

# Systematic Review of the Skin Photoaging and the Role of Sericin in its UV Protection

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**Abstract:** *Background:* Skin aging, and comprehending ultraviolet (UV) exposure, are significant health burdens with the rising UV radiation. Protective actions to delay the dry appearance, scalping, and wrinkling of the skin are absolutely crucial. Sericin has been the most customary skincare on the cosmetics market for many decades as a means of moisturizer and protection against UV. Consequently, the objective of this review was to systematically search for the role of sericin as skin photoaging in beauty skin society, which is the key thing to developing a new skincare product. *Methods:* Data was collected through the use of online databases such as Pubmed, EBSCO, Science Direct, and Google Scholar from 2003 to 2021. *Results:* The entire application of sericin can drastically protect the UVB irradiation on the skin. *Conclusion:* Based on the findings of a systematic review and meta-analysis, it is possible to infer that sericin is superior to UVB irradiation in improving the protection of the skin.

**Keywords:** Sericin, UVB irradiation, Skin Protection

## 1. Introduction

The emergence of chronic exposure to UV radiation has placed photo aging through the generation of reactive oxygen species (ROS) as global skin health at knifepoint; driving a need for newer natural compounds in neutralizing the effects of oxidative stress. Silk sericin is known to be a biopolymer and is utilized have diverse biological properties. In cells, 10 µg/mL *Antheraea assamensis* sericin treatment before 12 J/cm<sup>2</sup> UVA and 120 mJ/cm<sup>2</sup> UVB irradiations increased the viability of human keratinocytes. It equates to sericin treatment prior to UVA and UVB irradiation preserved the cells from apoptotic cell death by terminate the cell cycle at G1 phase. This has been reflected in a suppressed the interleukin (IL)-6 and IL-8, overexpressed p53 and reduce the deregulation of Bcl-2/Bax gene expression in the Sericin pretreatment. The available data on treatment prior to UVB irradiation significantly decreased skin inflammation, DNA fragmentation, and lipid peroxidation in the female SKH-1 hairless mouse skin. Therefore, it is of value to systematically establish the effective profile of *Antheraea assamensis* sericin in UVA and UVB radiation-induced skin damage<sup>[1]</sup>, to help inform future studies exploring possible clinical benefits in the preparation of skin care products.

Now, with recent research showed that cecropin B as well as sericin activity in the fusion protein gave better protection against UVB damage in human dermal fibroblasts as doable therapeutic agent for ROS-induced skin diseases<sup>[2]</sup>. Due to a paucity of adequate clinical data, it is difficult to reach consensus on an effective sericin dose that can be applied in skin care product for UV radiation-induced skin damage. To that end, this systematic review seeks to identify, appraise and synthesize evidence on the effective of sericin as a therapeutic agent for treating photo aging skin.

## 2. Materials and Methods

Data was collected through the use of online databases such as Pubmed, EBSCO, ScienceDirect, and Google Scholar from 2003 to 2021 was also carried out. This study is classified as a systematic review, and a meta-analysis. This study's population was the sericin on the skin. This study's sample is a scientific article on inclusion criteria include: articles were acknowledged as an original article, including experimental studies (randomized and placebo-controlled trials), observational studies (cohort, cross-sectional, and case-control studies), and reviews concentrating on sericin and photoaging skins were included. It was a full text published in English. A description of how sericin protects skin from UV was evaluated and defined in the methods section. The concentration of sericin and UVB radiation used in skincare the intervention was specified. Exclusion requirements studies included studies performed physical-chemical sericin molecule properties, sericin for antibacterial activity, sericin being wound dressing and skin tissue engineering, sericin as a drug carrier for cancer therapy, and sericin applied as skin carcinoma treatment were excluded. Articles reporting in letters to the Editor, abstracts from conferences, books, PhD theses were also excluded.

