***Review Article***

**THERAPEUTIC POTENTIAL OF THE SILKWORM (*Bombyx mori* L.):**

**A BIOMEDICAL PERSPECTIVE**

**ABSTRACT**

Silkworms (*Bombyx mori* L.), historically valued for silk production, are now gaining recognition as a source of diverse bioactive compounds with significant medicinal applications. This review synthesizes current knowledge on the pharmacological and therapeutic potential of silkworm derivatives - eggs, larvae, pupae, cocoons and moths highlighting their emerging role in modern biomedicine. Silkworm eggs are rich in glycoproteins and essential fatty acids, contributing to reproductive health, liver protection and embryonic development. Larvae, particularly during the fifth instar, exhibit potent antihyperglycemic activity due to high levels of 1-deoxynojirimycin, while their hemolymph contains antimicrobial peptides with immunomodulatory effects. Pupal extracts are rich in essential fatty acids, bioactive peptides, vitamins and chitin derivatives, offering antioxidant, hepatoprotective, neuroprotective, antihypertensive and anticancer benefits. Cocoon proteins, notably fibroin and sericin, show promise in wound healing, drug delivery and tissue regeneration. Silk moths, traditionally discarded post-mating, are now utilized in therapeutic formulations such as medicinal wines and natural oils. Together, these findings underscore the immense potential of *B. mori* as a valuable resource for functional foods, pharmaceuticals and cosmeceuticals, encouraging further research and sustainable utilization in human health applications.

*Keywords: Bombyx mori; medicinal applications; bioactive compounds; silkworm pupae; therapeutic*

**1. INTRODUCTION**

Human beings have used animal resources for therapeutic purposes since ancient times, creating remedies from animal body parts, metabolic products and materials like nests and cocoons. Insects and their products have been integral to medical systems across various cultures, directly and indirectly, for thousands of years, providing valuable natural products like honey, bee-wax, propolis, pollen, royal jelly and silk. Despite their historical significance, insects have been overlooked in modern medicine. Evaluating their use from "Entomophagy to Entomotherapy" highlights their potential in contemporary healthcare. In January 2004, the FDA approved maggots as a prescription-only medical device for debriding non-healing necrotic wounds and various ulcers (Rajkhowa *et al.,* 2016).

The world consists of most diverse group of organisms of which, insects comprise 80 per cent with one million species across 30 orders. predominantly Coleoptera, Diptera, Hymenoptera and Lepidoptera. Among them, more than 2,100 species are edible. Insects are a largely unexplored source of potentially useful compounds for modern medicine, offering immunological, analgesic, antibacterial, diuretic, aesthetic and anti-rheumatic properties (Rajkhowa *et al.,* 2016).

