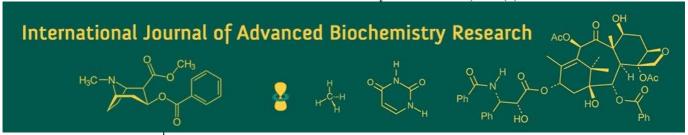
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Harnessing the medicinal benefits of silkworm, Bombyx mori

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Abstract

Sericulture, an agro-based industry centered on the production of raw silk through silkworm breeding, rearing, and host plant cultivation, has evolved significantly from its traditional focus on silk manufacture. Historically, byproducts of sericulture were discarded as waste. However, recent advancements have highlighted the medicinal potential of sericulture products and byproducts, expanding their applications beyond silk production. Silkworms have emerged as valuable tools in laboratory research, serving as model organisms in life sciences, environmental monitoring, and antimicrobial drug screening. Protein extracts from silkworm eggs are utilized for memory enhancement and weight management, while silkworm larvae provide blood glucose-lowering agents and other medicinal benefits. Additionally, silkworm pupae, a major byproduct of silk reeling, offer high nutritional value and therapeutic properties such as hepatoprotection, anticancer, and anti-aging effects, making them viable alternatives to traditional dietary supplements. This shift toward functional sericulture not only boosts farmer income but also contributes to healthcare innovations, underscoring its multifaceted potential.

Keywords: Sericulture, *Bombyx mori*, silkworm byproducts, therapeutic applications, functional foods, nutraceuticals, hepatoprotective effect, blood glucose regulation

1. Introduction

Animal-based substances have long been integral to traditional healing systems, with therapeutic applications involving body parts, metabolic products (such as secretions and excreta), and associated materials like cocoons and nests. Insects, in particular, along with their derivatives, have been consistently employed in medicinal practices across diverse human cultures throughout history. Insects are particularly significant in modern medicine due to their immunological, analgesic, antibacterial, diuretic, anesthetic, and antirheumatic properties. The chemicals that insects produce for self-defense hold immense potential as medicinal drugs.

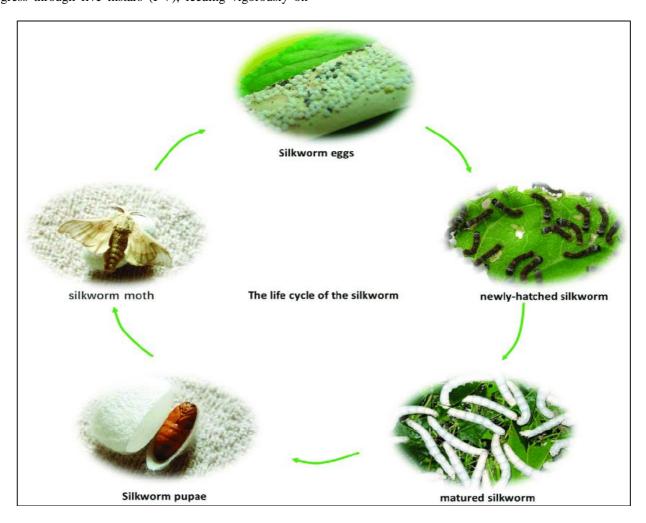
The search for new pharmaceuticals derived from natural biological materials has been guided by ethnobiological data. Investigating folk medicine has emerged as a valuable tool in bioprospecting for pharmaceutical compounds. Although insects have played a significant role in traditional and modern medicine throughout history and across continents, relatively little medical entomological research has been conducted since the revolutionary advent of antibiotics (Rajkhowa *et al.*, 2016) [17].

