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SERICIN- A GIFT OF NATURE: ITS APPLICATIONS

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ABSTRACT

Natural fibre silk consists of two proteins *i.e.* sericin and fibroin, which synthesized at the middle and posterior silk gland of silkworm, respectively. Sericin is glue proteins, which envelop the core protein fibroin and constitute about 15-25% of cocoon weight. It is hydrophilic in nature and composed of 18 different kinds of amino acids among these the serine, glycine, aspartic acid and threonine are most dominant one. Sericin possesses tremendous biological properties like antioxidant, antibacterial, anti-tyrosinase, UV resistance, anti-cancerous which open a wide scope for its application in various fields. Further, moisturizing ability of sericin serve as valuable ingredients for cosmetic industries for developing hydrating skin creams and protection against ultraviolet radiation as well as it also utilized as therapeutic agent for wound healing. In the present review the medicinal properties and its implication has been discussed.

***Keywords*: Silk, protein, sericin, antioxidant.**

Introduction

Silk is a natural polymer protein produced by the family of *Bombycidae* and *Saturniidae* of the order Lepidoptera (Jolly *et al.,* 1974). Silk fibre consists of two major proteins sericin and fibroin which is secreted from different regions of silk glands. Sericin is synthesized in middle silk gland (MSG) of mature silkworm larva, and fibroin is secreted from posterior silk gland (PSG) (Gamo *et al.,* 1977). Silk fibres constitutes 97% protein in which 70-80% is fibroin and 20-30%is sericin and remaining part is carbohydrate pigments waxes and minerals (Kongkachuichay *et al.,* 2002). Based on the feeding sources of silkworm sericin protein is classified into two major categories*i.e* mulberry and non-mulberry sericin. The mulberry sericin is synthesized by silkworm *Bombyx mori*, which solely feeds on mulberry food plants and synthesize sericin protein which have significant commercial values. Similarly, non-mulberry or vanya sericin is synthesized by *Samia cynthia ricini, Antheraea assamensis, Antheraea mylitta, Antheraea paphia*and etc. Further, sericin characteristics may depend on diversity of silkworm, primary host plant and other environmental conditions. Jena *et al.* (2018 and 2021) confirmed that the depending on the ecorace and food plants that the silkworm feeds on, affect the tasar sericin nature and properties. Sericin is basically glue protein for holding the silk filaments tightly. Tasar sericin is composed of 17 types of amino acid, among various amino acid it mainly consist of serine, histidine, glycine, threonine, tyrosine, glutamic and aspartic amino acid (Jena *et al.,* 2018a). Both sericin and fibroin protein play significant role in increasing the rigidity, strength and maintaining the constructional intrinsicity of cocoons.

Silk Protein

Silk protein consist of both fibroin and sericin. Fibroin is the hydrophobic glycoprotein which constitutes approximately 70-80% of cocoon. Molecular structure of fibroin revealed that it is heterodimeric ,consist of heavy chain H (MW 395kDa), light chain L(MW 25kDa) and small subunit P25 with (MW 27kDa). (Gamo *et al.,* 1997; Prudhomme *et al.,* 1985; Couble *et al.,*1983). The genes of Heavy and light chain are located on chromosome 25 and 14 respectively. (Kimura *et al.)* In case of both *B. mori* and *A. mylitta* expression of P25 gene is control during larval development (Prudhomme *et al.*, 1985). The fibroin microfibrils are clustered into fibril bundles, and when they are put together, they form a single silk thread. Two filaments are covered by sericin layer and produce silk thread during cocooning process (Padamwar and Pawar, 2006). Fibroin mainly exist in two forms β sheet which is crystalline form and other is non crystalline form. Sericin is glycoprotein, hydrophilic in nature and constitute about 15-25 % of cocoon total protein. It firmly holds the fibroin and together formed stable structural component of cocoon (Kaplan *et al.,* 1994; Vollrath *et al.,* 2001; Jin and Kaplan, 2003). Molecular weight of sericin protein differs depending upon the method of their isolation. A set of proteins with molecular weights ranging from 20 to 400 kDa are found in sericin, which is derived from the mulberry *B. mori* (Kumar *et al.,* 2017; Bari *et al.,* 2018 and Kunz *et al.,* 2016). It has extremely high serine content (40%) and a glycine content (16%) (Kundu *et al.,* 2008). Three distinct polypeptides, measuring 70 kDa, 200 kDa, and a greater percentage of more than 200 kDa, are present in the sericin of the Indian non-mulberry tropical silkworm *A. mylitta* (Dash *et al.*, 2014). Based on the isolation method, molecular weight of sericin also varies (Rajput and Singh, 2015 and Padamwar and Pawar, 2004). When sericin isolated from cocoon shell, polypeptide molecular weight is ranging between 40-400 kDa, and 80-310 kDa when extracted from silkworm, this further depend upon the various factors like temperature, pH, chemicals, weight, preparing time.

