



FROM SILK TO MEDICINE: THE PHARMACEUTICAL POTENTIAL OF SERICULTURE AND SILK BIOMATERIALS.

Neha Vijay Patil, Pranali Vilas Bodake, Madhubala Devkumar Fursule, Vaishali Vilas Gadhe, Prof. Pravin Gadakh.
M. Pharm, SPPU

Abstract: -

An interesting nexus between antiquated materials and contemporary science is presented by the investigation of silk's use in medicine. The article explores the many uses of silk, with a focus on silk fibroin, a protein that is taken from the cocoon of silkworms and has shown itself to be a perfect material for wound healing, medication delivery, tissue engineering, and regenerative medicine. This article highlights the continuing research and technologies that are transforming healthcare by analysing the special qualities of silk, such as its capacity to enhance tissue growth, encourage cell adhesion, and dissolve in the body without causing harm. The intriguing transformation of silk from a traditional textile to a cutting-edge substance in the medical industry is examined in this article. Silk's transformation from an antiquated luxury cloth to a crucial component of current health demonstrates the amazing fusion of traditional wisdom and cutting-edge science. By illustrating silk's transformation from a natural fibre to a key component of contemporary biomedical advancements, this analysis highlights the article's growing significance in the medical profession.

Keywords: -

Sericulture, Silk Pharmacy, Silkworm By-product, Pharmaceutical Silkworm Medication, Silk and Pharmacy, Silk healthcare, Evaluation of silk, Silk to Medicine, wound healing.

Introduction: -

Most emerging nations in the globe economically engage in sericulture, a method of growing silkworms; India is the world's second-largest producer of silk, after China. Four types of silk were produced in India: Muga (0.54%), Eri (13.32%), Tasar (6.8%), and Mulberry (79.23%) [2]. The increasing number of studies that use natural substances to cure different diseases these days indicates how significant this area of study is to the scientific world. Many of these investigations have been influenced by traditional Asian medicine, which is a great place to find ideas for investigating novel bioactive substances. The mulberry tree's leaves, which have several therapeutic benefits like anti-inflammatory, antibacterial, antiviral, detoxifying, wound healing, and blood pressure management, are the main food source for silkworms. Silkworm growth, health, and productivity are directly impacted by the quantity and quality of mulberry leaves. Fresh, soft mulberry leaves are ideal for silkworms, which are quite picky creatures.

Mulberries are used in the production cycle known as sericulture to feed the worms until the larvae spin their cocoon. Following degumming, the silk is utilised for the textile sector or certain emerging biomedical uses. A number of potentially useful medical compounds are produced during this process. Given the numerous uses for silkworms or silk proteins (fibroin and sericin) in Asia, this is not shocking [1]. Silk proteins offer a significant range of material alternatives for controlled drug release, biomaterials, and scaffolds for tissue engineering due to their remarkable mechanical capabilities [5].

In the spring, when the mulberry leaves—the sole food supply for *B. Mori*, an oligophagous insect—have reached their peak size, the silkworms create their best cocoons. Silkworm's silk, one of the *B. Mori* silk kinds, has become more significant due to its distinctive fabric qualities and huge availability. Although spider silk is stronger and more elastic, *B. Mori* silk has become more popular due to its much simpler cultivation. As a result, the silk moth has emerged as the primary source of silk, which is made up of two ingredients: sericin and fibroin. As holometabolous insects, silkworms go through four distinct developmental stages: egg, larva, pupa, and moth [4].

Table1: -Types of silk in India

Name: -	Mulberry	Tasar	Eri	Muga
Picture: -				
States: -	Karnataka, Andhra Pradesh, West Bengal, Tamil Nadu and Jammu & Kashmir	Jharkhand, Chhattisgarh and Orissa, besides Maharashtra, West Bengal and Andhra Pradesh	north-eastern states, Assam It is also Bihar, West Bengal and Orissa	specific to the state of Assam
Species of silkworm	Bombyx mori	A. paphia, A. royeli, A. peranyini	Altocus ricini	Anthraea assama
Food Plant	Mora alba	Terminalia species, Zizyphus zuzuba	Ricinius communis	Tetraantra

The Life Cycle of Silkworm: -

Stage 1: Egg: The silkworm's life cycle begins with the egg. The female moth, which is mostly the size of a small dot, lays the egg. A female moth can deposit up to 350 eggs at once. The eggs hatch in the spring because of the warmer air. This process takes place once a year.