### 2.1 Research Procedures

Data source and online database search strategies involve the databases Pubmed, EBSCO, ScienceDirect, and Google Scholar. The data sources examination was conducted until the data was analyzed. To establish three subcategories of citations, the following phrases were employed (1) sericin; (2) UVB; (3) protection. To generate a subset of citations relevant to the study issue, the three subgroups were merged using the Boolean operators 'AND'. The PRISMA flowchart from 2020 was employed to conduct the literature review<sup>[3]</sup>.

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Two researchers performed an independent literature review to determine citation lists of all major papers and the most updated literature review was performed to detect missing publications. Consensus was used to settle any differences in article selection and data extraction. Data were extracted separately by two researchers using the provided data extraction forms. Both intervention and without intervention of sericin, as well as properties scores were documented.

## 2.2 Data analysis

Regarding the data processing, the data collection was reviewed for reliability and consistency. The data will then be entered into the computer. Both intervention and without intervention of sericin, as well as properties scores were retrieved and entered into the form of data extraction. Comprehensive Meta-Analysis: A software application for Meta-Analysis, Version 3.0 was used to examine the systematic review and meta-analysis of mean differences between the experimental and comparison groups.

## 3. Results and Discussion

Comprehensive Meta-Analysis: A software application for Meta-Analysis, Version 3.3 was used to examine the systematic review and meta-analysis of mean differences

between the experimental and comparison groups. Data searches were carried out online at Pubmed, EBSCO, ScienceDirect, and Google Scholar with a time range till the study was completed. The search found 847 publications. After examining the title and eliminating any duplicates, we got 35 relevant article titles [4-29]. After reviewing the abstracts of these publications, 693 articles were eliminated including 9 primary research articles outside the topic of this meta-analysis. Nine complete papers were evaluated for acceptability and utilized in qualitative and quantitative research to assess the effectiveness of sericin as a protection on skin from UVB.

### 3.1 Research Characteristics

Descriptive analysis of research characteristics consisted of research design, number of samples, research subjects, and length of treatment. The majority of research sites were carried out in India (n=5), followed by Korea (n=1), Thailand (n=1), Japan (n=1) and China (n=1) in the period 2003-2020. Three studies used an in vivo design, 3 in vitro design and 4 in vivo, in vivo including cytotoxicity studies. The total sample of 9 studies is 151 samples. The nine studies selected sericin in UVB-irradiated as research subjects. Nine studies took samples of the total treatment events, namely 27 treatment samples and 10 control samples.

