Hidden Hazards in the Field: The Complex World of Venomous Moths and Caterpillars

Manjunatha M. J.
M. Sc. Scholar, Dept. of Entomology, University of Agricultural Sciences, Raichur, Karnataka- 584104
Corresponding Email: manjunathamj0@gmail.com

Introduction

Lepidoptera (moths and butterflies) is a highly diverse order with ~1,60,000 species across 133 families (Kawahara *et al.,* 2019). While many rely on defenses like crypsis, aposematism and Batesian mimicry, others possess secondary defenses such as spines, setae and venom production (Sugiura, 2020). Venom is reported in 576 species across 14 families (~2%) (Battisti *et al.*, 2024), likely evolved to counter predation, especially in vulnerable stages like eggs, larvae and pupae. Many venomous species are also significant agricultural pests, posing health risks and occupational hazards to humans and livestock.

Defining the Threat: Venom v/s Poison

To understand this hazard, it is essential to distinguish venom from poison. Venoms are complex mixtures of peptides, proteins and organic compounds, evolved to cause diverse physiological effects. They are actively injected through specialized structures like bites, stings or spines. In contrast, poisons are passively absorbed, ingested or inhaled.

The Evolutionary Marvel of Convergent Evolution

The occurrence of venom in Lepidoptera is a clear example of convergent evolution, with similar toxin types evolving independently across multiple lineages. Cladogram analyses show venomous species scattered across distant branches, confirming separate evolutionary origins driven by common selective pressures like predator defense.

Across insects, venom has evolved at least 13 times (Walker *et al.,* 2018). Lepidopteran venoms also resemble those of unrelated animals; for instance, Inhibitor Cystine Knot (ICK) peptides found in *Acharia stimulea* and *Parasa lepida* are also present in spiders, scorpions and cone snails, indicating shared evolutionary strategies (King, 2019).

Anatomy of Envenomation

Unlike many venomous animals, caterpillars lack a centralized venom gland. Instead, venom is produced by secretory epithelial cells and stored in hollow bristle-like structures arising from regions such as the abdominal tergite. These structures are supported by cells including epidermal, trichogen, tormogen, sensory and venom-producing cells.

Three main envenomation structures occur:

1. **True setae:** Found in Erebidae, Notodontidae and Saturniidae; hollow, toxin-filled hairs that break easily and penetrate skin to release venom (Fry *et al.,* 2009).
2. **Modified setae:** Present in Erebidae, Limacodidae and Lasiocampidae; contain an additional glandular cell for active venom production and controlled release (Fry *et al.,* 2009).
3. **Spines:** Seen in Megalopygidae, Limacodidae and Nymphalidae; larger structures with basal glandular cells, whose tips break on contact to rapidly deliver venom.

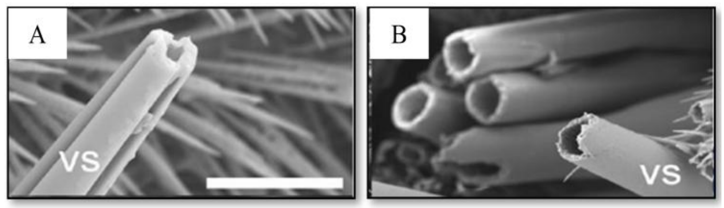

Fig. 1. Venom apparatus of the asp caterpillar. (A) Shows a broken venom spine near the tip with a trilobed cross-section due to longitudinal striations. (B) Shows a spine broken closer to the base with a circular cross-section.

Envenomation Symptoms: From Skin to Organs (Berger *et al.*, 2019)

Caterpillar venom is highly bioactive and targets mast cells, key mediators of allergic and inflammatory responses. Since these cells are abundant in exposed tissues (skin, respiratory and gastrointestinal systems), envenomation can cause rapid and severe effects.

- **Local Effects:** Common reactions include contact dermatitis with erythema, edema, urticaria, severe pain and localized tissue damage.
- **Joint Damage:** Some venoms cause Paranoma phalangeal periarthritis, leading to intense joint inflammation, swelling of fingers and possible cartilage loss.
- **Systemic Effects:** Severe envenomation disrupts haemostasis, triggering inflammation, thrombosis and internal bleeding. If venom enters circulation, it may cause Acute Kidney Injury (AKI) through inflammation, clotting and tissue necrosis in the kidneys, potentially leading to acute renal failure.

Key Lepidopteran Families and Their Toxins

The following table outlines the major venomous Lepidoptera families, highlighting the vast diversity of their venom apparatuses and toxins.

Table 1. Venomous Lepidoptera (Abbreviations: ACP, adipokinetic/corazonin like peptide; EAFL, equine amnionitis and fetal loss; ICK, inhibitor-cystine knot; Lopap, *L. obliqua* prothrombin activator protein; Losac, *L. obliqua* Stuart-factor activator; MRLS, mare reproductive loss syndrome; NA, not available; PLA2, phospholipase A2.) [Walker, 2025].

Family	Venom Apparatus	Envenomation Syndrome	Mode of Action	Known Toxins
Saturniidae	Spines, true setae	Pain, haemorrhagic syndrome, death	Activation of clotting factors	Lopap, Losac, PLA2, histamine
Limacodidae	Spines, modified setae	Pain	Membrane permeabilization	Cecropins, ACP-like, ICK, RF-amides, histamine
Megalopygidae	Spines	Pain	Membrane permeabilization	Megalysins
Erebidae	True setae, modified setae	Itch, pain, pararamosis	Enzymatic	NA
Lasiocampidae	Modified setae	Pain, itch, MRLS, dendrolimiasis	NA	NA
Notodontidae	True setae	Inflammation, pain, EAFL	NA	Tha p 1, Tha p 2

Saturniidae (*Lonomia* species):

These caterpillars are highly lethal, with branched spines delivering venom that causes severe hemorrhagic syndrome. Symptoms include headache, fever, pulmonary and cerebral hemorrhage, hematuria and acute renal failure. The venom disrupts hemostasis by increasing prothrombin and thrombin while depleting fibrinogen and factors V, VIII and XIII, resulting in unclottable blood (Zannin *et al*., 2003).