Stage 2: Silkworm: A hairy silkworm emerges from the ruptured eggs. The silkworms begin to enlarge at this point. Before going on to the next stage, they consume a lot of mulberry leaves for about 30 days.

Stage 3: Cocoon: After 30 days, the silk moth reaches this stage. The silkworm frequently becomes translucent and yellowish in color at this point. At this point, the silkworm is starting to surround itself with a protective coat. A cocoon is the name given to this protective layer. A single silk thread, nearly the size of a little cotton ball, makes up the cocoon. It takes around two days for the cocoon to fully grow.

Stage 4: Pupa: During this stage, the silkworm is only totally still. When they are at the pupa stage, the pupa is killed by unwinding the silk thread by immersing the cocoon into the bubbling water.

Stage 5: Moth: Before emerging, the silk moth must remain in the cocoon stage for 10 to 14 days. When the pupa turns into a silk moth, the life cycle is complete.

History: -

Silk was first utilized in biomedical applications in 150 A.D. when it was discovered to be a suture material. In the past, the ancient Greeks and Romans used insect silk nets to conceal wounds or halt bleeding. Nonetheless, the first sterile silk suture was advised in hospitals as early as 1869, while sterilizing silk sutures in bubbling oil has been documented as early as 1500. The first attempt to create recycled silk by inversely engineering silk cocoons was made at the turn of the 20th century. Using freeze-dried silk powders, silk films, and gels, wound dressings and blood vessels were patented in the 1990s. In the 2000s, research and business-related activities significantly increased. Silk has been widely used in the production of sutures, membranes, controlled drainage systems, and as substrates for cell development and research due to its anti-inflammatory and anti-thrombotic qualities. Silk is still widely used as a suture material in cardiovascular, neurological, and ophthalmic surgery, but it has also been used in a variety of other bodily tissues. These materials are very appealing for specialized and biological applications because of their non-toxic, biocompatible, and biodegradable nature, as well as their very good and stable mechanical qualities to one another. Additionally, it is important to note that throughout the lengthy history of Persian medicine, Persian physicians, known as hokama, such as Avicenna (AD 10th century), Mohammad Momen (AD 17th century), Agili Khorasani (AD 18th century), and Hakim Aazam Khan (AD 19th century), introduced silk, also known as Abresham, as a stimulant and tonifier of the psychic, vital, and natural spirit. Silk is hence liver-protective, cardioprotective, neuroprotective, and cardio-protective. It is hot and dry by nature. Silk is used to make a variety of medicines in Persian medicine, such as Tonica silk syrup and Mofareh abrishami syrup. Additionally, Silkworm dressing (Osro or Yasroo' Zamad) has been shown to be successful in mending amputated nerves and blood vessels by Hakim Aghili Khorsani in Makhzan-al-Adawiyah and Hakim Mohammad Momen in Tahfato-al-Momenin [4]. Our recent research focuses on the different biomedical uses of silk culturing.

Components of silk: -

The two self-assembled protein types that make up silk are fibroin (75% of the protein) and sericin (25%–30%). Other minor components of silk include wax (0.4–0.8), fat, colors (0.2), and mineral components that are created by the silkworm *B. mori* [4]. In these animals, silk proteins are typically made in specialized glands following biosynthesis in the gland-lining epithelial cells, followed by release into the gland lumen before spinning into threads. The cultivated silkworm (*Bombyx mori*) and certain spiders (*Nephila clavipes* and *Araneus diadematus*) produce the most thoroughly described silks.

Silkworm silk from *B. mori* consists primarily of two protein components: -

Although sericin is insoluble in cold water, it is readily hydrolyzed—that is, broken down into smaller portions by lengthy protein molecules—and becomes soluble in hot water. The unique characteristics of sericin protein—such as its resistance to oxidation, antimicrobial qualities, resistance to UV light, ease of absorption and release of moisture, and inhibition of tyrosine and kinase activity—make it beneficial. In order to make silk lustrous, sericin, a significant component of silk fiber, has been specifically extracted from fibroin using degumming during the silk manufacturing process. Fibroin fibers are held together by water-soluble proteins called sericins, which resemble glue.