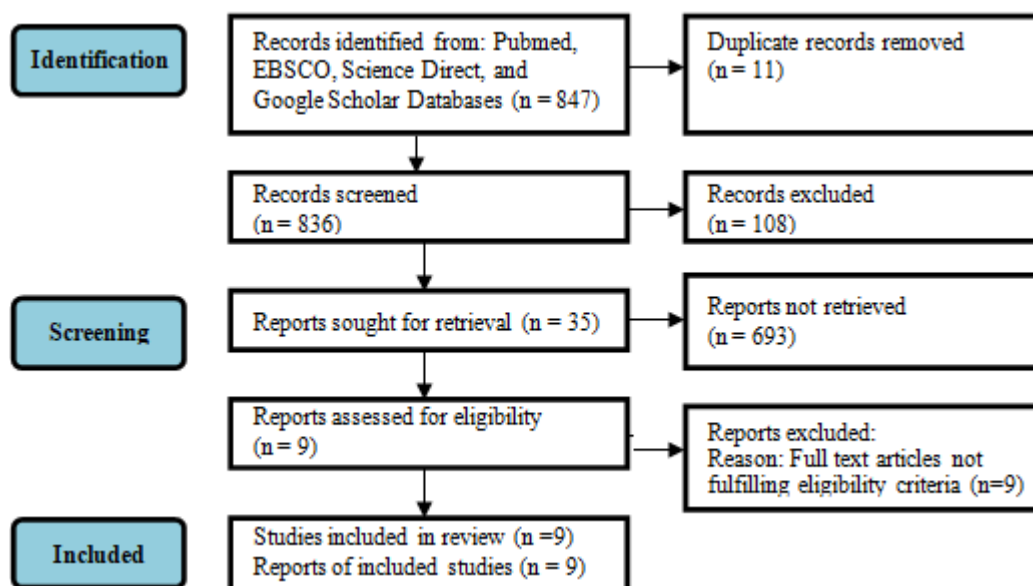


Figure 1: Flow diagram for the systematic review

### Result of Qualitative Data Analysis (Systematic Review)

#### 1) Kumar et al. 2018<sup>[30]</sup>

This research was carried out on topical delivery of potential antioxidants protects the skin against ultraviolet (UV) radiation-induced oxidative damage through maintaining redox balance. The selection of research samples into the treatment group was done by the protective activity of sericin against UVA and UVB radiation-induced skin damage. Methods of MTT and neutral red assays showed that Philosamiaricini sericin (PRS) and Antheraea assamensis sericin (AAS) (10 µg/mL) treatment prior to UVA (12 J/cm<sup>2</sup>) and UVB (120 mJ/cm<sup>2</sup>) irradiations enhanced the viability of human keratinocytes. The standard treatment for all study

samples was that the examination of cell cycle arrest and apoptotic/necrotic cell death using flow cytometer showed that sericin treatment before UVA and UVB irradiation protected the cells from apoptotic cell death by arresting the cell cycle at G1 phase. The outcomes assessed in the study were sericin pretreatment downregulated the interleukin (IL)-6 and IL-8, upregulated p53 and decrease the dysregulation of Bcl-2/Bax gene expression. Overall, AAS treatment prior to UVB irradiation significantly reduced skin inflammation, DNA fragmentation, and lipid peroxidation in the female SKH-1 hairless mouse skin.

**2) Dash et al. 2008<sup>[31]</sup>**

This research was carried out on the silk protein sericin identified as a potent antioxidant and photo protective agent against ultraviolet B (UVB) irradiation in mouse skin model. The standard treatment for all study samples was that the anti-apoptotic effect of sericin in UVB (30 mJ/cm<sup>2</sup>)-irradiated human keratinocytes. The outcomes assessed in this study were flow cytometry analysis has shown that pretreatment with sericin inhibits UVB-induced apoptosis. Overall the pre-treatment with sericin suppresses bax expression, up-regulates the expression of bcl-2, prevents both the activation of caspase-3 and cleavage of Poly (ADP-ribose) polymerase. The change in generation of intracellular hydrogen peroxide in UVB-treated keratinocytes is inhibited through pretreatment with sericin suggesting that sericin probably prevents mitochondrial damage.

**3) Zhaorigetu et al. 2003<sup>[32]</sup>**

This study was conducted on protective effect of an antioxidant protein, sericin, on UVB-induced acute damage and tumor promotion in mouse skin. Methods of in experiment 1, HR-1 hairless mice were treated with 180 mJ/cm<sup>2</sup> of ultraviolet B light (UVB) once daily for 1 and 7 days. The standard treatment for all study samples was the treatment for 7 days caused red sunburn lesions of the skin. The findings evaluated in this research were the intensity of red color and area of these lesions were inhibited by the topical application of sericin at the dose of 5 mg after UVB treatment. This result was increased in immunohistochemical analyses showed that the application of sericin significantly suppressed UVB-induced elevations in 4-hydroxynonenal (4-HNE), expression of cyclooxygenase-2 (COX-2) protein, and proliferating cell nuclear antigen (PCNA)-labeling index in the UVB-exposed epidermis. In contrast, experiment 2, HR-1 hairless mice were treated with 200 nmol of 7, 12-dimethylbenz [a] anthracene (DMBA) followed 1 week later by irradiation with 180 mJ/cm<sup>2</sup> of UVB twice weekly for 22 weeks. These results showed the protective effect of sericin was evident in terms of significant reduction in tumor incidence and tumor multiplicity at the dose of 5 mg. Both research groups applied the results suggest that sericin possesses photoprotective effect against UVB-induced acute damage and tumor promotion by reducing oxidative stress, COX-2 and cell proliferation in mouse skin.