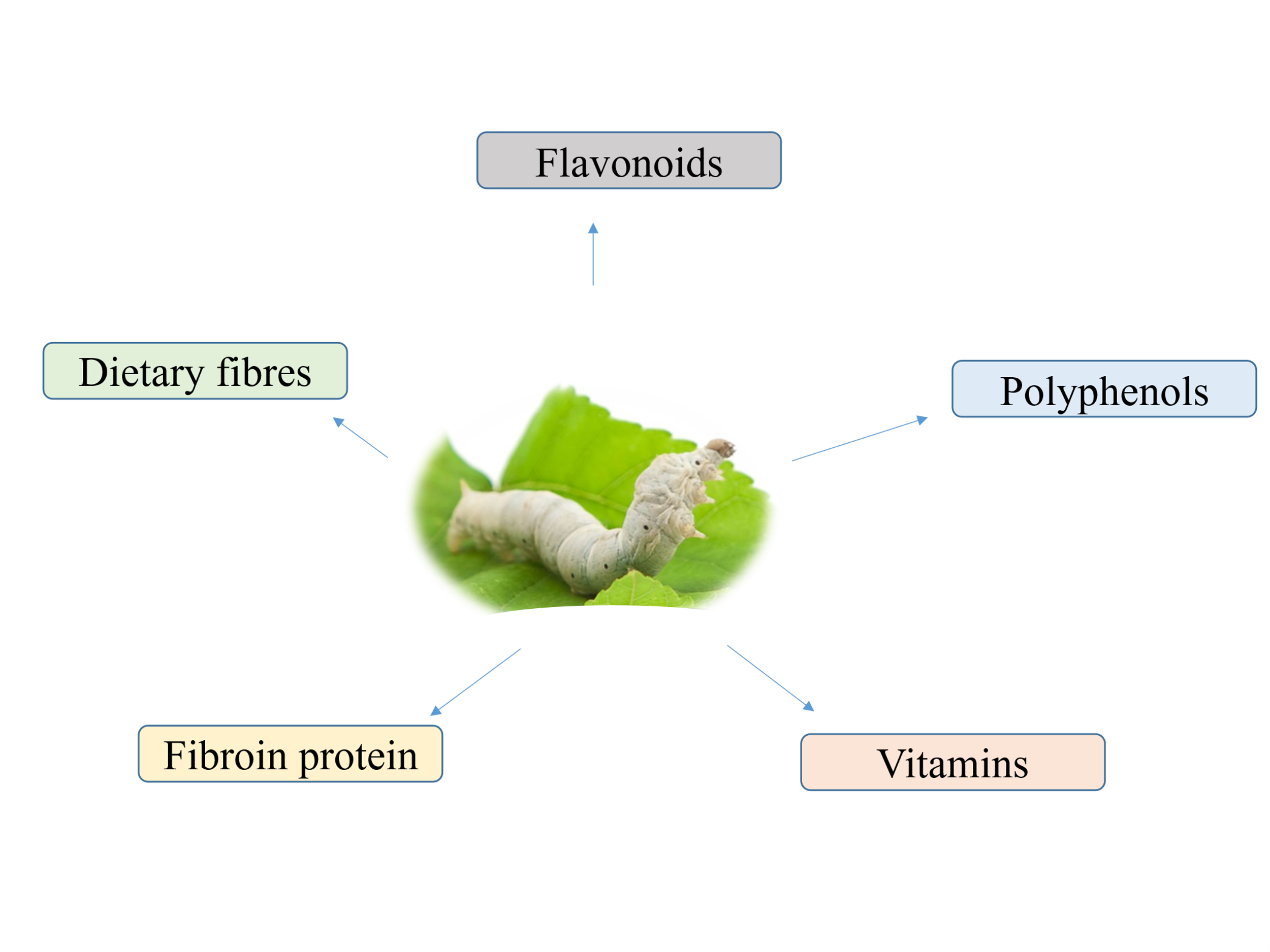
Silkworm (*Bombyx mori* L.) is a well-known and beneficial lepidopteran insect, that produces the sleek and sensuous silk fiber, often considered as “Queen of textiles”. The traditional Sericulture shifted from cocoon production to functional sericulture, in which the dress-centred textile business was moved into the advanced bio-industry emphasizing a diverse utility of sericulture products. One of such a big movement for new application of sericulture products is utilization of silkworm itself from the source of cocoon production to food stuff, medical sources and biotech applications. Example for food stuff is natural colouring extracted from silkworm excreta, for medical sources, pupal oil which contains omega-3 fatty acid and it raises good cholesterol level and for biotech applications, cocoon scaffolds for wound healing etc. They have been used in Chinese traditional medicine for at least three thousand years (Soumya *et al.,* 2017).

In sericulture, apart from silk, there are many other byproducts and waste products obtained at different stages of silkworm rearing. Eggs, larvae, pupae and feces find their use in pharmaceuticals, cosmetics and the paper and leather industry (Anon., 1996). In China, sericulture products are exploited considerably. Silk is made up of mainly two proteins, fibroin and sericin. Fibroin is secreted in the posterior part of the silk gland while sericin is from the middle part (Qader & Haque, 1996). Fibroin consists of many fine fibrillae bound together by sericin (Taraporewala & Shah,1995). Silk fibroin is reported to have a high proportion of the amino acids, glycine, alanine and tyrosine. The mulberry silkworm, *Bombyx mori* is reviewed in this paper as a potential medicinal insect providing a variety of products with wide applications (Majumder, 1997; Raju, 1996).

