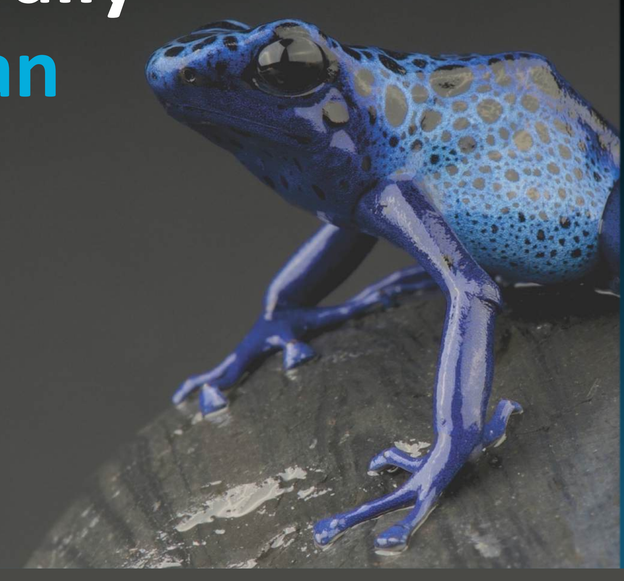
Butterfly Pea (*Clitoria ternatea*) - Remarkable, naturally pollinator safe, botanical one step closer to European market

Tom Hargreaves
Co-Owner and Group Director

Ann Vermaete
Regulatory & Development Manager

Nick Watts
Director

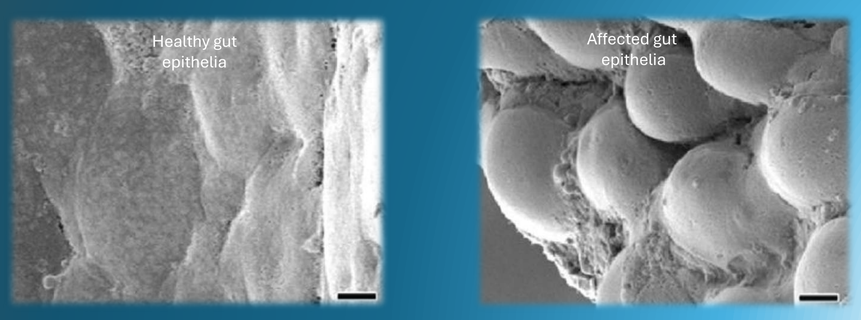


Background

- Researchers found that butterfly pea (*Clitoria ternatea*) fields next to pest-infested cotton remained mostly unaffected.
- Extract of the aerial parts of butterfly pea showed toxicity to phytophagous insect larvae in laboratory assays and also modified pest behavior, acting both as a feeding and oviposition deterrent.

Lepidoptera pest *Helicoverpa armigera* (cotton bollworm)

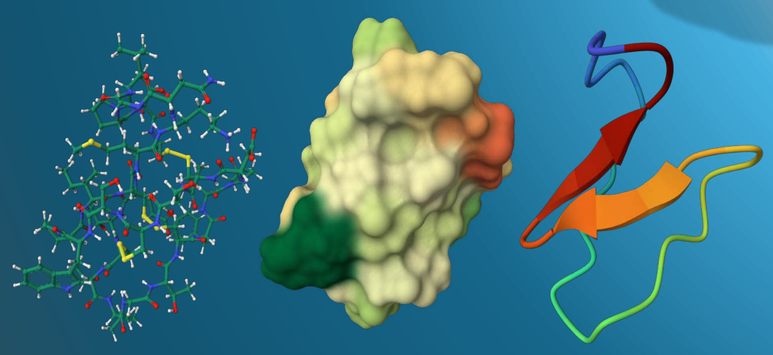
- Component analysis of the extract showed the presence of common phenolic compounds, but also significant amount of a new class of peptide - cyclotides.
- Isolated cyclotides where found to cause similar toxic (gut membrane disruption) effects to insect larvae as the extract.



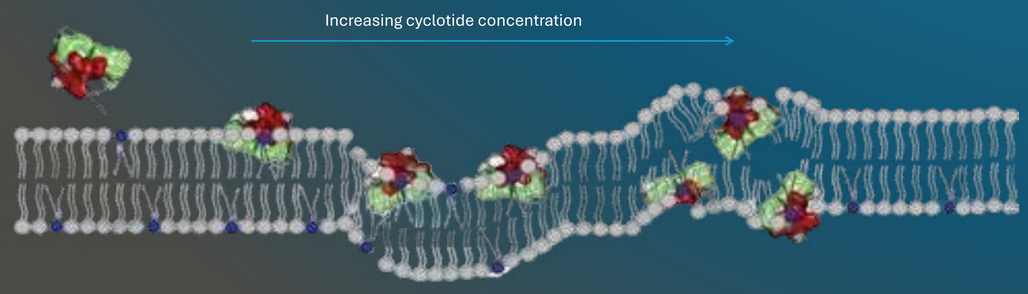
Henriques and Craik, 2017

Mode of action

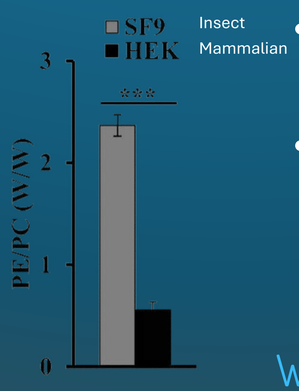
- Cyclotides: globular micro-proteins with a unique head-to-tail cyclized backbone, stabilized by three disulfide bonds forming a cystine knot.



- Hydrophobic face (green), bioactive face (orange/red).
- Highly stable, resistant to heat and enzymatic cleavage.
- Bioactive face binds phosphatidylethanolamine (PE) in lipid bi-layer membrane, hydrophobic face inserts into layer causing disruption leading to breach.



After Henriques *et al.*, 2015; Katala b1



Dawaliby *et al.*, 2016

- Specificity: Insects have > 4 x PE content in membranes compared to mammals.

Regulatory position

- A botanical extract must follow the data requirements of Part A of Regulation (EC) No 1107/2009, unlike microbials, there are no specific regulatory provisions.
- Previously, regulatory uncertainty and changing interpretations of requirements has hampered the submission in the EU, specifically regarding:
  - Specification of the active substance
  - Identification of relevant components of concern
  - Analytical methodology for the above
- Butterfly pea is widely consumed by human populations and is an excellent livestock forage and soil improving crop.
  - Unlikely to have any component of concern
    - Biocontrol through toxicity / repellence / deterrent
      - Regulatory position developed through common understanding of the issues after problem formulation with collaborative RMS (Ctgb)
        - Focus is on potential components of concern
        - Similar approach to microbial secondary metabolite assessment
          - Proving component fraction responsible for biocontrol activity; bio-guided fractionation

Blue Frog Scientific

- We specialize in handling complex regulatory challenges, combining innovation, logic, and determination.
- Our expertise spans agrochemicals, chemicals, pharmaceuticals, veterinary medicines, and biocides.
- Since 2010, we've grown from 2 staff to 34 across four locations in two countries.
- We are innovative problem solvers, building trusted relationships with clients.
- To find out more see our web site:

  www.bluefrogscientific.com

  or visit us at Booth 026

WE ARE BLUE FROG
ACHIEVING REGULATORY COMPLIANCE THROUGH THE APPLICATION OF GOOD SCIENCE, INNOVATIVE THINKING & CLARITY