Table 2: Amino Acid composition of the sericin obtained from different cocoon layers and silk fibroin residues/ 1000 residues

Amino acid	Cocoon Layer			Floss	B.mori fibre
	Inner	Outer	Whole		
Aspartic acid	18.61	18.30	18.46	10.20	13.0
Threonine	11.39	8.44	9.92	6.29	9.1
Serine	28.12	29.05	28.58	40.28	121.06
Glutamic acid	4.90	4.75	4.84	4.31	10.2
Proline	0.51	0.56	0.53	0.66	3.6
Glycine	16.90	16.70	16.80	18.17	446.0
Alanine	4.84	5.15	5.00	4.43	294.0
Cystine	0.42	0.64	0.53	trace	2.0
Valine	2.67	2.91	2.79	3.46	22.0
Methionine	0.10	0.11	0.10	0.12	1.0
Isoleucine	0.60	0.67	0.63	0.67	
Leucine	0.90	1.17	1.03	0.85	5.3
Tyrosine	3.28	3.39	3.33	4.09	51.7
Phenylamine	0.42	0.47	0.44	0.43	6.3
Lysine	2.26	2.89	2.58	1.89	3.2
Histidine	0.89	0.99	0.94	0.68	1.4
Arginine	3.03	3.41	3.22	3.30	4.7

The fibroin's water absorption, dyeing affinity, thermotolerance, insulating qualities, and luster are well-known. Heavy and light chain polypeptides joined by a disulfide bond make up silk fibroin. The protein of interest for biomedical materials is fibroin, which must be separated from the silkworm cocoon by removing sericin in order to be refined or extracted.

The field of biomaterials has shown interest in silks because of their biodegradability, biocompatibility, predictable breakdown rates, and adaptability in producing a variety of material formats, including as gels, fibers, and sponges. The use of silk-based biomaterials for cell culture and tissue creation has been investigated; proper cell adhesion, proliferation, and differentiation on or in silk biomaterials promote tissue regeneration. Silk proteins are intriguing candidates for biomedical applications because of their relative ease of processing into a range of material morphologies, flexible chemical functionalization options, processing in water or solvent, and associated biological properties of biocompatibility and enzymatic degradability [5].