**Table 1: Nutrient content of *Bombyx mori* L. in larval and pupal stages**

|  |  |  |
| --- | --- | --- |
| **Parameters (%)** | **larvae** | **pupa** |
| Crude protein content | 20.79±2.22 | 21.59±2.91 |
| Ash content | 6.34±0.84 | 5.50±0.51 |
| Moisture content | 7.92±0.98 | 8.26±0.66 |
| Fat content | 17.57±1.51 | 19.90±1.80 |
| Crude fibre content | 6.46±0.21 | 6.30±0.12 |
| Carbohydrate content | 40.93±3.20 | 38.47±4.24 |
| **Parameters mg/100g** |  |  |
| Na | 10.52±1.31 | 11.66±1.22 |
| Ca | 20.31±2.78 | 26.65±3.49 |
| Mg | 31.24±3.61 | 27.53±3.76 |
| Zn | 35.63±4.98 | 37.50±4.64 |
| Fe | 5.31±0.72 | 6.33±0.81 |

*Bombyx mori* L. have nutrient contents such as crude protein content, ash content, moisture content, fat content, crude fibre content, carbohydrate content and minerals Na, Ca, Mg, Zn and Fe. Pupa contains majority rich nutrient content compare to larva (Omotoso, 2015).



**Fig. 1: Bioactive compounds of *Bombyx mori* larva**

**Fig. 1: Bioactive compounds of *Bombyx mori* larva**

**1.1 Flavonoids:** Because of their antioxidant activity they help to regulate cellular activity and fight against oxidative stress (Cho *et al.*, 2016).

**1.2 Polyphenols:** They 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.

**1.3 Vitamins:** They help shore up bones, heal wounds and booster your immune system. They also convert food into energy and repair cellular damage.

**1.4 Fibroin protein:** Fibroin is a FDA-approved polymer that has been popularly used in numerous medical applications such as sutures, tissue regeneration, coating devices and drug delivery systems

**1.5 Dietary fibres:** They reduce serum LDL, cholesterol and blood pressure preventing heart diseases.

**2. EXPLORING THE BIOMEDICAL SIGNIFICANCE OF SILKWORM LIFE STAGES**

**2.1 Usage of *Bombyx mori* L*.* egg in medicinal field**

The silkworm eggs are shown to contain chorionins, cysteine proteinase (Xia *et al.*, 1989). The silkworm eggs contain three main types of glycoproteins namely vitellin, 30 kDa protein and egg-specific protein (ESP) which account for more than 90% of total (Maki and Yamashita, 1997). Silkworms produce numerous 30 kDa low-molecular-weight proteins, which account for 35% of the total soluble protein in the egg (Zhu *et al.*, 1986). More than thirty genes coding for 30 kDa proteins have been annotated from *Bombyx* genome. Silkworm eggs can be a potential nutritious food for nursing mothers due to presence of omega-3 polyunsaturated fatty acids. These unsaturated fatty acids are precursors of prostaglandins which has significant role in infants’ nutrition. Consumption of silkworm eggs increases the male sexual power and decreases erectile dysfunction as it increases GSH and nitric oxide synthetase levels in the corpus cavernosum. The silkworm eggs contain high amount of protein and vitamins B1, B2. In Romania food industry silkworm eggs are used as Human fort B product (Buhroo *et al.,* 2018). Silkworm eggs are said to cause heavy drinkers to stop drinking alcohol completely if they eat them (Popular tradition, India). Silkworm eggs are used as embryo inducer, hepatic protector, hypolipidic and hypoglycemic. The silkworm eggs are also used extensively in transgenic studies (Joy & Gopinathan, 1994).