Sericin is a versatile protein with lots of remarkable properties such as antioxidant, antibacterial, UVresistance, anti-tyrosinase which signifies its use in various cosmetic, pharmaceuticals, textile and food industries, for human beings it is a gift of a nature but in the field of sericulture it has been discarded for a long time. According to an estimation 50,000 tons of sericin discarded in waste water during degumming process in silk industries. (Gulrajni, 2005), which alleviate the biological and chemical oxygen demand of water bodies. (Fabiani *et al.,* 1996). The extraction of sericin from wastewater and its prospective utilization could have strong impact on economic, community, and environmental point of view. The purpose of this review paper is to explore the medical based applications of sericin.

Application of Sericin

Sericin has recently been used extensively in the cosmetics products, as an antioxidant and anti-apoptotic substances, as a support for enzyme immunobilization, as a supplement in animal cell culture media, as a dietary supplement, as well as a biomaterial for cell culture, drug delivery, and gene delivery (Lamboni *et al*., 2105 and Dash *et al.,* 2008). Addition of 0.5% sericin to cell culture medium improved the resistance to oxidative stress and quality of bovine embryos in vitro (Isobe *et al.,* 2014). Sericin contains polar amino acids that enable crosslinking to form blends with other polymers, increasing the mechanical resilience of SER-based biomaterials (Cao *et al.,* 2016 and He *et al.,* 2017).

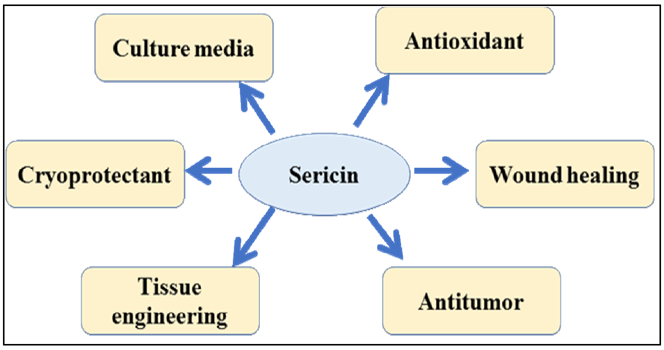

Fig. 1 : Attributes of Sericin

Sericin in Wound Healing

Sericin possess some of the tremendous properties like hydrophilicity, compatibility and biodegradability that make it good wound healing agent without causing any allergic reaction. Numerous studies demonstrated that sericin has an ability to promote collagen formation, migration, and proliferation which is correlated to its therapeutic effects (Aramwit *et al.,* 2007, 2009, 2010). Sericin contain sulphur rich amino acid methionine and cysteine which involved in the synthesis of collagen and play significant role in wound healing process (Aramwit *et al.*, 2009). Sericin enhanced the attachment and proliferation activity of primary cultured human skin fibroblast cell which are thought to be crucial steps in healing of skin leisons. Sericin concentration (100 ug/mL) facilitates the migration of fibroblast cell L929 and in *in vitro* injury model, the sericin treated wound recovered very quickly than control wound. (Aramwit *et al.,* 2013)