**4) Parashar et al. 2020<sup>[33]</sup>**

This fact-finding study was arranged on Naringenin (NAR) is a flavonoid found in citrus fruits such as grapes and oranges and has demonstrated its potential in inhibition of photoaging. The selection of research subjects into the treatment group was done by the efficacy of sericin (SR) gel loaded with NAR microemulsion (ME) to inhibit UVB-induced photoaging and prevention of epidermoid carcinoma in animal model. The standard treatment for all study samples was NAR-ME through Box-Behnken design. The optimized ME was loaded into sericin (SR) gel. Prior to the formulations were subjected to various in vitro, in vivo and cytotoxicity studies over A431 cell lines. Outcomes assessed in this study were the optimized ME revealed a globule size of 249.05 ± 3.78 nm, 6.7 ± 0.5 pH and 73.1 ± 2.11% release over a period of 24 h respectively. Overall, cytotoxicity studies revealed a depression in IC<sub>50</sub> value in NAR -ME

(65.11 ± 1.54 µg/ml) when compared with NAR (118.1 ± 2.09 µg/ml). The NAR-ME-SR gel displayed enhanced therapeutic potential when compared with plain NAR, in terms of augmented antiproliferative activity.

**5) Kumar et al. 2019<sup>[34]</sup>**

This research was performed on ultraviolet radiation (UVR)-induced redox imbalance in melanocytes triggers the activation of tyrosinase that results in melanogenesis and its related skin disorders. The methods of randomization, blinding and concealment of allocations were inhibited such melanogenesis. At the time of examination silk sericin (SS), a globular protein, is known to possess antioxidant and anti-tyrosinase activities along with other biological attributes. The examination was carried out in the inhibitory activity of SS against UVR-induced melanogenesis. The result assessed was Anti-tyrosinase activity of SS using mushroom tyrosinase, showing that *Antheraea assamensis* sericin (AAS) and *Philosamia ricini* sericin (PRS) inhibited 50% of its activity. Inhibitory activity of SS against UVR-induced melanogenesis was assessed by measuring the cellular melanin content, intracellular tyrosinase activity, and reactive oxygen species (ROS) levels in mouse melanoma. Overall, SS pretreatment significantly reduced cellular melanin and ROS production in UV irradiated melanocytes compared with SS untreated cells. AAS treatment before UVA or UVB irradiation significantly inhibited tyrosinase activity. The findings evaluated in this research were the skincare formulation prepared by the addition of AAS to the basic formulation minimally affected its flow properties and validate that AAS efficiently inhibited UVR-induced melanogenesis also it could be used as a potential antioxidant molecule in skin care cosmetics.

**6) Zhao et al. 2015<sup>[35]</sup>**

This research was carried out on exposure of the skin to ultraviolet B radiation causes oxidative stress that results in sunburn, photo aging, and skin cancer. The standard treatment for all study samples was to investigate the antioxidant, anti-inflammatory, and anticancer effects of a flavonoid extract (FE) from the sericin layer of Daizo silkworm cocoons. The findings evaluated in this research were the analytical HPLC result showed that the FE of the Daizo cocoon shell contains the flavonoid aglycones quercetin (21.76 ± 0.66 g kg<sup>-1</sup> FE) and kaempferol (4.62 ± 0.11 g kg<sup>-1</sup> FE). This assessment uses a skin tumor mouse model, the topical application of FE reduced the number of tumors per mouse from 5.1 in the model group to 3.2 and 2.6 in two sample groups (3 mg and 5 mg FE) prior to induction with UVB/DMBA. These results showed in vivo experimental results that the FE could reduce the phototoxicity of UVB at different cellular and molecular levels by decreasing the severity of dermal inflammation and keratinocyte proliferation through the modulation of oxidative stress and NF-κB. Prior to FE could increase antioxidant activity and decrease the levels of the inflammatory cytokines IL6 and TNF-α.