**2.2 Usage of *Bombyx mori* L*.* larva in medicinal field**

The hemolymph of silkworms is rich in glutamine, histadine, lysine, serine and glycine. The amino acid content is proportional to the weight of the silk gland. The amino acids weigh up to 140 mg/gland (Chitra & Sridhara, 1972). Three novel antibacterial lebocin peptides have also been reported from the hemolymph of silkworm immunized with *Escherchia coli* (Hara & Yamakawa, 1995; Abraham *et al.,* 1995). According to research findings, silkworms exhibit the most significant ability to reduce blood glucose levels when processed on the third day of their fifth instar stage, using a freeze-drying technique and consumed in powdered form, as compared to other preparation methods (Ryu *et al.*, 1997). This pronounced antidiabetic effect is primarily attributed to the presence of 1-deoxynojirimycin (DNJ), a compound they accumulate by feeding on mulberry foliage. DNJ levels vary considerably throughout the silkworm’s metamorphic development. Reverse-phase high-performance liquid chromatography (RP-HPLC) analysis revealed that larvae on the third day of the fifth instar contain the peak concentration of DNJ, reaching approximately 1512.46 mg per individual (Chen *et al.*, 2014). Traditionally, in East Asian countries such as China, Korea and Japan, silkworms have been utilized as a natural remedy for diabetes and contemporary research supports their blood sugar-lowering efficacy. Silkworm powder is easily digested and absorbed by the human body and may also support healthy gastrointestinal function (Ryu *et al.*, 1997). Dehydrated larvae that succumbed to white muscardine disease have also been used to manage symptoms such as abdominal cramps and bloating (Chen *et al.*, 2002). It is believed that silkworms nourished on mulberry leaves offer superior health-promoting properties compared to other varieties. Additionally, due to their high sensitivity to external chemicals including pesticides, pharmaceuticals and toxic metals, *Bombyx mori* serves as a valuable bioindicator for health risk assessment and environmental pollution studies (Abdelli *et al.*, 2018). Silkworm larval powder, prepared through boiling and freeze-drying of mature larvae, contains bioactive compounds such as proteins, peptides and immune-regulating molecules that exhibit notable liver-protective and anti-inflammatory effects. Its administration has been shown to lower levels of liver enzymes, reduce tissue damage and suppress the production of pro-inflammatory cytokines in experimental models of liver toxicity induced by diethyl nitrosamine. These findings highlight the potential of mature silkworm larval powder as a functional food ingredient with both therapeutic and preventive value in the management of liver-related disorders (Cho *et al.*, 2016). Steamed and freeze-dried mature silkworm larval powder demonstrates promising bioactive and therapeutic potential against chronic alcohol-induced fatty liver and liver fibrosis. Supplementation with this silkworm powder has been shown to regulate lipid metabolism by influencing key gene expressions such as sirtuin 1, adenosine monophosphate-activated protein kinase and acetyl-CoA carboxylase, thereby reducing fat accumulation and improving the ratio of low-density lipoprotein to high-density lipoprotein. Furthermore, it alleviates liver fibrosis by downregulating pro-collagen type 1 and alpha-smooth muscle actin, while enhancing antioxidant defenses and reducing hepatic levels of malondialdehyde and tumor necrosis factor-alpha. These findings support the use of silkworm larval powder as a functional dietary intervention for the prevention and management of alcoholic fatty liver disease (Hong *et al.*, 2018).

**2.3 Usage of silkworm cocoon in medicinal field**

In their final larval stage, silkworms spin a protective shell known as a cocoon to transition into an immobile pupal phase. The cocoon primarily comprises fibroin (about 75.38 %), with smaller amounts of sericin (17-25 %) and minor traces of other elements like pigments, waxes, sugars and plant-derived compounds (approximately, 1-4 %). Beyond their use in sericulture, cocoons have also found applications in the cosmetics sector. Traditionally, the cocoon is sectioned and immersed in warm water, then gently rubbed onto the face by hand, as sericin is known for its hydrating properties (Biganeh *et al.,* 2022).

Sericin, a natural silk protein obtained from the cocoon of *Bombyx mori*, exhibits significant wound healing properties by increasing epidermal thickness and vascularization, while reducing inflammation, edema, oxidative stress and tissue damage. These findings highlight its potential for use in biomedical applications, especially in skin repair and regeneration (Ersel *et al.*, 2016). Silkworm cocoons contain valuable proteins like fibroin and sericin. When processed into cocoon scaffolding, they show improved water absorption and retention. Compared to untreated samples, tissues treated with cocoon scaffolds showed increased blood vessel formation. Among the treated groups, scaffolds combined with platelet-rich components showed the most effective wound healing due to the presence of platelets. Overall, cocoon scaffolding is a promising natural material for use in wound care and tissue regeneration (Liu *et al.*, 2017).