Sericin based cream formulations (8% sericin in silver zinc sulfadizine) have significant role in preventing second degree burn wound without causing any severe reactions. In a clinical trial on 29 patients with 65 burns, treated with sericin the result showed that 70% restoration of epithelium tissue on the surface of burn area and enhanced the process of healing in only 5-7 days than control group (treated withstandard silver zinc sulfadizine). Further Aramwit *et al.,* 2007also concluded that impact of sericin on wound healing process in rats. The author concluded that application of 8% sericin cream was effective in recovery of 90% wound and accelerated the reduction of size of wound without showing any ulceration with little inflammatory response. (Aramwit *et al.,* 2007).

Sericin significantly enhanced antioxidant activity and wound healing. Sericin-based formulations can accelerate the healing of incision wounds.*In vitro* wound healing experiment on mouse, Ersel *et al.,* 2016 confirmed that 1% sericin gel was superior to treat the incision area of mouse. Sericin act by increasing epidermal thickness which is related to collagen synthesis by fibroblast cell and decreases the vascularized necrosis. Histo immuno chemical analysis indicated increased level of superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPX) that revealed the positive antioxidant activity in mouse treated with sericin (Aramwit *et al*., 2013).

In addition to biomaterials for wound healing (Gilotra *et al.,* 2018) and artificial skin (Bhowmick *et al.,* 2018), sericin nano formulations are also available for regeneration tissues (Mehrotra *et al.,* 2019). Studies have demonstrated that SER can stimulate the proliferation of skin keratinocytes and fibroblasts (Kunz *et al.,* 2017) and may also aid in the healing of wounds by promoting the deposition of collagen (Tsubouchi *et al.,* 2005). Several sericin based nano formulation revealed positive impact in alleviating recovery of wounds. Dialdehyde carboxymethyl cellulose and silk sericin have also been used in other biomedical applications, including tissue engineering, artificial skin, and wound dressing (Yang *et al.,* 2019; Wang *et al.,* 2019).

A dressing material with exceptional qualities and antibacterial activity is sericin hydrogel. By utilising these qualities, Tao *et al.* (2019) created a brand-new, non-toxic hydrogel with antibacterial activity and super-absorbent qualities that has the potential to be used as a wound dressing. They created a biomaterial with combination of sericin with PVA (poly vinyl alcohol) and silver nitrate nanoparticles. AgNPs-sericin/poly (vinyl alcohol) dressing shows excellent properties like high permeability, good compressibility and absorpitivity which showed outstanding biocompatibility and could load and release both small molecules and Ag-ENPs. It also worked by inhibiting the growth of *Staphylococcus aureus, Escherichia coli* and *Pseudomonas aeruginosa*.

Liu *et al.* (2018) created a film with durable antibacterial properties. It was created using Ag-ENPs-polydopamine sericin/Agar and demonstrated outstanding cytocompatibility on fibroblast NIH/3T3 cells. It also demonstrated significant potential as a novel wound dressing. Using PVA-SER blended mats, Gilotra *et al.* (2018) also investigated the potential of silk sericin based nanofibrous mat for treatment of chronic wound like diabetic foot ulcers. This is novel dressing materials having scavenging potential, microbicidal activity, and bulging capacity ,also PVA mats release slowly releases the sericin which heals wound approximately threefold greater speed than conventional dressing material they claim that SER-based dressing is a promising ENMs candidate.