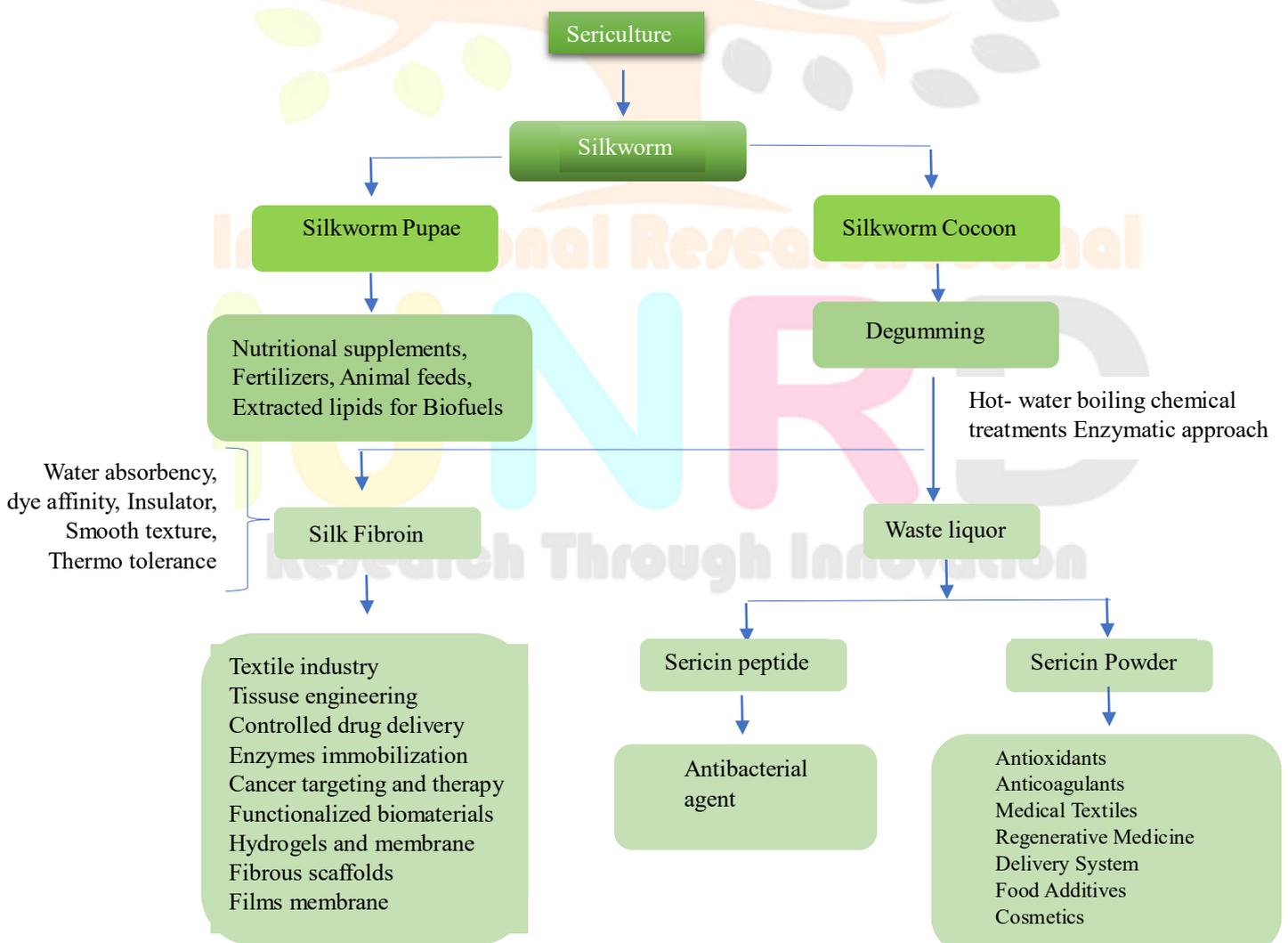


Fig1: -Potential application of silkworm product and by-product

Sericulture in Pharmaceutical Industry: -**1) Silkworm excreta's potential for pharmaceutical use: -**

The prospective uses of silkworm excreta, also known as *Bombyx mori* excreta or silkworm droppings, in the biotechnological and medicinal sectors have been investigated. Numerous bioactive compounds, including proteins, amino acids, and peptides, have been discovered in silkworm excreta.

Excreta from silkworms is cylindrical, 2-3 mm long, and dark green in color. It is used in both the culinary and medicinal industries. In China, Korea, and certain Eastern Asian nations, silkworm feces have been utilized as a medicinal substance in traditional medicine to cure headaches, stomachaches, and infectious disorders.

The main chemical components of silkworm excrement that have been documented are flavonoids, carotene, xanthophylls, and chlorophyll and its derivatives. Silkworm (*Bombyx mori*) excreta contained chlorophyll derivatives CpD-A, -B, -C, and -D. Of these, CpD-A was thoroughly investigated to elucidate its function as a "photosensitizer" for photodynamic treatment (PDT) of malignancies in vitro. Excreta has yielded three beneficial compounds: β -sitosterol, lupeol, and 1-tritriacontanol. Of these, 1-tritriacontanol is probably produced in the silkworm's intestine, but lupeol and β -sitosterol are derived from mulberry leaves that the silkworms ate and are expelled in an unaltered form. They are also used to treat inflammation. Furthermore, research has shown that silk and polyamide materials may be readily dyed using a natural dye derived from silkworm excrement, yielding a yellowish brown hue [7]. Silkworm excrement is also a valuable source of natural colorant for the food sector. These bioactive compounds may be useful for antiviral, antimicrobial, and antioxidant activities (enzymes that can be used in drug formulation, including enzymes that help break down complex substances). Antioxidant properties may be useful in the development of formulations aimed at reducing oxidative stress or protecting against age-related diseases. Because silkworm excrement is high in proteins and other organic compounds, it may be used to make biodegradable medicine delivery systems. The potential use of proteins generated from silkworms for the controlled release of medicinal substances has been investigated. Because of its natural composition, the excreta may have benefits like biocompatibility (being a natural product, silkworm excreta may be less toxic and more compatible with human tissues), sustainability (being a more sustainable alternative to synthetic drug delivery materials), and drug encapsulation (drugs may be better stabilized and bioavailable when encapsulated in proteins and peptides found in the excreta).