From a medical standpoint, silkworm silk fibers have long been a preferred source for silk-based biomaterials, especially in suturing. These fibers have demonstrated versatility and efficacy in numerous therapeutic contexts. (Tsubouchi, 1999a) developed a silk fibroin-based wound dressing that promotes rapid healing and can be removed without damaging the regenerated skin. This wound covering formed an amorphous fibrin layer ranging from 10 to 100 μm in thickness, maintaining moisture content between 3–16%. Another wound dressing was developed using a blend of fibroin and sericin (Tsubouchi, 1999b).

Cocoon-derived powder is incorporated into various skincare formulations, such as facial cleansers and masks. It is also applied as a wound covering for severe (third-degree) burns. Silk proteins have been employed in an array of personal care products like silk-infused lotions, creams (day and night), hand creams, baby creams and even toothpaste due to their proven ability to lock in moisture and protect against ultraviolet rays. Additionally, silk extracts are included in functional beverages aimed at promoting health (Nazim *et al.*, 2017).

Sericin also possesses potential as a hair conditioning agent, making strands soft and manageable. Furthermore, it offers skin benefits, functioning as a moisturizer, anti-irritant, anti-aging agent and sunscreen due to its hydrating, rejuvenating and UV-blocking properties (Kumaresan and Sinha, 2007). Through sulfonation, both fibroin and sericin can be converted into materials with blood-thinning (anticoagulant) abilities (Kato *et al.*, 1998). The antioxidant nature of silk protein was first confirmed by (Tamada, 1997), who found that sericin suppressed lipid oxidation in laboratory tests. It was also shown to inhibit tyrosinase activity an enzyme linked to skin pigmentation making sericin a promising natural additive for both food and skincare.

Sericin shows strong affinity to keratin, the protein found in human hair and skin. Biomedical research has also expanded the applications of fibroin. Silk powder processed to retain its natural aesthetic characteristics has been shown to absorb and release moisture based on surrounding humidity and temperature ideal for inclusion in pressed powders, blushes, eye shadows, lipsticks and nail polishes due to its ultra-fine texture (approximately 11.3 μm in size). Recently, both sericin and fibroin have been evaluated for their role in drug delivery systems. (Wu *et al.*, 1996) investigated the properties and potential of fibroin-based membranes for protecting wounds, which are believed to support effective tissue repair.

Matta *et al.* (2004) reported that fibroin hydrogels, either infused with 30% glycerol or formed from a 2% (w/v) aqueous silk fibroin solution stored at 4 °C, can act as scaffolds to assist bone regeneration. Both lab and animal studies are underway to evaluate fibrin's suitability in sustained-release oral medications. Interestingly, sulfated silk fibroin exhibited anti-HIV-1 properties in vitro by completely blocking virus binding to CD4+ cells at a concentration of 100 µg/mL.

**2.4 Usage of silkworm pupa in medicinal field**

Silkworm pupae (SP), a by-product of sericulture, have garnered increasing attention for their remarkable nutritional and medicinal potential. Rich in essential fatty acids (EFAs), bioactive peptides, vitamins and minerals, SP are now recognized for their multiple therapeutic functions, ranging from cardiovascular protection to neuroprotection.

The oil extracted from SP is particularly rich in polyunsaturated fatty acids (PUFAs), including alpha-linolenic acid and linoleic acid, which are essential in human diets due to the body’s inability to synthesize them. These EFAs play crucial roles in preventing and managing various diseases such as cardiovascular disorders, inflammatory conditions and metabolic syndromes. Additionally, the high levels of unsaturated fatty acids in SP contribute to lowering blood pressure, improving vascular health and enhancing lipid metabolism (Hăbeanu *et al.*, 2023; Zhou *et al.,* 2022). Fatty acids compositions of pupa are shown in table 2.

According to researchers, bioactive compounds derived from SP exhibit significant antioxidant, anti-inflammatory, anti-apoptotic, anticancer, hepatoprotective and neuroprotective activities. SP oil enriched with sodium salts has been shown to improve blood circulation and aid in treating vascular complications (Kim *et al.*, 2020). The presence of long-chain unsaturated fatty acids such as oleic, linoleic and alpha-linolenic acids further contributes to antibacterial properties, particularly effective against Gram-positive bacteria (Saviane *et al.*, 2021).

