared with the untreated control. Nevertheless, for the regeneration of bone tissue, the conjugation of sericin with hydroxyapatite or other calcium phosphate-based materials is the most common blend of biomaterials used to produce scaffolds.[32] since these biomaterials enable the mimicking of the organic and inorganic matrixes of the bone, respectively. Furthermore, since sericin has poor mechanical properties, its mixture with other biomaterials is crucial to obtain scaffolds with suitable mechanical properties for bone regeneration.

9.5. Drug Delivery

Scaffolds, films, hydrogels, fibers, foams, spheres, capsules and microneedles, among others, can be used for local and systemic drug delivery. Since sericin has an amphiphilic character (polar side chains and hydrophobic domains), it can be used as a vehicle because it easily binds charged therapeutic molecules or hydrophobic and hydrophilic drugs.[33] In addition, sericin has a long half-life in vivo and high moisture absorption and desorption abilities, which are also favorable properties for its application for drug delivery purposes.[34]

Sericin-based structures, mostly hydrogels, prepared by cross linking, ethanol precipitation, or blending with other polymers, can be used for drug delivery.

10. Literature review

Chandrashekhar et al. (2013) opined that the foliar contents of major and secondary nutrients may vary from region to region and also season to season. Pandey (1995) studied on seasonal variation in Oak leaf quality of Quercus serrata and its impact on oak tasar silkworm rearing and revealed that leaf proteins was high between March and April and then declined in summer and autumn months. Conversely, crude fibre content was minimum during March. During spring (March) the moisture content was highest along with carbohydrate and crude protein while during April, the leaf moisture decreased with increase of crude protein and mineral contents.

The productivity and quality of cocoon, however, depends upon quality food supply, favorable environmental conditions and utmost hygienic condition (Yadav and Mahobiam, 2010). Seasonal variation such as variation in temperature, humidity, sunshine, rainfall, etc. of a particular place, which is governed by different geographical parameters influences the rearing performance of silkworm (Murthy et al., 1996; Clarke 2003; Tamiru et al., 2012 and Bhatia and Yousuf, 2014).

Insect, being cold blooded organisms, the performance of all insect species solely depends on temperature changes (Singh et al., 2009 and Petzoldt and Seaman, 2013). The ideal range of temperature for the growth of eri silkworms ranges from 20°C to 40°C, however, increase in temperature beyond 35°C causes less spinning, mortality of larvae and pupae and poor moth emergence and sterility at adult stage (Sugai and Takashashi, 1981 and Sahu et al., 2006).

Tanaka (1964) reported that crude protein of mulberry leaves decreased with the advancement of leaf maturity**. Rupa et al. (1993a)** worked on positional nutrient status of mulberry leaves and observed that the concentration of organic constituents in themulberry leaves such as crude protein, non-reducing sugar and total sugar was significantly higher in tender leaves than in medium and mature leaves. Sinha et al. (1993) analyzed the variation of chemical constituents in relation to maturity of leaves of mulberry varieties under the agro-climatic condition. They opined that the values of moisture, total nitrogen, total minerals and crude fibre generally decreased gradually with maturity of leaves.

Rupa et al. (1993a) also studied the effect of soil properties in nutrient constituent of mulberry leaves and established that the nutrient of mulberry was significantly influenced by the available soil nutrient statu.

Pathak et al; (1988) estimated the composition on the leaves of different food plants of eri silkworm and reported that the moisture content was highest in gulancha followed by tapioca, kesseru while it was lowest in castor. Crude protein content was highest in castor and lowest in gulancha. Crude fat, total soluble in sugar and reducing sugar contents were highest in kesseru. While the lowest amount of crude fat was recorded on gulancha. Tapioca leaves possessed lowest amount of total soluble sugar and reducing sugar content. In all the food plants leaves moisture and crude protein content decreased gradually with the maturity of leaves while crude fat, soluble sugar and reducing sugar increased gradually with the age of leaves.

Dutta et al. (1997) analyzed the foliar constituents of four different food plants of muga silkworm, A. assama and found differences in values of nutrient constituents. With significantly low percentage of crude fibre and high amount of total nitrogen, protein, starch and calcium contents, mezankari (Listaea citrata) leaves were best in nutritive value followed by som (Machilus bombycina) and soalu (L. polyantha) leaves. Digloti (L. salicifolia) occupied the last position in these respect. Shaw (1998) analyzed the chemical composition of three Ailanthus species in relation to growth, nutrition and cocoon characters of eri silkworm and found that with higher amount of moisture, total nitrogen, crude protein, crude fat and lower amount of crude fibre, A. grandis emerged out as the most efficient host plant for rearing of eri silkworm.