Two key toxins are involved: Lopap, a lipocalin that activates prothrombin independently, causing excessive thrombin formation and disseminated intravascular coagulation; and Losac, a hemolin that activates Factor X, further promoting uncontrolled clotting. Lonomia antivenom developed by the Butantan Institute effectively neutralizes these toxins.

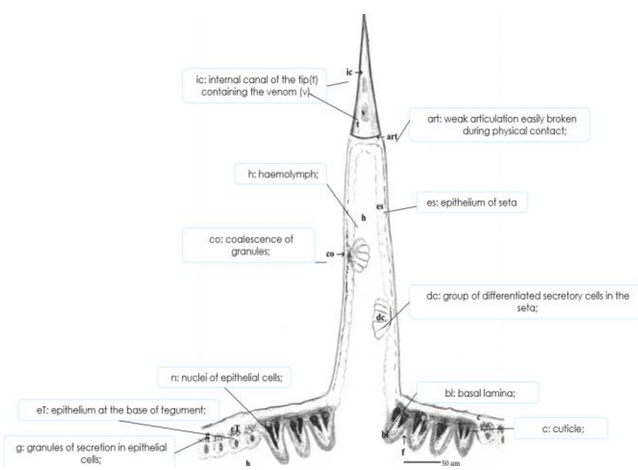

Fig. 2. Schematic model illustrating the complex system involved in the production and active injection of venom by the highly dangerous *Lonomia obliqua* caterpillar. (Veiga *et al.*, 2001).

Limacodidae (Stinging caterpillars):

Species like *Doratifera vulnerans* have cylindrical venom spines rich in histamine (Itokawa *et al*., 1985), causing vasodilation, itching, burning and swelling. Their venom also contains cecropin-like peptides positively charged, amphipathic molecules that disrupt cell membranes by forming pores, leading to nerve damage and intense pain, similar to melittin. Additionally, neurohormone-like peptides such as antimicrobial cationic peptides (ACP) activate GPCRs, while RF-amide peptides mimic human neuropeptides and bind NPFF1 receptors, modulating pain responses.

Megalopygidae (Puss caterpillars):

Species like *Megalopyge opercularis* have highly venomous spines hidden beneath soft hairs. Stings cause intense pain, bruising, blistering, respiratory distress and tissue necrosis (Foot, 1922). Their venom contains megalysins pore-forming toxins likely acquired from *Aeromonas* bacteria via horizontal gene transfer (Walker, 2023). These toxins degrade basement membrane proteins (collagen, laminin, fibronectin, elastin), forming pores that lead to cell death and blood vessel rupture.

Processionary and Lasiocampid Caterpillars:

Processionary caterpillars such as *Thaumetopea pityocampa* and *Ochrogaster lunifer* possess vast numbers of urticating hairs, with later instars carrying up to 2.5 million setae (Perkins *et al*., 2016). They pose serious risks to livestock: *T. pityocampa* is linked to Equine Amnionitis and Fetal Loss (EAFL) via inflammatory toxins Tha p 1 and Tha p 2 (Cawdell-Smith *et al*., 2012). Likewise, Lasiocampidae caterpillars cause dendrolimiasis in humans and are associated with Mare Reproductive Loss Syndrome (MRLS), leading to fetal loss in horses (Sebastian *et al.,* 2008).

Biotech Applications: Harnessing the Venom

Despite their risks, Lepidopteran venoms show strong potential in biotechnology and agricultural medicine. Inhibitor Cystine Knot (ICK) peptides from limacodid caterpillars are being explored as antiparasitic agents, with variants shown to inhibit larval growth of *Haemonchus contortus*, a major ruminant parasite, offering promise for veterinary treatments. Additionally, cecropin-like peptides exhibit broad-spectrum antimicrobial activity, acting as antimicrobial peptides (AMPs) that can inhibit or kill harmful bacteria.

Field Management and Precautions

Given the serious occupational risks, rapid first-aid response is essential. Recommended steps include:

1. Wash the affected area with soap and water and dry without contact (use a fan or hair dryer).
2. Use adhesive tape to remove embedded hairs.
3. Remove tight clothing or jewellery to prevent complications from swelling.
4. Apply isopropyl alcohol and an ice pack for cooling; tetanus prophylaxis is also advised.

Conclusion and Future Prospects

Lepidopteran venoms are highly evolved larval defenses causing effects from localized pain to fatal haemorrhagic syndromes and veterinary conditions like Equine Amnionitis and Fetal Loss. Despite their ecological and medical importance, they remain understudied compared to snake or spider venoms. However, they offer strong potential for biotechnology, medicine and agriculture, with toxins such as megalysins and knottin-like (ICK) peptides showing promise for pain control, anticancer therapy and eco-friendly antiparasitic agents.

Advancing this field requires multidisciplinary research, including anatomical studies, venom transcriptomics, proteomics and recombinant approaches, particularly in peptide-rich families like Limacodidae and Megalopygidae. Integrating insect ecology with drug discovery could unlock their potential in clinical toxicology and sustainable pest management.

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