

Venoms of Lepidoptera: Evolution, Composition, Delivery Mechanisms and Biological Significance

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ABSTRACT

Lepidoptera, comprising butterflies and moths, are generally perceived as harmless insects; however, growing evidence demonstrates that several species possess potent venoms, particularly during the larval stage. Lepidopteran venoms have evolved primarily as defensive adaptations against predators, parasitoids, and accidental human contact. These venoms are delivered through specialised structures such as urticating setae, spines, and venomous scales, which release bioactive compounds upon contact. Venomous caterpillars, including *Lonomia obliqua*, *Doratifera vulnerans*, and *Comana monomorpha*, can cause a range of effects from localised pain and dermatitis to severe haemostatic disorders. Lepidopteran venoms are biochemically diverse, comprising peptides, proteins, enzymes, and inflammatory mediators, and have evolved independently across multiple lineages. Beyond their medical relevance, these venoms represent promising sources of novel bioactive molecules with potential applications in agriculture, medicine, and biotechnology.

INTRODUCTION

Lepidoptera may inadvertently affect human health through specialised scales and toxic substances used for

defence. Although traditionally regarded as non-venomous, several butterflies and moths, particularly in their larval stages, possess

effective venom systems delivered through urticating setae, spines or modified scales that break on contact and release bioactive compounds (Battisti *et al.*, 2024). Consequently, contact with these structures may cause irritation, pain or more severe reactions in humans. Venoms are complex biochemical secretions evolved across animal groups for defence or competition, and in Lepidoptera venomous traits have arisen independently in multiple families, reflecting convergent evolution driven by predation and environmental pressures. Their venoms exhibit marked biochemical diversity, including peptides, proteins, enzymes and inflammatory mediators affecting neurological, haematological and cellular pathways (Walker, 2025). Medically significant species such as *Lonomia obliqua*, *Doratifera vulnerans* and *Hylesia* are linked to coagulopathy, intense pain and dermatological reactions; consequently, beyond predator deterrence, these venoms are increasingly recognised as valuable sources of novel bioactive compounds, stimulating renewed interest in toxinology and applied biological research.

Which Lepidopterans Are Venomous???

Venomous Lepidoptera are distributed across multiple taxonomic families, with venom expression occurring predominantly during the larval stage. Unlike predatory venom systems, lepidopteran venoms function mainly as defensive adaptations against predators, parasitoids, and accidental vertebrate contact. Medically significant venomous species are primarily reported from families such as Saturniidae, including *Lonomia obliqua* (Walker, 2025) and *Hylesia* spp.; Limacodidae, represented by *Doratifera vulnerans* and *Acharia stimulea*; Megalopygidae, commonly known as asp caterpillars; Notodontidae, notably *Ochrogaster lunifer* (Cawdell-Smith *et al.*, 2012); and selected members of Erebiidae. These taxa possess specialized venom-delivery

structures such as urticating setae, spines, or detachable scales capable of releasing toxins upon mechanical stimulation. Phylogenetic evidence suggests that venomous traits have evolved independently in different lepidopteran lineages, indicating convergent evolution driven by ecological pressures rather than shared ancestry. While adult butterflies and moths are generally non-venomous, some species retain venomous hairs or scales that contribute to human envenomation incidents.

Evolution of Lepidopteran Venoms

The evolution of venom in Lepidoptera represents a specialised defensive adaptation shaped by strong ecological and evolutionary pressures. Unlike predatory venoms, lepidopteran venoms have evolved primarily for defence, particularly during the larval stage when caterpillars are slow-moving and highly vulnerable to predators and parasitoids. Phylogenetic studies indicate that venomous traits have emerged independently across several lepidopteran families, including Saturniidae, Limacodidae, Megalopygidae, and Notodontidae, demonstrating clear patterns of convergent evolution (Yang & Zhu, 2025).

Selective pressures such as vertebrate and invertebrate predation, along with parasitism, have driven the diversification of venom composition and delivery systems. Key evolutionary innovations include the development of urticating setae, spines, and venomous scales that enhance toxin release upon mechanical contact (Walker, 2025). At the molecular level, venom evolution involves gene duplication, diversification of toxin families, and in some lineages, horizontal gene transfer contributing to novel bioactive compounds. Together, these processes have enabled lepidopteran larvae to deploy rapid and effective chemical defences, highlighting venom as an important adaptive trait influencing survival and ecological interactions.