Bhowmick *et al.* (2018), created a skin substitute for second-degree burn care made of mPEG-PCL-grafted-gelatin (Bio-Syn)/hyaluronan/chondroitin sulfate/SER nanofibers. It was found that the nanofibers (which primarily contained 1 percent of sericin) displayed enhanced levels of epithelial protein expression as well as better performance. Similar wound dressing devices are also described by Tao *et al.* (2019) and Bakhsheshi-Rad *et al.,* (2020) while creating sericin-based poly(vinyl alcohol), chitosan, and tetracycline porous nanoparticles and sericin-based poly(vinyl alcohol), chitosan, respectively. When tested on animals, these materials demonstrated improved wound healing abilities, and they performed better than the control in terms of re-epithelialization and collagen deposition. In addition, various sericin regenerative devices have been developed for the regeneration of articular cartilage (Yuan *et al.*, 2020), sheaths for the regeneration of peripheral nerves (Rao *et al.,* 2017), cardiac patches for the repair of the heart after myocardial infarction (Dong *et al.*, 2020) and bone tissue engineering (Albu *et al.,* 2016 and Chen *et al.,* 2015).

Use of sericin as antitumor

Chemotherapy that are used in the treatment of cancer has been showing adverse side effect, affecting both normal and malignant cells, and due to its high cytotoxicity it affect the vital organ of body which limits its therapeutic potential (Cheok, 2012). Additionally, another issue is the development of chemotherapeutic drug resistance having reduced toxicity and biocompatibility which serve as potent antitumor drugs and in this regard silk protein sericinserve as great source (Huang *et al.*, 2004).

Zhaorigetu *et al.* (2001) investigated the impact of supplementing the diet of an animal model of colon carcinogenesis with 30% sericinand revealed that dietary sericin reduce the proliferation of colon adenoma via suppressing the expression of c-myc and c-fos oncogenes. Sericin's antitumor impact is accompanied by a decrease in cell proliferation, oncogene expression, and oxidative stress. Similar results with sericin supplementation were also reported by Sasaki *et al.* (2000) in a colon cancer model. This study demonstrated the sericin possess antitumor effects by reducing the frequency of aberrant crypt foci after a 5-week supplementation of 3 percent sericin. Kaewkorn *et al.* (2012) studied the effect of sericin against proliferation of colon tumour cells. Sericin has potential to inhibit the proliferation of colon cancer by accelerating cell apoptosis rate via reducing the expression of bcl-2 gene. Studies showed that small molecular weight sericin (61-132 Da) had significantly reduced the proliferation of colorectal cancer cells (SW480) when compared to normal fetal colonic mucosal cells (FHC).

Nanoparticles have frequently been used as the delivery system for chemicals and biomolecular pharmaceuticals, such as anticancer drugs and therapeutic proteins. Proteins are a suitable alternative to the synthetic polymers typically used in the production of nanoparticles because of their safety. In general, protein nanoparticles are advantageous due to their biocompatibility and biodegradability (Kunz *et al.*, 2016 and Zhao *et al.*, 2015). Furthermore, neither the production of protein nanoparticles nor the following encapsulation process involved the use of any hazardous chemicals or organic solvents (Jain *et al.*, 2018).

Medicine that has been studied as a guest molecule on SER-nanoparticles is Doxorubicin (DOX), which serve as one of the most popular anticancer agents. SER-based nanoparticles showed promising effects attributed to molecular mechanisms involving integrated events started by (i) Drug-loaded SER nanoparticle internalisation caused by clathrin-modulated endocytosis (ii) drug release into lysosomes after nanoparticle breakdown, acid pH (observed into tumour environment) (iii)the stimulation of cell death processes such as apoptosis mediated by caspase-3, Bcl-2 down regulation, and Bax protein over expression and (iv)Accumulation of nanoparticles in tumour cells as a result of the EPR effect (Elahi *et al.*, 2021 and Kaewkone *et al.*, 2012).

