Multi-omics approach applied to the discovery of biopesticides from endophytic fungi

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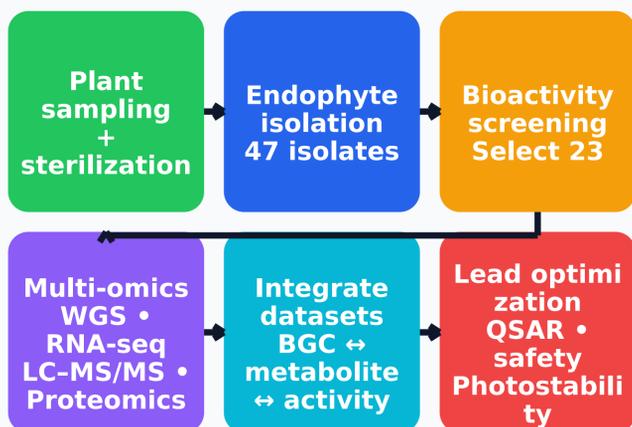Contact: baburbiotechnology@gmail.com

Background

Endophytic fungi are a rich source of secondary metabolites for sustainable pest control. Traditional screening often misses silent pathways and chemical diversity. This work uses an integrated genomics–transcriptomics–metabolomics–proteomics framework to accelerate discovery and de-risk leads.
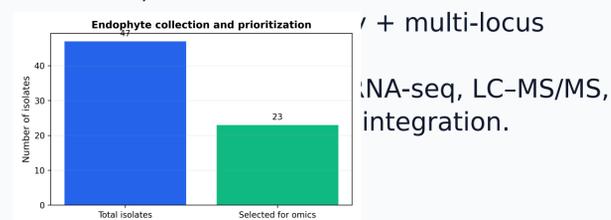
Objectives

• Build a multi-omics pipeline from endophyte isolation to active compound identification.
• Link biosynthetic gene clusters (BGCs) to metabolites and pesticidal activity.
• Prioritize leads with improved stability and reduced mammalian toxicity.

Discovery Workflow

Plant sampling + sterilization → Endophyte isolation 47 isolates → Bioactivity screening Select 23

Multi-omics WGS • RNA-seq LC-MS/MS • Proteomics → Integrate datasets BGC ↔ metabolite ↔ activity → Lead optimization QSAR • safety Photostability

Source plants: Azadirachta indica, Withania somnifera, Ocimum sanctum.
... + multi-locus
... RNA-seq, LC–MS/MS,
... integration.
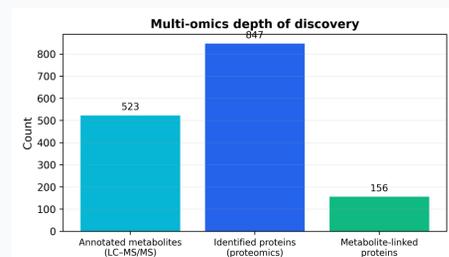

Endophyte collection and prioritization

Genomics and Gene Cluster Mining

Genome size: average 42.3 Mb.
BGC richness: 58–72 clusters per isolate (PKS, NRPS, terpene).
Transcriptomics: ~38% of clusters significantly upregulated under stress conditions.

58-72 BGCs per isolate
Genome mining reveals rich biosynthetic capacity
Biosynthetic gene clusters per isolate (BGCs)
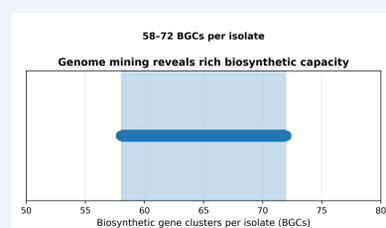
## Metabolomics and Proteomics

Multi-omics depth of discovery

Metabolome: 523 annotated secondary metabolites (LC–MS/MS).
Proteome: 847 proteins detected; 156 linked to specialized metabolite production.

Unlocking Silent Chemistry

Genome mining revealed silent biosynthetic gene clusters. Epigenetic modulation using histone deacetylase inhibitors activated hidden pathways, yielding 18 additional compounds beyond standard cultivation.

Bioactivity Results

Bioactivity highlights: fractions to leads
Lead compound potency (LC$_{50}$, nM; log scale)
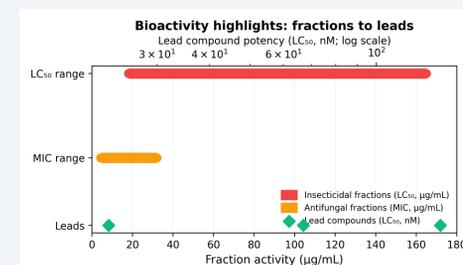
Targets tested: Helicoverpa armigera, Spodoptera litura, Tetranychus urticae; and phytopathogens (Fusarium oxysporum, Botrytis cinerea).
Active fractions: 12 insecticidal (LC$_{50}$ 18–165 µg/mL) and 8 antifungal (MIC 4.2–32 µg/mL).
Leads: LC$_{50}$ of 23 nM, 67 nM, and 142 nM against H. armigera larvae.

Mode of Action and Environmental

Mechanism-of-action and environmental behavior
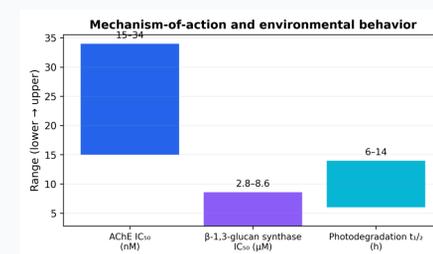
Insect mode of action: AChE interference (IC$_{50}$ 15–34 nM).
Antifungal mode of action: β-1,3-glucan synthase inhibition (IC$_{50}$ 2.8–8.6 µM).
Environmental fate: rapid photodegradation (t$_{1/2}$ 6–14 h under sunlight).

Conclusions and Impact

• A comprehensive multi-omics framework accelerates the route from endophyte to validated biopesticide leads.
• Data integration enables BGC–metabolite–activity linking for faster prioritization.
• Lead optimization improved photostability 3.5–6× and reduced mammalian cell toxicity by 40–60%.
• Minimal non-target effects in screening (Daphnia LC$_{50}$ > 500 mg/L; honeybee LD$_{50}$ > 100 µg/bee).