Among lepidopteran insects, the silkworm (*Bombyx mori* L.), renowned for producing the luxurious silk fiber often called the "Queen of Textiles," has traditionally been valued for its role in sericulture. However, modern sericulture has evolved from focusing solely on cocoon production to a more comprehensive approach known as functional sericulture (Mahanta *et al.*, 2023) ^[14]. This transition has led the silk textile industry to diversify into advanced biotechnological fields, significantly broadening the applications of sericulture products. Notably, silkworms are now being explored for their potential as food sources, in medical applications, and within biotechnology. The use of silkworms in traditional Chinese medicine dates back at least three thousand years.

2. Silkworm at different stages in medicinal field

The silkworm is a lepidopteran insect that belongs to the family Bombycidae and Saturniidae. Silkworm, an endopterygote lepidopteran insect, undergoes complete metamorphosis through four life stages: egg, larva, pupa, and adult. After mating, adults lay eggs in batches, known as Disease-Free Layings. The eggs hatch into larvae, which progress through five instars (I-V), feeding vigorously on

host plants and producing silk. Late instar larvae spin sericigenous material to form cocoons, within which the pupae develop. Silkworm larvae and pupae are emerging as nutritious insect-based food sources, rich in proteins, oils, polyphenols, vitamins, and chitosan. Each stage of the silkworm's life cycle offers potential health benefits (Singh *et al.*, 2002) [20].



2.1 Potentiality of silkworm egg in medicinal field

Silkworm eggs are rich in biologically active compounds and nutrients, making them a subject of increasing interest in both nutritional and biomedical research. They predominantly consist of three major glycoproteins vitellin, 30 kDa protein, and egg-specific protein (ESP) which together account for over 90% of the total protein content. In addition to these, various other proteins such as enzymes, proteases, and their inhibitors have also been identified, reflecting the complexity of the silkworm's metabolic system. Notably, cathepsin B-like acid cysteine proteinase has been detected in the eggs, indicating active proteolytic Nutritionally, silkworm processes. eggs approximately 56% albumin, 19.2% fat, and 7.7% carbohydrates. They are also a good source of vitamins B1 and B2, and contain significant amounts of omega-3 polyunsaturated fatty acids. These fatty acids serve as precursors to prostaglandins, which play an essential role in infant development and maternal health, suggesting potential benefits for nursing mothers.

Additionally, traditional practices attribute several healthpromoting properties to silkworm egg consumption. Some reports suggest that they may enhance male reproductive health by increasing glutathione (GSH) and nitric oxide synthase activity in the corpus cavernosum, potentially alleviating erectile dysfunction. Folk medicine in parts of India even claims that regular consumption may reduce alcohol dependence. Furthermore, silkworm eggs have demonstrated pharmacological potential, being explored for their hepatoprotective, hypolipidemic, and hypoglycemic effects. They are also extensively utilized in genetic and transgenic research due to their biological and developmental characteristics (Mahanta et al., 2023) [14]. After hatching, silkworm egg shells are mostly discarded. Silkworm egg shells is also known for major source of chitin with as high as 74% in chicken eggs. Chitin is one of the most widely used polymers next only to cellulose. Rather than chitin, its deacetylated form chitosan is more widely used for commercial applications. Silkworm egg shell chitosan has antibacterial and anti-fungal activity similar or better than commercially available chitosan. With large availability and limited applications, egg shells can be used as renewable and sustainable sources for chitosan. The protein extract of egg shell is sold as the Humanofort B product in Romania (Naan et al., 2024) [15].

2.2 Bioactive compounds of *Bombyx mori* larva

- Polyphenols: Polyphenols can help manage blood pressure levels and keep your blood vessels healthy and flexible, promoting good circulation. They also help to reduce chronic inflammation risk factor for heart disease.
- **Fibroin protein:** Fibroin is an FDA-approved polymer that has been popularly used in numerous medical applications such as sutures, tissue regeneration, coating devices, and drug delivery systems
- Dietary fibres: Dietary fibres reduce serum LDL, cholesterol and blood pressure preventing heart diseases
- **Flavonoids:** It has an antioxidant property. They help to regulate cellular activity and fight against oxidative stress
- **Vitamins:** They help shore up bones, heal wounds, and booster your immune system. They also convert food into energy, and repair cellular damage (Soumya *et al.*, 2017) [13].