**7) Thomas et al. 2020<sup>[36]</sup>**

This research was carried out on chronic exposure to UVB radiation causes photo aging, immunosuppression, and ultimately photocarcinogenic through the generation of reactive oxygen species (ROS). The standard treatment for

all study samples was Silk sericin, a biopolymer is reported to have diverse biological properties. Overall, the antioxidant and anti-UVB are potential of recombinant sericin and sericin-cecropin B proteins against oxidative stress using human primary dermal fibroblast cells. The findings evaluated in this research were treating the cells with recombinant sericin (RS) or sericin-cecropin B (RSC) prior to exposure to UVB and H<sub>2</sub>O<sub>2</sub>, effectively increased the cell viability by approximately 30% and 50%, respectively, in comparison to non-treated control. The result assessed was a reduction in LDH release of at least 16 and 33% with RS and RSC treatments, respectively, in comparison to exposed control. This indicates, elevated levels of catalase and superoxide dismutase (SOD) activity were observed. Importantly, the RSC fusion protein exhibited enhanced protective effects than cells treated with RS alone.

#### 8) Pongcharoen et al. 2013<sup>[37]</sup>

This fact-finding study was arranged on Lutein and zeaxanthin are carotenoids present in high concentrations in the human retina which are involved in the photoprotection of the human eye. The standard treatment for all study samples was lutein may also protect the skin from ultraviolet (UV)-induced damage. Overall, the present study investigated the protective effect of lutein extracted from yellow silk cocoons of *Bombyx mori* on human keratinocytes against UVB irradiation. A human keratinocyte cell line and primary human keratinocytes were used to investigate the UVB protection effects of silk lutein and plant lutein. Silk lutein showed no cytotoxicity to keratinocytes. Treatment with silk lutein prior to UVB irradiation enhanced cell viability and cell proliferation, and reduced cell apoptosis. The protective effects of silk lutein may be superior to those of plant lutein. Silk lutein may have a benefit for protection of keratinocytes against UVB-irradiation.

#### 9) Cheong et al. 2017<sup>[38]</sup>

This research was performed on ultraviolet (UV) light, a main cause of photoaging, leads to collapse of skin structure, resulting in wrinkle formation and dehydration. The standard treatment for all study samples assessed the anti-photoaging and moisturizing effects of *Bouea macrophylla* extract (BRE). UVB-irradiated hairless mice were orally administered with BME (300 mg/kg/day) for 8 weeks. BME ameliorated wrinkle formation, skin thickening, and inelasticity. BME upregulated COL1A1, COL3A1, COL4A1, and COL7A1 mRNA levels through activation of the transforming growth factor- $\beta$  (TGF- $\beta$ )/Smad pathway, thereby recovering the content of collagen reduced by UVB. Further, BME suppressed UVB-induced matrix metalloproteinase (MMP)-3 and MMP-13 expression and

inhibited MMP-2 and MMP-9 activity by mediating the mitogen-activated protein kinases (MAPKs)/activator protein-1 (AP-1). BME improved moisture content by stimulating the expression of certified envelope proteins and filaggrin-processing enzymes. Overall, the results show that BME prevents photoaging and promotes miniaturization in UVB-irradiated hairless mice, suggesting its potential as a nutraceutical candidate for anti-photo aging and moisturizing effects.

#### Quantitative data result (Meta-analysis)

Meta-analysis result effect of sericin on UVB irradiation

The mean score difference of the treatment and the control which got sericin and UVB-irradiation is presented in Table 1.

**Table 1:** Mean score difference of sericin on UVB irradiation treatment group compared to controls

No	Name of Researcher	Treatment		Control	
		Average $\pm$ SD	n	Average $\pm$ SD	n
1	Cheong, 2017	2.125 $\pm$ 1.273	18	0.754 $\pm$ 1.273	18
2	Dash, 2008	3.000 $\pm$ 1.528	4	1.099 $\pm$ 1.528	4
3	Kumar, 2019	2.118 $\pm$ 1.192	21	0.750 $\pm$ 1.192	10
4	Kumar, 2018	5.377 $\pm$ 1.112	58	1.682 $\pm$ 1.112	58
5	Parashar, 2020	4.200 $\pm$ 1.295	8	1.435 $\pm$ 1.295	8
6	Pongcharoen, 2013	2.143 $\pm$ 1.280	16	0.762 $\pm$ 1.280	16
7	Thomas, 2020	2.000 $\pm$ 1.190	6	0.693 $\pm$ 1.190	6
8	Zhao, 2015	3.600 $\pm$ 1.232	13	1.281 $\pm$ 1.232	13
9	Zhaorigetu, 2003	4.500 $\pm$ 1.323	7	1.504 $\pm$ 1.323	7