Sogand Schäfer MD et al; 2023: Silk proteins in reconstructive surgery: Do they possess an inherent antibacterial activity? A systematic review.

In this systematic review, the following question was addressed: Do silk proteins, SF and SS, possess an intrinsic antibacterial property and how could these materials be tailored to achieve such a property?

S. Mowafi et al; 2023: Production and Utilization of Keratin and Sericin-Based Electro-Spun Nanofibers: A Comprehensive Review.

This article review is devoted to throw the light on the unique characteristics of keratin- and sericin-based electro-spun nanofibers which make them suitable for various applications in different fields. The principles of electro-spinning together with the various devices usually used to fabricate nanofibers are also highlighted.

Lei Zhang et al; 2023: Novel Applications of Silk Proteins Based on Their Interactions with Metal Ions.

This review focuses on discussing and summarizing advances in the use of silk fibroin and sericin for heavy metal ion-contaminated water remediation, biosensing materials, and electrochemical materials from the perspective of the interaction between silk proteins and metal ions.

Kanoujia et al; 2023: Mini-Review on Analytical Methods Applied for Analysis and Characterization of Sericin.

This mini-review illustrates the reported methods for the characterization of extracted sericin and quantification in pharmaceutical formulations. The review covers analytical methods like UV-Visible Spectroscopy, Fouriertransform infrared spectroscopy, amino acid analysis, mass spectroscopy, and high-performance liquid chromatography with a brief explanation of every analytical method.

Andreia S.silva et al; 2022: Silk Sericin: A Promising Sustainable Biomaterial for Biomedical and Pharmaceutical Applications.

Silk is a natural composite fiber composed mainly of hydrophobic fibroin and hydrophilic sericin, produced by the silkworm Bombyx mori. In the textile industry, the cocoons of B. mori are processed into silk fabric, where the sericin is substantially removed and usually discarded in wastewater.

Su-jin seo et al; 2022: Silk Sericin Protein Materials: Characteristics and Applications in Food-Sector Industries.

There is growing concern about the use of plastic in packaging for food materials, as this results in increased plastic waste materials in the environment. To counter this, alternative sources of packaging materials that are natural and based on eco-friendly materials and proteins have been widely investigated for their potential application in food packaging and other industries of the food sector.

Biaou Oscar Ode Boni, et al; 2022: Immune Response to Silk Sericin–Fibroin Composites: Potential Immunogenic Elements and Alternatives for Immunomodulation.

The unique properties of silk proteins (SPs), particularly silk sericin (SS) and silk fibroin (SF), have attracted attention in the design of scaffolds for tissue engineering over the past decades. Since SF has good mechanical properties, while SS displays bioactivity, scaffolds combining both proteins should exhibit complementary properties enhancing the potential of these materials.

Reyhaneh Fatahian et al; 2022: A Review on Potential Applications of Sericin, and its Biological, Mechanical, and Thermal Stability Characteristics.

Silk sericin exhibits biodegradability, non-toxicity, oxidation resistance, UV resistance, and moisturizing characteristics. The present review is mainly focused on considering the mechanical and biological characteristics of silk sericin, as well as its applications in many industries, especially in the medical industry. In addition, one of the most notable limitations of sericin forms in many application fields is their lack of mechanical properties.

Sogand Schäfer MD et al; 2022: Silk proteins in reconstructive surgery: Do they possess an inherent antibacterial activity? A systematic review.

The field of reconstructive surgery encompasses a wide range of surgical procedures and regenerative approaches to treat various tissue types. Every surgical procedure is associated with the risk of surgical site infections, which are not only a financial burden but also increase patient morbidity.

Lei Zhu et al; 2022: Recent Advances in Environmentally Friendly and Green Degumming Processes of Silk for Textile and Non-Textile Applications.

Silk has been widely used not only in the textile field but also in non-textile applications, which is composed of inner fibrous protein, named fibroin, and outer global protein, named sericin. Due to big differences, such as appearance, solubility, amino acid composition and amount of reactive groups, silk fibroin and sericin usually need to be separated before further process

11. CONCLUSION

Silk protein sericin is a natural polymer produced and secreted by the silk gland insect *B. mori*. Sericin is a water-soluble glycoprotein and comprises 25 to 30% of the cocoon weight; it is characterized by the presence of 18 amino acids, with strong polar side groups (hydroxyl, carboxyl, and amino groups) and high content of serine, aspartic acid, and glycine, resulting in a hydrophilic protein. Sericin is splicing alternative product of genes *Ser1*, *Ser2*, and *Ser3*, which provides a high molecular heterogeneity, 20 to 400 kDa, and variation on amino acid molar percent.

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