Live pupae have also been used as a biological medium for synthesizing antibacterial peptides in vivo (Koul *et al.,* 1994) and live healthy pupae are utilized in the preparation of antibacterial proteins (Lakshminarayan & Rao, 1970; Rajiv & Vijayakumar, 1996). A therapeutic tar derived from pupae has exhibited superior bactericidal and antihistaminic activity compared to plant sources (Kanebo Ltd., 1980). Additionally, pupal oil has traditional applications in treating liver and blood disorders (Koul *et al.*, 1994).

SP oil has been found effective in ameliorating liver injury, particularly in acetaminophen-induced hepatotoxicity models, by reducing oxidative stress and inflammation (Zhou *et al.,* 2022). Similarly, dietary SP oil intake has been associated with gastric ulcer reduction and improved gastric pH regulation (Kim *et al.*, 2020).

Neurologically, SP has shown promise in managing neurodegenerative diseases. In an experimental model of Alzheimer’s disease, Wattanathorn *et al.* (2012) demonstrated that SP significantly improved memory performance and preserved neuronal density in the hippocampus. These effects were mediated by increased cholinergic activity and decreased oxidative stress, as evidenced by reduced malondialdehyde levels. Additionally, peptides from SP can inhibit nitric oxide production in immune cells, enhancing their role in controlling neuroinflammation and oxidative damage (Yoon *et al.*, 2019).

From an antihypertensive perspective, peptide hydrolysates of SP proteins (MW <5000 Da) have been shown to inhibit angiotensin-I-converting enzyme (ACE). Oral administration of these hydrolysates to hypertensive rats resulted in significant, dose-dependent reductions in systolic blood pressure, with comparable efficacy to captopril and no observed toxicity indicating strong potential for use in hypertension management (Wang *et al.*, 2014).

SP has also demonstrated anticancer potential. Protein hydrolysates obtained from SP inhibited the proliferation of MGC-803 gastric cancer cells in vitro. The mechanism involved cell cycle arrest at G0/G1, cytoskeletal disintegration and apoptosis induction, suggesting SP peptides may function as natural chemopreventive agents (Li *et al.*, 2022).

Chitin, accounting for approximately 4% of the pupal dry weight and its derivatives such as chitosan, chitin sulfate and sodium carboxymethyl chitin, are obtained from the pupal skin. These biopolymers have proven useful in wound dressing, controlled drug release systems and contact lens materials and can enhance the solubility and delivery of poorly bioavailable drugs (Katti *et al.*, 1996; Singh & Jayasomu, 2002).

Moreover, SP hydrolysates have demonstrated antigenotoxic effects, potentially due to the presence of polyphenols and fatty acids like linoleic acid. SP are also rich in essential vitamins (A, B-complex, C, E) and minerals (iron, calcium, selenium, zinc), which contribute to their nutritional and therapeutic value (Kumar *et al.*, 2015; Wu *et al.*, 2021).

Although some anti-nutritional factors such as phytates, tannins and saponins have been detected in SP, their concentrations remain within safe limits for human consumption. However, researchers have noted that SP may cause allergic reactions in sensitive individuals, warranting further investigation before their large-scale incorporation into food or medicinal products (Wu *et al.*, 2021; Zhou *et al.*, 2022).