Composition of Lepidopteran Venoms

Lepidopteran venoms display marked biochemical diversity, reflecting their defensive role and evolutionary origins. These venoms are complex mixtures of bioactive molecules, including peptides, proteins, enzymes, and low-molecular-weight compounds (Yang & Zhu, 2025). Key components include neurotoxic and pain-inducing peptides, membrane-permeabilising proteins, inflammatory mediators, and, in certain species, toxins that modify blood coagulation. For example, *Lonomia obliqua* venom contains factors that disrupt haemostasis, while limacodid caterpillars produce peptides responsible for intense nociceptive responses. Many lepidopteran venom peptides are small, cysteine-rich, and structurally stable, enhancing their biological activity. The compositional complexity of these venoms allows them to act on multiple physiological pathways simultaneously, increasing defensive efficiency (Walker, 2025). Consequently, lepidopteran venoms represent an important yet underexplored source of biologically active compounds with significant ecological and biomedical relevance.

Anatomy of Venom Production and Delivery

In venomous Lepidoptera, venom production and delivery are anatomically specialised to function primarily as defensive mechanisms during the larval stage. Venom is synthesised in modified epidermal or glandular cells associated with specialised cuticular structures such as urticating setae, spines, and venomous scales (Yang & Zhu, 2025). These hollow or brittle structures store and release venom upon mechanical contact. True setae and modified spines commonly penetrate the skin and fracture, allowing toxin release, while detachable scales or hairs can cause envenomation without direct contact (Walker,

2025). This passive, mechanically activated delivery system ensures rapid toxin release and reflects adaptive specialisation for effective predator and parasitoid deterrence.

Molecular Modes of Action

Lepidopteran venoms act through diverse molecular mechanisms that enhance their effectiveness as defensive adaptations. Unlike predatory venoms, these toxins rapidly deter predators and protect against accidental human contact by targeting multiple physiological systems simultaneously. The venoms comprise complex mixtures of peptides, proteins, enzymes, and small bioactive molecules that act synergistically. Key mechanisms include membrane permeabilization, resulting in cell lysis, tissue damage, and intense pain, and neuroactive effects that activate nociceptive pathways (Goudarzi *et al.*, 2024). In certain species, such as *Lonomia obliqua*, venoms disrupt haemostatic pathways, causing haemorrhage and coagulopathy. Inflammatory and immunomodulatory responses further contribute to venom potency, making lepidopteran venoms highly effective defensive tools with significant biomedical relevance.

Medical and Ecological Significance

Medically, species such as *Lonomia obliqua* are notorious for causing severe haemorrhagic syndromes in humans. Contact with its urticating spines may result in coagulopathy, extensive internal bleeding, haematuria and, in critical cases, acute renal failure. Similarly, *Comana monomorpha*, commonly known as the electric caterpillar, produces venom that induces intense pain, inflammation and progressive skin lesions. Such envenomations represent a significant public health concern in endemic regions and necessitate improved clinical awareness and management (Goudarzi *et al.*, 2024).

Ecologically, venom functions primarily as a defensive adaptation, deterring predators and enhancing larval survival. These chemical defences influence predator-prey interactions, shape community dynamics and contribute to evolutionary selection pressures. Moreover, studying these venoms provides insight into toxin evolution and biodiversity. Their bioactive compounds may also hold promise for pharmaceutical development, highlighting the broader ecological and biomedical relevance of venomous Lepidoptera.

CONCLUSION

Venomous Lepidoptera represent a unique and underexplored component of insect chemical defence. Their venoms, primarily expressed during the larval stage, have evolved as effective protective adaptations involving specialised delivery structures and complex bioactive compounds. These venoms play an important role in ecological interactions by deterring predators and parasitoids, while also posing significant medical risks to humans in certain species. Advances in molecular and evolutionary studies have revealed the diversity and functional significance of lepidopteran venoms, highlighting their potential as valuable sources of novel bioactive molecules for biomedical and applied research.

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