AGRI MAGAZINE
(International E-Magazine for Agricultural Articles)
Volume: 02, Issue: 07 (July, 2025)
Available online at http://www.agrimagazine.in

Silkworm as a Model Organism: A New Era of Scientific Discovery

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For centuries, the silkworm (*Bombyx mori* L.) has been celebrated for spinning the fine threads that fuel the global silk industry. But today, beyond the looms and textiles, this humble insect is making waves in the world of science. With its small size, short life cycle, well-mapped genome and ethical advantages, the silkworm is emerging as a powerful model organism, a living laboratory for discoveries in genetics, molecular biology, immunology, biotechnology and pharmacology. This transformation is not accidental. It is built on decades of research, combined with modern technologies like CRISPR and transcriptomics, which have unlocked the silkworm's true potential. As scientists seek new models that are ethical, cost-effective and biologically insightful, Bombyx mori is stepping into the spotlight not just as a producer of silk but as a contributor to science and medicine.

From Domesticated Insect to Genetic Resource

Silkworms have been domesticated for more than 5,000 years, with humans selectively breeding them for improved silk yield, growth rate and disease resistance. This long history of domestication has created a genetically rich species one that offers insights into both evolutionary biology and artificial selection. A groundbreaking study by Tong *et al.* (2022) who resequenced 1,078 silkworm individuals and assembled high-quality genomes for 545 strains. The pan-genome revealed 3.4 million structural variants, identified over 7,300 new genes and pinpointed loci associated with domestication traits such as silk yield, cocoon quality and ecological adaptations. This genetic diversity provides researchers with a powerful toolkit for exploring how genetic variations influence physiology and development not only in insects but across the entire animal kingdom.

Silkworms in Genetic Engineering and Functional Genomics

In recent years, genome editing tools such as CRISPR/Cas9, TALENs and zinc-finger nucleases (ZFNs) have been applied to silkworm research. This has enabled precise gene manipulation and functional analysis of genes involved in development, silk synthesis, disease resistance and metabolism. One particularly revolutionary development is the use of the silkworm (*Bombyx mori*) as a bioreactor for producing recombinant proteins. Xu *et al.* (2019) developed a transgenic *B. mori* strain that produces recombinant human lactoferrin in the silk glands. The yield was approximately 12 mg per gram of cocoon shell, with nearly 95 per cent purity and the protein demonstrated antibacterial and anti-inflammatory activity in cell models. Moreover, techniques such as CRISPR/Cas9 and RNA interference (RNAi) are widely used to knock out or suppress genes, enabling reverse genetics studies that clarify gene functions and their roles in physiological pathways (Kumar *et al.*, 2022). This molecular toolbox positions *B. mori* as an invaluable model not only for phenotypic screening but also for mechanistic studies that dissect gene–environment interactions and drug responses.

Immune System Insights from the Silkworm

Though it lacks an adaptive immune system like that of vertebrates, the silkworm has a robust and well-organized innate immune system, offering valuable insights into immune signaling and pathogen response. A recent study by Liu *et al.* (2024) identified the BmToll9-1 receptor, which becomes highly upregulated when the silkworm encounters *E. coli* or *Beauveria bassiana*. This receptor regulates antimicrobial peptides (AMP) expression through RNAi pathways and offers a new target for understanding broad-spectrum immunity.

Fungal Immunity and Infection Models

Silkworms are commonly infected by the fungal pathogen *Beauveria bassiana*, offering a natural model to study fungal immunity. In the confirmed study by Geng *et al.* (2016), researchers showed that:

The JAK/STAT signaling pathway in silkworms is strongly activated during fungal infection. Silencing pathway components or the pattern recognition receptor BmCTL5 through RNA interference significantly reduced antifungal activity in the hemolymph and led to higher larval mortality. This study confirms JAK/STAT as a key defense mechanism in silkworm innate immunity. In addition, Ye *et al.* (2021) demonstrated the role of 30K proteins especially BmLP1 and BmLP4 in cellular immunity. These proteins help hemocytes recognize, bind and encapsulate fungal spores, effectively blocking the spread of infection.

Advantages Over Traditional Model Organisms

Why use silkworms over mice and fruit flies? The answer lies in a combination of biological, ethical and practical advantages:

Ethical edge: As invertebrates, silkworms face fewer ethical concerns in experimentation, helping reduce reliance on vertebrate testing.

Low maintenance: They require simple, non-sterile environments and can be reared on artificial diets or mulberry leaves.

High-throughput screening: Hundreds or even thousands of larvae can be tested simultaneously, making them ideal for drug discovery.

Conserved physiology: Silkworms have many metabolic and immune pathways similar to mammals, especially in detoxification and response to pathogens.

Because of these strengths, silkworms are used in a growing number of toxicology, oncology and pharmacokinetics studies.

Applications in Drug Screening and Toxicology

Silkworms metabolize chemicals through enzymes like cytochrome P450, just like humans and mice. This makes them useful for early-stage drug screening and toxicology testing. Researchers have used silkworms to test plant-derived compounds, antibiotics and even nanoparticle-based therapies. Their immune response (*e.g.*, hemocyte count, AMP production) and survival rate can be used as biomarkers for therapeutic efficacy. This model has helped reduce reliance on vertebrates, aligning with the ethical 3Rs principles (Replacement, Reduction, Refinement). Li *et al.* (2022) conducted tissue-specific transcriptomic analyses in *Bombyx mori* (midgut, head, fat body) to evaluate how different diets or drug-like compounds affect gene expression and cellular responses.

Biomaterials and Spider Silk Integration

Another breakthrough use of silkworms is in biomaterials engineering. Scientists have inserted spider silk genes into the silkworm genome to produce fibers that are stronger, lighter and more elastic than natural silk. In a groundbreaking study, Mi *et al.* (2023) successfully engineered silkworms to produce full-length spider silk proteins, resulting in hybrid fibers with exceptional strength and toughness. These bioengineered silks show great potential for use in medical sutures, biodegradable scaffolds, and wearable sensors, illustrating the powerful convergence of synthetic biology and materials science.

A Tool for Science Education and Public Engagement

Silkworms aren't just tools for advanced science, they are also powerful educational models. Their metamorphosis from egg to larva to pupa to moth captivates students, offering a live example of genetics, physiology and ecology in action. Silkworms (*Bombyx mori*) are increasingly incorporated into science outreach and education programs in countries such as Japan, South Korea and India. Their complete metamorphosis, observable larval markings and docile, non-toxic nature make them ideal for classroom demonstrations and citizen-science activities (Kato *et al*., 2017; IBSD, 2021).

Conclusion

Once known only for its silk, *Bombyx mori* has now become an ambassador for scientific progress. It offers a unique combination of genetic malleability, low cost, ethical acceptability and biological relevance that no other model organism can match in totality. As we enter an era of precision medicine, sustainable materials and ethical science, the silkworm is poised to play a larger role bridging the gap between insects and insights, between tradition and transformation. Whether you're a molecular biologist, pharmacologist, educator, or student, it's time to look again at the silkworm not just as a spinner of silk, but as a spinner of solutions for science. So, the silkworm tiny insect with a huge future

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