In Table 1 the difference in the value of sericin and UVB irradiation the treatment and the control group the value was positive. This indicates an increase in the sericin values after applying UVB irradiation. The research of Kumar et al. 2018 showed that the sericin values after UVB irradiation, which was 5.377 $\pm$ 1.112, was higher than the control, which was 1.682 $\pm$ 1.112. In the study of Thomas et al. 2020 showed the value of sericin after treatment, 2.000 $\pm$ 1.190 lower than the control, 0.693 $\pm$ 1.190.

In Table 2 the findings of a meta-analysis on the efficacy of sericin on UVB irradiation. The heterogeneity result demonstrates Q's value=0.802 df=8 P=0.348 I<sup>2</sup>=0.000. This indicates that the data are homogenous, as indicated by the statistical Q test and heterogeneity results, the I<sup>2</sup> test outcomes are not significant, indicating that the data are homogeneous. Since this data were homogenous, the analysis was conducted using a fixed effect model. The meta-analysis findings found that the statistical Q value of Z value=0.938 (P = 0.348). This demonstrates that the entire application of sericin can drastically protect the UVB irradiation on skin.

**Table 2:** The meta-analysis results of the sericin effectiveness on the UVB irritation in skin

Model	Study name	Cumulative statistics					Cumulative odds ratio (95% CI)				
		Point	Lower limit	Upper limit	Z-Value	p-Value	0.01	0.10	1.00	10.00	100.00
	Cheong, 2017	2.125	0.175	25.775	0.592	0.554					
	Dash, 2008	2.448	0.360	16.645	0.915	0.360					
	Kumar, 2019	2.309	0.525	10.161	1.107	0.268					
	Kumar, 2018	3.016	0.886	10.272	1.766	0.077					
	Parashar, 2020	3.211	1.065	9.681	2.072	0.038					
	Pongcharoen,	3.007	1.095	8.258	2.137	0.033					
	Thomas, 2020	2.820	1.116	7.125	2.192	0.028					
	Zhao, 2015	2.910	1.225	6.913	2.419	0.016					
	Zhaorigetu, 2003	3.040	1.338	6.907	2.655	0.008					

The meta-analysis findings as a whole uncovered the fact that the total of standardized mean difference in Sericin values between samples receiving UVB irritation compared to those receiving control was  $3.229 \pm 1.269$  (95% CI, 0.592 to 2.655). These findings imply that the total sericin values of the group receiving UVB irritation was substantially higher than the controls as a whole ( $P=0.348$ ).

The limitation of this review is the lack of publications related to sericin, especially those related to the function of sericin as UV protection. There is a need to study several aspects of ideal sericin molecule in skincare formulation against UV, including animal and human testing. Further clinical trials are needed to support the acclaim of sericin as potential UV protective.

#### 4. Conclusion

Based on the findings of a systematic review and meta-analysis, it is possible to infer that sericin is superior to UVB irradiation in improving protection of skin.

#### Ethics

Data was collected through the use of online databases such as Pubmed, EBSCO, ScienceDirect, and Google Scholar from 2003 to 2021.

#### Funding

The authors received no financial support for the research.

#### Author Contributions

**Fitria Agustina:** Conceptualization, Investigation, Methodology, Validation, Data curation, Resources, Formal analysis.

**Wimpie Pangkahila, Anak Agung Gde Putra Wiraguna,:** Conceptualization, Methodology, Formal analysis, Data curation, Review and editing and Supervision.

#### Declaration of competing interest

The authors declare "No conflict of interest".

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