2.3 Potentiality of silkworm larvae in medicinal field

Bombyx mori larvae are highly nutritious, with 100 grams containing 54% protein, 8% fat, 6% fiber, 6% ash, and 390 kcal. Their high protein content makes them a valuable supplement for young animals, including reptiles. They are also used in pharmaceuticals for their anti-diabetic properties and as nutraceuticals in the food industry (Mahanta et al., 2023) [14]. According to the research, silkworm powder prepared from freeze dried method have better efficacy in lowering the blood glucose level due to minimum denaturation of silkworm component during drying process is an important factory for an efficacy. In addition, later than the third day of 5th instar may deteriorate the quality of powder per unit because silkworm develops its silk and it occupies 40 per-cent of silkworm weight (Ryu et al., 2002) [19]. 1-Deoxynojirimycin (DNJ) content in silkworm powder (0.39% to 0.58%) was higher than that in mulberry leaf powder (0.08% to 0.12%). The alphaglucosidase inhibitory activity of silkworm powder was more potent than that of mulberry leaves and green tea. Additionally, the DNJ in silkworm powder remained stable when heated to 121 °C for up to 15 minutes. silkworm powder can be used as supplement for decrease the blood glucose level in type 2 diabetic patients (Ryu et al., 2002) [19]. Silkworms have long been employed in traditional medicine for managing diabetes, particularly in East Asian countries such as China, Korea, and Japan. Recent scientific investigations have validated their hypoglycemic properties, demonstrating a significant blood glucose-lowering effect. Additionally, silkworm powder is known to be easily digested and absorbed by the human body (Mahanta et al., 2023) [14].

A wide array of bioactive compounds has been isolated from silkworm ($Bombyx\ mori$) larvae, including β -N-acetylglucosaminidase, DOPA(3,4-dihydroxyphenylalanine), quinone amine conversion factors, adipokinetic hormone (AKH), insulin-like growth factor II (IGF-II), and the sex pheromone bombykol {(10E, 12Z)-10,12-hexadecadien-1-ol}. In traditional Chinese medicine, male silkworms have been utilized in the formulation of specific medicinal preparations aimed at inducing male infertility (Hai-bo, 1989) [8]. Experimental studies have shown that $B.\ mori$ extracts exert androgen-like effects in rodent models, including rats and mice (Cai $et\ al.$, 1991) [3]. Furthermore,

larval extracts are included as active ingredients in dermatological formulations such as anti-acne creams, which have demonstrated high efficacy and minimal side effects in clinical settings. Notably, proteins such as D66b and human carcinoembryonic antigen-like proteins have also been detected in silkworm larvae (Song & Wang, 1994; Yamanaka *et al.*, 1996) [21, 28], underscoring their potential biomedical significance.

Silkworm haemolymph contains a high concentration of essential amino acids, notably glutamine, histidine, lysine, serine, and glycine. The total amino acid content has been found to correlate with the mass of the silk glands, suggesting a metabolic link between silk production and amino acid profiles. Additionally, dehydrated larvae of silkworms that succumbed to white muscardine disease have been traditionally used for the treatment of ailments such as abdominal cramps, bloating, and related gastrointestinal disorders. The intestine of silkworm larvae is used to produce a unique kind of thread that is utilized in surgery. The intestine of silkworms and their glands are used to prepare the surgical gut. The braided scaffolds revealed higher tensile strength and strain at break values in the case of Samia cynthia ricini and Bombyx mori materials with a potential application in tissue engineering (Naan et al., 2024) [15].