2) Cell culture application in silkworms: -

Applications for silkworm cell culture, especially in *Bombyx mori*, are numerous and mostly in the domains of genetics, biotechnology, and sericulture. Following a severe serum deficit, sericin stimulates cell development and reduces cell death, exhibiting substantial biological activity. To enhance the culture of mammalian cells, a novel technique for making sericin as a mitogenic component has been created. Researchers have looked into sericin's increased impact on islet culture. The study concluded that sericin functions as a substitute supplement to boost the serum-free culture of rat islets and encourage the growth of the rat insulinoma cell line. By preventing oxidative stress, sericin has been shown to have a positive effect on the pre-implantation growth of the bovine embryo culture separately. By preventing oxidative stress, the researchers found that adding 0.5% sericin to in vitro culture increases pre-implantation proliferation and the quality of separately cultured cow embryos. The activities of collagen-derived matrices produced using stem cells from human adipose tissue can be improved by the addition of sericin. Silkworm-derived cell culture can be used to test the effects of a variety of substances, such as chemicals, medications, or pesticides. Because silkworm cells have some cellular similarities to other higher organisms, they are frequently used as a model system for toxicity research. They are also helpful in understanding cellular processes like differentiation, development, and hormone impacts, as well as in developing environmentally friendly techniques of controlling agricultural pests.

3) The Hypoglycemic Action of Silkworm: -

High blood sugar, insulin resistance, and other problems are frequently associated with diabetes, particularly Type 2 diabetes, a metabolic disease. As previously mentioned, silkworms and mammals share a similar mechanism for the uptake and storage of sugars. These similarities allow for the use of silkworm models to evaluate antidiabetic medications for both kinds of diabetes (I and II). In this study, two different forms of hyperglycemia were created in silkworms: one using a diet high in glucose and the other using sucrose. Our ability to determine whether the mechanism of action of this possible hypoglycemic impact is associated with suppression of glucose absorption or, conversely, is more closely tied to inhibition of α -glucosidase activity is aided by this. The expression of the glucose transporter (SGLT1) of the human intestinal epithelial cell line Caco-2 has been shown to be inhibited by silkworm powder; insects occasionally exhibit this type of transporter [1]. Peptides obtained from silkworms have demonstrated promise in blood sugar regulation. Silkworms have peptides that have characteristics similar to those of insulin, which may help lower blood sugar levels and offer possible therapeutic benefits for diabetes patients. Blood glucose levels can be lowered by silkworm products, such as extracts from silkworm larvae and pupae. Like certain antidiabetic medications, the precise process might entail the stimulation of specific enzymes involved in glucose metabolism. One of the main causes of insulin resistance in diabetes is chronic inflammation. Bioactive substances found in goods obtained from silkworms have the potential to improve insulin sensitivity and avoid complications from diabetes by reducing inflammation. According to a few animal studies, extracts from silkworm pupae and protein hydrolysates can improve insulin sensitivity, lower blood glucose levels, and restore normal lipid profiles, all of which can have antidiabetic effects.

4) In hyperlipidemia, silkworm: -

Unusually high blood lipid (fat) levels are a symptom of hyperlipidemia, a disorder that raises the risk of cardiovascular illnesses. How silkworms can be used to treat hyperlipidemia It has been discovered that the silkworm protein sericin contains a number of bioactive qualities. Because they are antioxidants, enhance lipid metabolism, and lessen oxidative stress, sericin and other silk proteins may help lower blood lipid levels. Through their effects on the liver's lipid production and absorption pathways, these substances may be able to alter cholesterol levels. Unsaturated fatty acids, which have been demonstrated to promote cardiovascular health and lower cholesterol, are among the many beneficial fats found in silkworm pupae. Although the nutritional value of silkworm fatty acids is frequently the primary source of interest, they may also

be useful in controlling lipid profiles in hyperlipidemic patients. Silkworms also synthesize complex sugars called polysaccharides, which have been demonstrated to have hypolipidemic effects. Through improving gut health and fat absorption, or by increasing the activity of enzymes involved in lipid breakdown, these polysaccharides may help decrease blood cholesterol and triglycerides. Hyperlipidemia and cardiovascular disorders are largely caused by oxidative stress and chronic inflammation. The anti-inflammatory and antioxidant qualities of several sericulture products, especially sericin, may aid in the fight against these root causes of lipid abnormalities.