Sericin nano formulations are being linked to additional active components, such as vitamin B12-conjugated sericin micelles (Guo *et al.*, 2019). According to Mandal and Kundu 2019, micellar nanoparticles made of paclitaxel-loaded SER-Pluronic F-127 induced cytotoxicity by causing quick uptake by breast cancer cells and subsequent activation of the pro- and anti-apoptotic proteins Bax and Bcl-2. In this experiment sericin (extracted from cocoon of *A. myllita*) mixed with pluronic F-127 and F-87 to developed appropriate nanoparticle with size range (100-110 nm). This nanoparticle is unique in terms of carrying both hydrophilic (FITC-inulin) and hydrophobic (paclitaxel). Sericin loaded paclitaxel nanoparticle have shown positive result against breast cancer MCF-7 cell by inducing programmed cell death. Annexin Staining revealed that it acts by increasing the level of Bax and reducing the expression of Bcl-2. In general, for cancer chemotherapy, isolated SER anti-tumoral effects were previously reported considering its integrated proapoptotic activities like decrease in caspase-3 expression, down regulation of Bcl-2, and human colorectal cancer cell cycle arrest (Kaewkon *et al.*, 2012). To target tumors and respond to pH, sericin was used as a doxorubicin prodrug (Huang *et al.,* 2016).

Sericin based nanoparticle play significant role in drug delivery process. In this regard Hu *et al.,* 2017 developed charged reversal sericin based nanoparticle (SSC@NPs) by fusing sericin and chitosan. SSC@NPs showed charge transition according to pH of environment, at neutral pH SSC@NP is negative and at acidic pH surface charge of SSC@NP is positive. More significantly, HeLa cellular uptake was encouraged by the charge-reversal feature of SSC@NPs. Additionally, DOX was loaded onto SSC@NPs before being pH-dependently released. HeLa cells have the ability to take up DOX-SSC@NPs, which then build up in endosomes and lysosomes where DOX was previously released into cancer cell nuclei. In conclusion, the surface charge-reversal SSC@NPs can act as a functional nanocarrier with great promise for pH-responsive drug delivery systems.

Tumor treatment with phototherapy, which includes photodynamic therapy (PDT) and photothermal therapy

(PTT), have high efficiency to cure the metastasis growth (Gai *et al.,* 2018; Jung *et al.,* 2018). Recently Dong *et al.,* 2020 prepared (FA-Ser-Chol/IR780),a type of sericin conjugated with Folic acid cholesterol micelles loaded with IR780(a hydrophobic cation which shows absorption spectra at infrared region) for treatment of gastric cancer. VB12-sericin -PBIG-PTX micelles have excellent biocompatibility and right particle size enable them to diffuse in the cell and target the CD320 receptor that are over expressed in gastric cancer cells. Micelles activates the apoptosis pathways, alter the transmembrane potential of mitochondria and significantly reverse the drug resistance phenotype.

Use of sericin in tissue engineering

In the field of biomedical and tissue engineering, naturally occurring polymers silk fibroin and sericin have received a lot of attention. (Wang *et al.,* 2006). For tissue engineering biomaterial scaffolds is key components and sericin possesses various properties that serve as an ideal scaffold material as it supports cell adherence, migration, proliferation and differentiation as well it is biodegradable and biocompatible to the host immune system.

Teramoto *et al.* (2005) formed the sericin hydrogel simply by adding 10% alcohol to a sericin solution without using any additional cross linking agents or radiation. This research identifies sericin hydrogel as a natural biomaterial. Despite its potential, pure sericin creates brittle films and this limits its used to employ as a biomaterial in tissue engineering (Mandal *et al.*, 2009). Various methods have been used to improve the physical characteristics of sericin (Lamboni *et al.*, 2015). Using sericin from an *A. mylitta* cocoon and glutaraldehyde as a cross linking agent, Mandal *et al.* (2009) created sericin/gelatin blended 2D films and 3D scaffolds. The combination of sericin and gelatin had a similar pore distribution, homogeneous morphology, increased mechanical strength, and good water uptake capacity. In an in vitro experiment, feline fibroblast cells (AH 927) attached and proliferated on sericin/gelatin-blend 2D films and 3D scaffolds, which turned cytotoxic at higher sericin concentrations. But the sericin membrane cross linked with glutaraldehyde, Nayak *et al.* (2012) found that the physical qualities of the membrane increased along with the rate of enzymatic degradation and the viability and attachment of fibroblast cells. This finding offers insight into the role of sericin as a biomaterial.