**Table 2**: Centesimal Composition of Fatty Acids in Total Lipid Extracts of Silkworm Pupae (*Bombyx mori*)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Fatty Acids (%)** | **Male** | **Female** | **Total** | **Reference** |
| C16:0 (palmitic) | 28.60 | 22.80 | - | Nakasone and Ito, 1967 |
| 24.90 | 19.50 | Kotake-Nara *et al.*, 2002 |
| - | - | 21.3–28.30 | Pereira *et al.*, 2003 |
| 24.20 | Tomotake *et al.* 2010 |
| 23.18 | Kumar *et al.*, 2021 |
| 23.18 | Zhou *et al.,* 2022 |
| C16:1n-7 (palmitoleic) | 3.10 | 1.80 | - | Nakasone and Ito, 1967 |
| 0.80 | 0.60 | Kotake-Nara *et al.*, 2002 |
| - | - | 0.60–0.70 | Pereira *et al.*, 2003 |
| 1.70 | Tomotake *et al.* 2010 |
| 1.07 | Kumar *et al.*, 2021 |
| 1.07 | Zhou *et al.,* 2022 |
| C18:0 (stearic) | 2.60 | 4.30 | - | Nakasone and Ito, 1967 |
| 5.40 | 6.30 | Kotake-Nara *et al.*, 2002 |
| - | - | 5.5–9.20 | Pereira *et al.*, 2003 |
| 4.50 | Tomotake *et al.* 2010 |
| 4.69 | Kumar *et al.*, 2021 |
| 4.69 | Zhou *et al.,* 2022 |
| C18:1n-9 (oleic) | 29.0 | 27.20 | - | Nakasone and Ito, 1967 |
| 24.30 | 22.60 | Kotake-Nara *et al.*, 2002 |
| - | - | 30.6–38.0 | Pereira *et al.*, 2003 |
| 26.00 | Tomotake *et al.* 2010 |
| 28.32 | Kumar *et al.*, 2021 |
| 28.32 | Zhou *et al.,* 2022 |
| C18:2n-6 (linoleic) | 7.30 | 8.50 | - | Nakasone and Ito, 1967 |
| 6.30 | 7.70 | Kotake-Nara *et al.*, 2002 |
| - | - | 5.81–8.57 | Pereira *et al.*, 2003 |
| 7.30 | Tomotake *et al.* 2010 |
| 3.88 | Kumar *et al.*, 2021 |
| 3.88 | Zhou *et al.,* 2022 |
| C18:3n-3  (alpha-linolenic) | 29.20 | 34.90 | - | Nakasone and Ito, 1967 |
| 36.00 | 40.70 | Kotake-Nara *et al.*, 2002 |
| - | - | 17–33.40 | Pereira *et al.*, 2003 |
| 36.30 | Tomotake *et al.* 2010 |
| 38.25 | Kumar *et al.*, 2021 |
| 38.25 | Zhou *et al.,* 2022 |

**2.5 Usage of silk moth in medicinal field**

The silk moth undergoes a non-feeding, post-pupal stage prior to emergence from the cocoon, during which its primary biological function is to reproduce and lay eggs for the continuation of the species. Silk moths that are not utilized for seed production, as well as those that perish post-mating, are often discarded into pits and left to decompose without being put to any further use. However, according to practices in traditional Chinese medicine, these post-reproductive silk moths are now being repurposed for therapeutic applications, such as the preparation of medicinal wines. One of the most notable examples is the male silkworm moth wine developed by the Shaanxi Sericultural Technology Station, which is traditionally employed in the treatment of impotence, menstrual disorders and menopausal symptoms (Gui and Zhuang, 2000).

Furthermore, silkworm moths serve as a valuable source of a specialized oil that contains approximately 75 per cent fatty substances. This oil is well-suited for the production of high-quality soaps and textile dyes (Gui and Zhuang, 2000). The residual matter obtained after oil extraction can be further utilized for the production of monosodium glutamate or used as animal feed. Additionally, silk moths can yield biologically active components such as cytochrome C, uric acid and neurohormones including prothoracicotropic hormone (PTTH) and diapause hormone (DH), which have pharmaceutical relevance (Gui *et al.*, 2001). The leftover biomass can also be processed into hay and employed as supplementary feed for livestock.

**3. CONCLUSION**

New diseases are emerging at unprecedented rate disrupting people’s health and causing social and economic impact. Hence, dependence on chemicals have been increased. However, while using these chemicals as drugs, awareness of their potential hazards for health and environment is required. Therefore, the world is looking for easily available and better physiologically compatible system of medicine and holistic approach to avert such problem and provide basic healthcare to all. Silkworms are rich in proteins and the reports have mentioned about their extensive utilization in Chinese traditional medicine. Silkworm, cocoon, pupa and moths were used in development of drugs against hepatotoxicity, wound healing, hypertension and diabetes. Therefore, the aforementioned biological activities of silkworms may be exploited for the welfare of mankind.

**4. DISCLAIMER (ARTIFICIAL INTELLIGENCE)**

Author(s) hereby declares that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

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