5) Silkworm Treatment as a Cancer Medication: -

Cancer is one of the biggest health and financial problems in the world. Even though research on cancer has advanced significantly and novel treatments have been developed, cancer remains one of the primary causes of mortality. Significant strides have been made in recent years to overcome the drawbacks of traditional cancer treatments. Chemotherapy and radiotherapy are the most often utilized treatment techniques for cancer. It is commonly known that these treatments have a wide range of adverse side effects, including psychological issues and systemic toxicity, in addition to the development of significant drug resistance in the tumor cells [9]. The antitumoral effects of various sericin concentrations on two triple-negative human breast cancer cell lines—one of the most aggressive cancer types—have been studied. The MTT assay was used to assess the cell survival following the sericin treatment, and the findings demonstrated that sericin has a dose-dependent antitumoral impact. Furthermore, sericin inhibited the rate of colony formation and proliferation. Additionally, apoptosis and cell cycle progression were examined using flow cytometry, and the findings showed that the natural chemical caused cell cycle arrest, particularly in the G0/G1 phase. By measuring the expression levels of multiple target proteins, such as cyclin D1, Cdk4, E2F3, P21, and P27, these findings were validated. Furthermore, the apoptotic rate was assessed, which confirmed that sericin causes tumoral cell apoptosis. Another study assessed the antitumoral activity of sericin on three distinct tumoral cell lines, namely breast adenocarcinoma (MCF-7), tongue carcinoma (SAS), and squamous carcinoma (A431). Silk sericin treatment at a dosage of 1 mg/mL had no effect on the vitality of the cancer cells; however, when the concentration was increased to 4 mg/mL, all tumoral cell lines showed a decline in cell viability. The scientists found that sericin is more lethal to tumoral cell lines than to healthy cells when they compared the viability of normal and tumoral cells following treatment with silk sericin [9].

6) The role of sericulture in skin regeneration and wound healing: -

As a wound healing agent: The silk that silkworms generate, which is mainly made up of the proteins fibroin and sericin, has shown a number of advantageous qualities that make it useful for fostering skin regeneration, wound healing, and tissue repair. The primary protein found in silk fibers, silk fibroin, has been researched for its ability to heal wounds. It is extremely biocompatible, which means that when given to the body, it does not cause any noticeable immune reactions. It is therefore a perfect material for skin grafts and wound dressings. Additionally, it gives scaffolds and wound dressings flexibility and structural support, preserving the integrity of the wound while permitting mobility. Numerous cell types involved in wound repair and regeneration, including fibroblasts, keratinocytes, and endothelial cells, are supported in their proliferation by silk fibroin. Because of this, it works well as a scaffold for skin regeneration. Numerous cell types involved in wound repair and regeneration, including fibroblasts, keratinocytes, and endothelial cells, are supported in their proliferation by silk fibroin. Because of this, it works well as a scaffold for skin regeneration. Silkworm's sericin has hydrating and moisturizing properties that help enhance the environment surrounding a lesion and hasten its recovery. Tyrosine and serine, two amino acids with antioxidant qualities, are also found in sericin. These aid in lowering oxidative stress, which can hinder skin regeneration and wound healing. Sericin can speed up the healing process when coupled with fibroin. It has been demonstrated to aid in promoting the dermis (inner skin layer) and epidermis (outer skin layer) to regenerate.

When silk fibroin is combined with growth factors, stem cells, and other regenerative materials, it can speed up the dermal and epidermal regeneration process, improving the skin's ability to function after injury. The potential for wider tissue engineering applications is highlighted by the fact that silk fibroin's adaptability also extends to regenerative therapy for other tissues, such as bone and cartilage. Silk has been utilized for wound healing, and its use in cancer treatments may help cancer patients recover from radiation therapy or surgery. Silk fibers' fibroin is well known for encouraging tissue regeneration, which may help repair radiation burns or surgical wounds and enhance quality of life while undergoing cancer treatment. Nanofibers of silk fibroin are being employed as cutting-edge materials for wound healing. These fibers can be engineered to promote tissue growth and enhance the healing process, which includes skin tissue regeneration. Silk has been used to heal wounds, and its usage in cancer therapies may help cancer patients recover from radiation therapy or surgery. Silk fiber's fibroin is well known for encouraging tissue regeneration, which could help cure radiation burns or surgical wounds and enhance quality of life while undergoing cancer treatment [10].