With the aim of creating a successful tissue-engineered skin replacement, Nayak*et al.* (2013) created 3D porous sericin matrices by using co-cultured of keratinocytes on the upper surfaces of matrices and fibroblast on the lower surfaces, utilising genipin as a crosslink and chitosan matrices as a control. Proliferation of sericin matrices observed for 28 days. Sericin matrices produce epidermal and dermal components in vitro, as shown by the multilayered stratified epidermal layer of keratinocytes that was revealed by histological investigation. In macrophages cultured on the sericin matrices, involucrin, collagen IV, and fibroblast surface protein are present, but there is minimal production of proinflammatory cytokines (TNF-, IL-1, and nitric oxide).The existence of paracrine signalling between keratinocytes and fibroblasts, which is necessary for skin tissue repair, is shown in histochemically stained sections. 3D sericin matrices are skin-equivalent tissues for wound healing because they are biostable and have strong biocompatibility.

Dinescu *et al.* (2013) developed 3D collagen-sericin scaffold with 10% hyaluronic acid and 5% chondroitin sulphate produced a uniform porous, homogenous structure resembling the extracellular matrix of cartilage having pore size 20–150 µm. Human adipose-derived stem cells were able to quickly expand and move on the scaffold, with increased cell adhesion and proliferation, and provided PPAR2 over expression, which upregulated expression of adipogenic markers and creating a viable biomaterial for cartilage tissue engineering.

Now a days sericin based biomembrane used in stem cell technologies and tissue engineering. Inthanon *et al.,*(2016) developed poly(L-lactic-co-ε-caprolactone)-sericin (PLCL-SC) copolymer membrane which support the growth of human Wharton's jelly mesenchymal stem cells (hWJMSC). These membranes are non-cytotoxic and promote the proliferation of human Wharton's jelly mesenchymal stem cells (hWJMSCs) by increasing the concentration of cyclin A and also promote the cell attachment due to increased focal adhesion kinase level. hWJMSC began to differentiate into a neuronal lineage on membrane topography. These findings imply that the PLCL-SC electrospun membrane has some qualities that will be advantageous for tissue engineering and medicinal applications. A hydrogel prepared from collagen, hyaluronic acid and sericin used for human dermal tissue engineering (Vulpe *et al.*, 2018). Fibroblast growth factor (FGF-1)-sericin hydrogel are also used for same purpose (Wang *et al.*, 2018). Pankongadisak *et al.* (2018), prepared a chitosan/sericin hydrogel which is thermosensitive and have porous nature and is suitable for attachment of mouse fibroblast cell line (MC3T3-E1) and also it is non toxic to mouse which may be further utilized in bone tissue engineering. Siavashani *et al.* (2020) also revealed that fibroin /sericin 3D sponges, promising candidate for bone tissue engineering.

As Antioxidant

Due to research on the effects of free radicals in the body, which can have detrimental effects if their products are not neutralised by a powerful antioxidant system, dietary antioxidants have garnered a lot of interest (Sorg, 2004). For the first time in an in vitro investigation, Kato *et al.* (1998), demonstrated that sericin prevents lipid peroxidation in rat brain homogenate. The unstable polyunsaturated fatty acid-derived lipid peroxides can breakdown into malondialdehyde, which has been linked to cardiovascular risk factors such hypertension, diabetes, and hyperlipidemia (Walter *et al.,* 2004). The effectiveness of sericin in inhibiting tyrosinase, an enzyme involved in the browning of numerous foods as well as the production of melanin, as well as its role in cancer and neurological illnesses, underscores the demand for the investigation of compounds with antityrosinase activity (Cavalicri *et al*., 2002)