Interleukin-3 produced from the silkworm is reported to be biologically identical to IL-3 produced from mammalian cells (Datta, 1994) ^[6]. A lutein binding protein has also been purified from fifth instar larvae (Jouni & Wells, 1996) ^[10]. Pretreatment with boiled mature silkworm larval powder (BMSP) may have a protective effect against acute liver injury by inhibiting necrosis and inflammatory response in DEN-treated mice Cho *et al.* (2016) ^[6]. Steamed and freezedried Mature Silkworm larval Powder (SMSP) exerted protective effects in ethanol-induced gastritis via the regulation of anti-oxidative and pro-inflammatory signaling pathway, suggesting SMSP could be anticipating remedy for the treatment of ethanol-induced gastric injury.

2.4 Potentiality of silkworm pupae in medicinal field

Silkworm pupae are recognized for their rich and diverse nutritional profile, making them a valuable functional food source. They primarily consist of 50-60% protein, 25-35% fat, and 8-10% carbohydrates. In addition to these macronutrients, they also contain significant amounts of vitamins, minerals, polyphenolic compounds, and other bioactive substances. Among silkworm species, *Bombyx mori* is particularly noted for its high protein content, which constitutes the majority of its dry weight.

The biologically active peptides found in pupae, composed of multiple amino acids, are involved in various physiological processes and contribute to their therapeutic potential. Silkworm pupae are especially rich in vitamins, including A, B-complex (B1, B2, B3, B5, B7, B9, B12), C, and E. Additionally, they contain phospholipids and several forms of tocopherols, such as α -, β -, γ -, and σ -tocopherol, as well as γ -tocotrienol, all of which contribute to their antioxidant properties.

Mineral content in pupae is equally impressive, with up to 25 distinct minerals identified. Notably, they are a good source of phosphorus, iron, calcium, zinc, manganese, and chromium—often in higher concentrations than those found in chicken eggs. These minerals play crucial roles in numerous physiological functions.

Oil ranks second only to protein in abundance within the pupae and is associated with a range of pharmacological effects. Regular consumption of silkworm pupae has been linked to potential benefits in preventing non-communicable diseases such as hypertension, cardiovascular disorders, and stroke. Their bioactive components are known for exerting multiple therapeutic effects, supporting their relevance in both nutrition and medicine (Mahanta *et al.*, 2023) [14].

Chitin, a component of pupal skin, is commonly utilized in post-operative therapies such conchotomy, deviatory, and polypectomy due to its ease of administration, reduced hemophase, improved pain management, and faster wound healing. Chitin is an effective anti-microbial agent against Staphylococcus aureus, Klebsiella pneumoniae, Aspergillus niger, and Trichophyton equinum. It also acts as a buffer against acids and can be used as a food additive to reduce carcinogenicity. Chitin can be utilized as an immunoadjuvant, bacteriostatic, fungistatic, and anti-sordes agent to prevent carcinogenic microorganisms from teeth, as well as a biocompatible barrier to control bleeding during major surgeries. Silkworm pupa is mostly used as animal feed and fertilizer in South East Asia and are also used as food insects. Asian nations either consume it directly as food or in the form of powder or oil.

Serrapeptidase, a protein derived from silkworms, is widely used in pharmaceuticals for its anti-inflammatory and antitumor properties. It is also applied in dental procedures such as fillings, cleanings, and tooth extractions. Additionally, artificial fibers and membranes created from pupal proteins show promising medical applications. Silkworm pupae are rich in n-3 omega fatty acids, with α-linolenic acid as a primary component, making them a high-quality protein source and an essential nutrient (Naan et al., 2024) [15]. The active components of silkworm pupae serve various pharmacological purposes and exhibit therapeutic effects on numerous disorders. These potent pharmacological properties have been validated through both in vivo and in vitro studies.

