

Bugs, plants and peptides – Unleashing the power of chemical ecology for sustainable crop protection

Aurélien Bigot

Syngenta Crop Protection AG, Schaffhauserstrasse 4332 Stein, Switzerland
aurelien.bigot@syngenta.com

Farmers face globally a shrinking toolkit for crop protection amid tighter regulations, increased public demand for residue-free food, challenges from resistance, and the negative impacts of climate change. At Syngenta Biologicals we are committed to enhancing agricultural productivity in concert with sustainable practices. We pledge to bring to market cutting-edge biocontrol solutions, and one such pioneering approach in our arsenal is the development of peptide-based insecticides. These novel bioinsecticides are designed to provide growers with a targeted and environmentally benign approach to insect pest management, ensuring no residual presence as they degrade into harmless natural amino acids.

Peptide toxins from natural insect predators, such as spiders and scorpions, represent attractive candidates for this purpose as they have been long known for their specificity, potency and rapid onset of toxic effects when injected into insect herbivores (1). However, their effectiveness is markedly diminished when administered orally, a route for which they have not naturally adapted through evolution, particularly in combating the highly damaging pests of the Lepidoptera order (2). We have uncovered that peptides of plant origin from the cyclotide family, kalata B1 and B2, when combined with various animal-derived neurotoxins significantly enhance their potency in controlling highly destructive caterpillars through oral ingestion (3). We report herein our efficacy findings on this concept and our mechanistic investigations, proposing a mode of action wherein cyclotides disrupt the structural integrity of the lepidopteran midgut barrier. This disruption facilitates the translocation of neurotoxins across the gut epithelium into the hemocoel, where they can manifest their lethal effects on the nervous system of insects.



1. T.N.T Ho, A. Turner, S.H. Pham, H.T. Nguyen, L.T.T. Nguyen, L.T. Nguyen, *et al.* Cysteine-rich peptides: From bioactivity to bioinsecticide applications. *Toxicon* **2023**, *230*, 107173-.
2. G.F. King, M.C. Hardy, Spider-venom peptides: structure, pharmacology, and potential for control of insect pests. *Annu. Rev. Entomol.* **2013**, *58*, 475–496.
3. F. Benfatti, A. Bigot, D.J. Craik, Y.H. Huang, Q. Kaas, M. Schiebler, *et al.* Compositions comprising cyclotides and other insecticidal peptides and uses thereof. WO2022136442A2, **2022**