7) Silkworm pupa in the food and medical industries: -

After reeling, silkworm pupae are an immediate byproduct of the reeling industry. On a dry weight basis, India produces over 40,000 MT of silkworm pupae annually. Crude 50–60% proteins, 25–35% lipids, 5–8% free amino acids, 8–10% sugar, calcium, phosphorus, and the vitamins E and B1 are all present in pupae. 100g of dried silkworm pupae can provide 75% of the daily protein required by an individual. The pupae are more nutrient-dense due to the presence of minerals like calcium, selenium, and phosphorus, as well as vitamins like pyridoxal, riboflavin, thiamine, ascorbic acid, folic acid, nicotinic acid, and pantothenic acid. High-quality edible liquids found in silkworms are utilized as basic materials in medicine. By triggering apoproteins and lipid-metabolizing enzymes, silkworm pupae control the levels of lipoproteins and plasma lipids in rats' serum. Therefore, hyperlipidemia may be treated with it. Silkworm pupae also contain lecithin, which has antioxidant properties. Over 70% of the oil derived from silkworm pupae is unsaturated fatty acid, with oleic acid and α -linolenic acid making up the majority. In the cosmetics industry, oil produced from boiling silkworm pupae is used to make moisturizers and soaps, which were used to degum silk. 1-Deoxynojirimycin (DNJ), a strong alpha glucosidase inhibitor used to treat diabetes, is also included in palpal oil. Pupa and pupal oil from silkworms are valuable resources because they are abundant in ALA (alpha linoleic acid) and omega-3 fatty acids, both of which are critical for human health. Paints, varnishes, medicines, soaps, candles, plastic, and biofuel are among the industrial goods that employ the precious pupae oil [7].

Future Scope And Conclusion: -

The production of silk and goods derived from it is the main purpose of sericulture, the practice of silk farming. However, because of the special qualities of silk proteins—particularly fibroin and sericin—its possible use in the pharmaceutical sector is gaining attention. It has been discovered that these proteins have bioactive qualities that can be applied to a number of therapeutic applications. Here is a summary of sericulture's function in pharmaceuticals:

- 1) Biodegradability and Biocompatibility: Silk proteins, particularly fibroin, are both biocompatible and biodegradable, which makes them great options for tissue engineering, drug delivery, and wound healing applications. The body can naturally break down these compounds without any negative consequences.
- 2) Wound Healing and Regenerative Medicine: Biomaterials derived from silk have demonstrated potential in fostering tissue regeneration and wound healing. Because silk dressings retain moisture and promote healing, they have been used to treat chronic wounds.
- 3) Drug Delivery Systems: Hydrogels or nanoparticles with regulated drug release are made from silk proteins. Their capacity to encapsulate pharmaceuticals and release them gradually improves the therapeutic efficacy of a range of treatments.
- 4) Medical Sutures: Silk strands have been utilized as surgical sutures for ages due to their strength and flexibility. Bioactive substances are even being added to contemporary silk sutures to encourage quicker healing and lower infection rates.
- 5) Silk proteins have been investigated as potential delivery systems for anticancer medications. Their special qualities reduce the negative effects of conventional chemotherapy while aiding in the targeting of cancer cells.
- 6) Tissue Engineering: In tissue engineering applications, silk scaffolds promote cell development, facilitating the regeneration of bone, cartilage, and skin tissues. They are perfect for these uses because of their mechanical qualities and porous nature.

To sum up, sericulture in the pharmaceutical industry provides cutting-edge approaches to tissue regeneration, wound care, and medication administration. Silk proteins' biocompatibility, adaptability, and biodegradability make them a viable material for pharmaceutical research that could transform a number of treatments. The further investigation of materials obtained from sericulture in medicine has great promise for enhancing patient care and treatment results.

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