Silkworm pupae demonstrate a broad spectrum of therapeutic properties, such as antimicrobial, anticancer, antiapoptotic, antioxidant, blood pressure-lowering, immune system-modulating, lipid and glucose metabolismregulating, as well as liver-protective activities. In terms of cardiovascular health, silkworm protein hydrolysates have shown significant antihypertensive properties. Oral doses of 5, 20, and 60 mg/kg led to a dose-dependent reduction in systolic blood pressure (SBP) within 1.5 hours. Prolonged treatment with 80 mg/kg for four weeks resulted in a 25mmHg reduction in SBP, an effect comparable to standard captopril therapy. Importantly, no changes were observed in normotensive rats, indicating selective action in hypertensive models. The mechanism underlying this effect is linked to the inhibition of angiotensin-I-converting enzyme (ACE), which reduces the production of angiotensin II, thereby lowering vascular resistance and blood pressure. These findings were reported by Wattanathorn et al. (2012) [27] and Wang et al. (2014) [26]. The use of a baculovirussilkworm pupae system to express the VP60 protein, which self-assembled into virus-like particles (VLPs) resembling Rabbit Hemorrhagic Disease Virus (RHDV). The system yielded high expression levels, reaching up to 107 Hemagglutination Units (HAU) per pupa. A single intramuscular dose of 10⁴ HAU provided full protection in rabbits against RHDV for at least 180 days, and up to 360

days when formulated with Freund's complete adjuvant. These findings support the use of silkworm pupae as an efficient and cost-effective platform for producing VLP-based vaccines.

This effectiveness is likely due to the high protein expression capacity of silkworm larvae and pupae estimated to be 50-1000 times higher than insect cell lines. Given that silkworm pupae are inexpensive by-products of the silk industry, especially in countries like China, their use as bioreactors offers an economical solution for large-scale vaccine production. This effectiveness is likely due to the high protein expression capacity of silkworm larvae and pupae estimated to be 50-1000 times higher than insect cell lines. Given that silkworm pupae are inexpensive by-products of the silk industry, especially in countries like China, their use as bio-reactors offers an economical solution for large-scale vaccine production (Zheng *et al.*, 2016) [31].

2.5 Potentiality of silkworm moth in medicinal field

The silk moth undergoes a non-feeding stage before emerging from its cocoon to mate and lay eggs for the next generation. Moths not used for seed production, along with the dead moths, are usually discarded in a pit and left to decompose without any specific purpose. Adult moths are used in making wine and medicines. The Shaanxi Sericultural Technology Station's male silkworm moth wine is the most well-known. Impotence, irregular menstruation, and menopausal symptoms can all be treated with this drink (Naan et al., 2024) [15]. Male moths are used in Chinese medicine to treat sterility. A unique lipophilic peptide (VAP peptide) has been isolated from the heads of male moths. It acts as a bioactive material for inducing egg diapause (Singh and Jayasomu, 2002) [20]. The butterflies can also release cellular cytochrome C for medicinal application, uric acid or hormones, and sex messengers of the PTTH (hormone of the central nervous system) and DH type sexual hormone (Naan et al., 2024) [15]. Female silkworm moth powder significantly enhanced all immunological indexes in the immunosuppressed mice, improving non-specific immune function, humoral immunity, and cellular immunity. This might be due to the female silkworm moth has high nutritional value that there was rich protein, amino acids, trace element and large amounts of unsaturated fatty acids. The female silkworm moth also contained steroid substances such as progesterone and estradiol (Gu et al., 2010) [7]. The exploration of silkworm moths as a resource for pharmaceuticals, nutraceuticals, and functional foods is expanding, reflecting a shift toward sustainable and circular utilization of sericultural by-products. In addition to their biological activities, silkworm moth derivatives are being considered for potential roles in anti-aging, neuroprotective, and antioxidant therapies (Chen et al., 2022) [4].

The beneficial effects are attributed to the rich composition of proteins, essential amino acids, trace elements, and unsaturated fatty acids. Moreover, female moths contain steroid hormones such as progesterone and estradiol, which may contribute to hormonal regulation and immune system stimulation (Zhang *et al.*, 2011; Liu *et al.*, 2016) ^[29, 13].