Dash *et al.* (2008), compared the antioxidant potential of sericin derived from mulberry cocoon and non mulberry tasar cocoon and found that sericin which has extracted from tasar cocoon shell has high antioxidant activities. The method of extraction of sericin protein greatly influences the biological potential and thermal properties. Miguel *et al.* (2020) also confirmed that antioxidant properties of sericin varies according to the extraction method. Sericin extracted from urea method has high antityrosinase activity, further author confirmed that flavonoids and carotenoids pigment present in cocoon responsible for tyrosinase inhibition. Kato *et al.* (1998), first provided the evidence that sericin have antityrosinase potential and also inhibit the lipid peroxidation. Amino acid serine and threonine responsible for antioxidant potential because it inhibit the tyrosinase enzyme responsible for browning reaction in food and also biosynthesis of melanin, for darker colour of skin so it serve as valuable ingredients in food and cosmetic industries. Takechi *et al.,* 2014 also confirmed that sericin possesses antioxidant potential against various free radicals and serve as important ingredients in food industries. Antioxidant activity was clarified by DPPH, chemiluminescence, oxygen radical absorbance capacity (ORAC) and electron spin resonance (ESR). Sericin possess anti tyrosinase, anti-elastase and ROS scavenging properties. Apart from this sericin exhibit immunological properties like TNF α, IFN-γ and IL-10. All these properties of sericin clarified that it serves as good ingredients in food industries, due to its antioxidant activities it reduces the oxidation of food and increases the shelf life of food.

Sericin in culture media and cryopreservation

Cryopreservation is regarded one of the basic method in cellular engineering for preservation of various cells, tissue and for ease of various cell culture-based medicinal therapies as well as for generating functioning cell lines in a constant supply (Sasaki *et al*., 2005). Fetal bovine serum (FBS) supplemented with 10% DMSO are generally used in animal cell culture for maintaining the cell line, but FBS are prone to virus such as bovine spongiform encephalitis and other infections. So sericin can be alternatively used as cryprotectant, serum free media for culturing of human dermal fibroblasts, human epidermal keratinocytes, the rat phaeochromocytoma cell line PC12 and insect (*Spodoptera frugiperda*) cell line Sf9 (Sasaki *et al*., 2005). Terada *et al.,* 2005 used the different molecular weight of sericin in cell culture medium. The sericin with molecular weight 5 to 100 kDa called sericin S stimulates the proliferation of hybridoma cells. The sericin with higher molecular weight, 50 to 200 kDa, also stimulates cell proliferation, but it had not effective sericin S. The result also proved that the sericin S serve as substitute of cytokine IL2, which is used as supplement in culture media, and successfully enhanced the proliferation of established T lymphocytes cell line CTLL-2.

Kumar *et al.* (2014), reported that sericin can be used as cryopreservative for preservation of buffalo sperm. Different concentration of sericin 0.25,0.5,1.5 and 2% is used in media supplement and found that 0.25 and 0.5% sericin improved the antioxidant status of freezing media and semen motility by lowering the lipid peroxidation and increasing the integrity of plasma membrane of sperm. Morikawa *et al.* (2008), uses the sericin in place of fetal bovine serum (FBS) for the culture of rat islet cells. Sericin is alternative supplement for culturing and proliferation of rat insulinoma cell line RIN-5F (Ogawa *et al.,* 2004)

Terada *et al.* (2010) found that 0.01 to 0.1% sericin is effective for proliferation of murine hybridoma 2E3-O cell line. Sericin is used to culture four different varieties of mammalian cell line human hepatoblastoma HepG2, human epithelial HeLa and human embryonal kidney 293 cells in place of fetal bovine serum, which is the source of many infections and contaminations. Sericin support the proliferation of mammalian cell in dose dependent manner, and does not affected by autoclaving. Sericin is used as substitute of fetal bovine serum. 1% sericin in 10% dimethylsulfoxide have proved to be effective cryoprotectant medium for primary human mesenchymal stromal cells (hMSCs) as compared to immortalized human osteoblast as determined by cell viability and colony forming unit (Verdanova *et al.,* 2014).

