Mind-controlling molecules from wasp venom could someday help Parkinson's patients

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After being stung by a parasitic wasp, the American cockroach loses control of its behavior, becoming host to the wasp's egg. Days later, the hatchling consumes the cockroach alive. While this is a gruesome process for the cockroach, scientists now report in ACS' journal *Biochemistry* the discovery of a new family of peptides in the wasp's venom that could be key to controlling roach minds, and might even help researchers develop better Parkinson's disease treatments.

Scientists have long studied venoms, such as that of the wasp, seeking out novel and potent molecules to treat disease, among other applications. In the case of the enigmatic wasp *Ampulex compressa*, it uses its venom in a two-pronged approach against the cockroach, with an initial sting to the thorax to paralyze the front legs and a subsequent sting directly to the brain. This second sting causes the roach first to vigorously groom itself, then to fall into a state of lethargy, allowing the wasp to do whatever it wants. This immobile state resembles symptoms of Parkinson's disease, and both may be related to dysfunction in the dopamine pathway. In this study, Michael E. Adams and colleagues wanted to identify the ingredients in wasp venom that dictate this behavior.

The researchers milked wasps for their venom and then analyzed the components using liquid chromatography and mass spectrometry. They identified a new family of alpha-helical peptides and named them

ampulexins. To test their function, the team injected the most abundant venom peptide into cockroaches. Afterward, the bugs needed, on average, a 13-volt electric shock to the foot to get them moving, while an average of 9 volts sufficed prior to the injection, suggesting the peptides help the wasp immobilize its prey. Future work will focus on identifying cellular targets of ampulexins, and potentially generating a useful animal model for the study of Parkinson's disease treatments.

More information: Eugene Moore et al. Ampulexins: A New Family of Peptides in Venom of the Emerald Jewel Wasp, Ampulex compressa, *Biochemistry* (2018). DOI: 10.1021/acs.biochem.7b00916

Abstract

The parasitoid wasp Ampulex compressa injects venom directly into the brain and subesophageal ganglion of the cockroach Periplaneta americana, inducing a seven to ten day lethargy termed hypokinesia. Hypokinesia presents as a significant reduction in both escape response and spontaneous walking. We examined aminergic and peptidergic components of milked venom with HPLC and MALDI-TOF mass spectrometry. HPLC coupled with electrochemical detection confirmed presence of dopamine in milked venom, while mass spectrometry revealed that the venom gland and venom sac have distinct peptide profiles, with milked venom predominantly composed of venom sac peptides. We isolated and characterized novel alpha-helical, amphipathic venom sac peptides that constitute a new family of venom toxins termed ampulexins. Injection of the most abundant venom peptide, ampulexin-1, into the subesophageal ganglion of cockroaches resulted in a short-term increase in escape threshold. Neither milked venom nor venom peptides interfered with growth of Escherichia coli or Bacillus thuringiensis on agar plates and exposure to ampulexins or milked venom did not induce cell death in Chinese hamster ovary cells (CHO-K1) or Hi5 cells (Trichoplusia ni).

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