2.6 Potentiality of cocoon in medicinal field

The silkworm cocoon (SC), both as a traditional Chinese medicine and as the raw material for biocompatible carriers, has been extensively used in the medical and biomedical fields. The primary chemical components of SC include silk fibroin (SF), silk sericin (SS), and other flavonoid-like bioactive compounds demonstrating various biological effects (Kundu et al., 2012) [12]. These include hypoglycemic, cardioprotective, hypolipidemic, inflammatory, antioxidant, Tissue engineering, delivery systems and antimicrobial actions, which highlight its potential therapeutic benefits (Tian et al., 2024) [23]. Recent studies highlight that SC also contains flavonoid-like bioactive compounds with various health-promoting effects. include These antioxidant, anti-inflammatory, hypoglycemic, hypolipidemic, and cardioprotective activities, making it a potential candidate for preventing or managing chronic diseases such as diabetes, cardiovascular disorders, and metabolic syndrome (Tian et~al., 2024; Aramwit et~al., 2010) [23, 1]. Notably, cocoon-derived compounds show promising action in tissue engineering, drug delivery, and antimicrobial therapies, further expanding their relevance in regenerative medicine and pharmaceuticals (Altman et al., 2003; Rockwood et al., 2011) [2, 18]. Cocoon powder, derived from whole or degummed cocoons, is widely applied in wound dressings, especially for third-degree burns, due to its high moisture retention, antibacterial activity, and healing-promoting properties (Vepari & Kaplan, 2007) [25]. Silk proteins, particularly sericin, are integrated into various cosmetic formulations such as silk lotions, night creams, baby creams, hand creams, and even silk-based toothpastes. These formulations benefit from sericin's unique ability to bind water, acting as a natural moisturizer, and to protect against ultraviolet (UV) radiation damage (Zhaorigetu et al., 2003; Kato et al., 1998) [30, 11].

Additionally, sericin-enriched silk extracts are included in nutraceuticals and health drinks, owing to their antioxidant

and anti-aging properties. In biomedical engineering, silkworm silk fibers have long been used in surgical sutures, and more recently, in biodegradable scaffolds for skin, bone, and vascular tissue regeneration (Jin et al., 2005) ^[9]. Silk sericin has shown remarkable properties in cosmeceuticals it promotes skin hydration, acts as an anti-wrinkle and anti-irritant agent, and absorbs UV rays, protecting skin from photodamage (Padamwar & Pawar, 2004) ^[16]. Its ability to make hair soft and manageable adds to its value in haircare products. Furthermore, when sericin and fibroin are chemically modified, such as through sulfonation, they can be transformed into biomaterials with anticoagulant properties, opening avenues for blood-contact medical devices (Naan *et al.*, 2024; *Um* IC et al., 2001) ^[15, 24].

Cocoon powder is used as a wound dressing for third-degree burns. Silk proteins are utilised in a range of cosmetic goods, including silk lotion, silk cream, silk night cream, silk hand cream, silk baby cream, and silk toothpaste, as research has shown that they may retain moisture and prevent UV radiation. Silk extracts are also used in health drinks. In biomedical applications, silkworm silk fibers have been the predominant source of silk-like material, especially for sutures. A combination of both fibroin and subsequently, the wound dressing along with sericin. In addition to being able to shape hair by making it soft and flexible, the silk protein sericin has the potential to be used as a skin moisturizer, anti-irritant, anti-wrinkle, and sun protector due to its saturation, revitalizing, and UV ray absorption qualities. By sulfonating sericin and fibroin, silk protein can be transformed into a biomaterial with anticoagulant qualities (Naan et al., 2024) [15].