Role of Sericin in Cosmetic Industries

Sericin properties such as biocompatibility, biodegradability, and wettability have been employed in skin, hair, and nail cosmetics alone or in conjunction with silk fibroin. Sericin, when utilized in lotions, creams, and ointments, demonstrates a raised skin elasticity, anti-wrinkle, and anti-aging impacts (Padamwar and Pawar, 2004). Sericin based moisturizer have been developed for preventing the dryness of top layer of skin (Ziolkowsky, 1998) Moisturizers come in a wide range of types. Wetting agents such vegetable glycerine, water, jojoba oil, vitamin E oil, and sorbitol are included in the components (Kirikawa *et al*., 2000). Sericin gels containing hydroxyproline increase the epidermal layer and reduce skin impedance, which shows the moisturizing properties of sericin. Sericin have moisturizing ability and it reduces the trans epidermal water loss from the skin (Padamwar and Pawar, 2005) Sericin's moisturising impact on human skin was demonstrated in in vivo studies, which also revealed that it increased the level of hydroxyproline and hydrated the epidermal cells while reducing impedance. The increase in hydration was linked to sericin's proline content, which aids in the production of collagen and has an occlusive action that prevents the transepidermal water loss that causes skin dryness. Sericin retained the water layer in the upper layer of stratum corneum essential for smooth and plump skin. Thus, sericin itself possesses effective ingredients in moisturizing formulations of skin.

Atopic dermatitis and ictiosis, which cause a drop in free amino acids in the stratum corneum, are two skin conditions that exhibit the dryness. Kim *et al.,* found that 1% of sericin is an effective in the treatment of skin dryness of atopic dermatitis(AD).Dietary intake of sericin improved the epidermal hydration due to increase in filaggrin and free amino acid in stratum corneum. The induced gene expression of peroxisome proliferator-activated receptor (PPARγ), peptidylarginine deiminase-3 (PAD3), and caspase-14, molecules responsible for profilaggrin gene expression .Thus sericin serve as potent therapy for treatment of dry skin conditions.

Sericin is highly hygroscopic molecules and inhibit the melanin synthesis (responsible for darker skin tone) in cortical layers it serves as valuable ingredients for cosmetic industries. Application of silk sericin on skin depends on its molecular weight. 12000-17000 Da molecular weight is generally preferred for hair care purpose and 5000-70000 is generally applied for skin cosmetic purposes (Jia young *et al.,* 2013). Author further argued that the natural moisturizing factor present in stratum corneum of skin which maintain the moisture content of skin have very similar amino acid composition as that of found in sericin (Jia young *et al.,* 2013). A lotion with 1% weighted sericin and 4% weighted D-glucose provides a hydrating and conditioning effect (Dao *et al*., 2018; Yamada, 2001). Sericin-containing creams with cleansing qualities that are better and less irritant to the skin (Sakamoto and Yamakishi, 2000; Takechi and Takamura, 2014; Tsukada,1994). Sericin enhances the light-screening effects of UV filters such triazines and cinnamic acids ester in sunscreen formulations (Yoshioka *et al*., 2001). It also serves other purposes, such as the absorption of sweat and fat from the skin's sebaceous glands (Miyashita *et al*., 1999).

Conclusion

The silk fibre is an excellent source of renewable protein and due to its superior biocompatibility and unique mechanical qualities is being utilized in pharmaceuticals and cosmetic industries. Sericin is a valuable protein which is going to waste during reeling and degumming process, it could be beneficial bioresources if an economically efficient recovery process could be set up. Many researches have been conducted on the biomedical application of sericin. Significant advancements in the disciplines of tissue engineering and healthcare have been made possible by nanotechnology, especially considering the applications of a natural product for the development of new pharmaceutical formulations and biomaterials. SER-based formulations are a great example of nano-technological tools applied to the design of commercially feasible, biocompatible, and biodegradable compound, as well as its use as nanomedicine.

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