Silkworm pupae demonstrate a broad spectrum of therapeutic properties, such as antimicrobial, anticancer, antiapoptotic, antioxidant, immune system-modulating, lipid and glucose metabolism-regulating, as well as liver-protective activities

Antitumor	Protein hydrolysates	Silkworm-derived compounds have demonstrated notable anticancer potential by suppressing the proliferation of human gastric cancer cell line SGC-7901.
	Protein hydrolysates	In MGC-803 gastric cancer cells, treatment induces marked structural alterations in
		intracellular organelles, resulting in vacuolization and eventual cell rupture
	Protein extracts	Additionally, in MCF-7 breast cancer cells, a significant reduction in pro-inflammatory
		cytokines such as IL-6, IL-1, and TNF-α has been observed, along with decreased levels of
		cellular proteins and nucleic acids.
Antioxidant	Protein hydrolysates	Enhances ABTS radical scavenging capacity, aiding in the prevention of disorders linked to
		oxidative stress.
	Protein hydrolysates	In HepG2 liver cells, it exhibits increased reactive oxygen species (ROS) suppression and
		upregulation of superoxide dismutase (SOD) expression.
	Polyphenols	Exhibited significant efficiency in scavenging reactive oxygen species (ROS).
Antibacterial	Chitin and chitosan	Exhibits stronger antifungal activity compared to commercially available chitosan and serves
		as a sustainable alternative source.
	Peptides	Peptide sequences with high potential bioactivity were identified using Peptide Ranker and
		the CAMP database, receiving top scores.
	Oil	Shows potent antibacterial effects against gram-positive bacteria, including <i>Bacillus subtilis</i>
		and Staphylococcus aureus.
Antiapoptotic	Silkworm Protein 30Kc6	The 30Kc6 protein inhibited oxidized LDL-induced apoptosis in HUVEC cells by
		suppressing MAPK signaling pathways, indicating its potential role in the prevention and
		treatment of cardiovascular diseases.
	Silkworm haemolymph	Silkworm haemolymph may interfere with the apoptosis pathway triggered by baculovirus
		infection or enhance the expression of anti-apoptotic viral genes like p35 in baculovirus-
		infected insect cells (Sf9).
	Recombinant 30 K	In both human (HeLa) and insect (Sf9) cells, recombinant 30K proteins inhibit apoptosis
	protein	induced by viral infections or chemical agents.
Blood pressure reduction	Protein hydrolysates	Silkworm protein hydrolysates exhibit inhibitory activity against angiotensin I-converting
		enzyme (ACE).
Antiageing	Oils and sericin	Silkworm-derived oils and sericin demonstrate in vitro tyrosinase inhibition and antioxidant
		properties, supporting their use in cosmetic formulations for skin whitening.

(Mahanta et al., 2023) [14]

3. Conclusion

Entomotherapy, the use of insects in healing practices, is a part of traditional medicine in many regions of the world. These practices are often embedded within broader cultural beliefs that include rituals, symbolic objects like amulets and charms, and actions such as gestures or transferences intended to restore health and spiritual balance. In this context, insects are not only valued for their physical properties but also revered for their supposed mystical or magical roles in healing. Silkworms (Bombyx mori), long recognized for their economic value in silk production, have recently attracted attention for their potential therapeutic applications. Compounds derived from silkworms—such as proteins, enzymes, and sericin—have shown a variety of beneficial biological properties, including antioxidant, antimicrobial. anti-inflammatory, and wound-healing activities. These properties make silkworms a promising candidate for use in the development of medicinal products and health-promoting supplements. The application of silkworm-derived substances in healthcare reflects a new frontier in natural product research. As scientists continue to explore and validate the bioactive compounds found in silkworms, there is great potential for creating new, sustainable, and affordable medical treatments. These could range from topical formulations for skin repair to orally administered supplements for metabolic disorders.

In summary, silkworms offer a unique opportunity to bridge traditional knowledge with modern therapeutic innovations. By advancing research in this area, and ensuring scientific rigor in the development of silkworm-based remedies, we can unlock new possibilities in healthcare that are both effective and environmentally sustainable.

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