

## Resistance to Microbial Agents: A Growing Challenge in Sustainable Pest Management

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### 1. Introduction

Sustainable agriculture increasingly relies on biological control agents to reduce dependence on chemical pesticides. Among these, microbial biocontrol agents- including bacteria, viruses and fungi- have emerged as eco-friendly and target-specific alternatives. *Bacillus thuringiensis* (Bt), nucleopolyhedroviruses (NPVs), granuloviruses (GVs) and entomopathogenic fungi such as *Beauveria bassiana* and *Metarhizium anisopliae* are widely used for managing insect pests in agricultural ecosystems.

Initially, microbial agents were considered less likely to induce resistance compared to synthetic insecticides. However, continuous exposure, large-scale adoption of Bt crops and repeated field applications have led to the evolution of resistant insect populations. Resistance to microbial agents refers to a heritable reduction in susceptibility that enables insects to survive doses that previously caused mortality. This emerging issue poses a serious threat to the long-term sustainability of biological pest management (Cory, 2017).

### 2. Microbial Biocontrol Agents and Their Mode of Action

Microbial agents suppress insect pests through highly specific infection or toxin-mediated mechanisms.

#### 2.1 Entomopathogenic Bacteria

*Bacillus thuringiensis* produces crystalline (Cry) proteins during sporulation. When ingested by susceptible larvae these protoxins are activated in the alkaline midgut and bind to specific epithelial receptors such as cadherins, aminopeptidase N (APN), alkaline phosphatase (ALP) and ABC transporters. Binding results in pore formation, midgut cell lysis, septicemia and eventual larval death (Cory and Franklin, 2012).

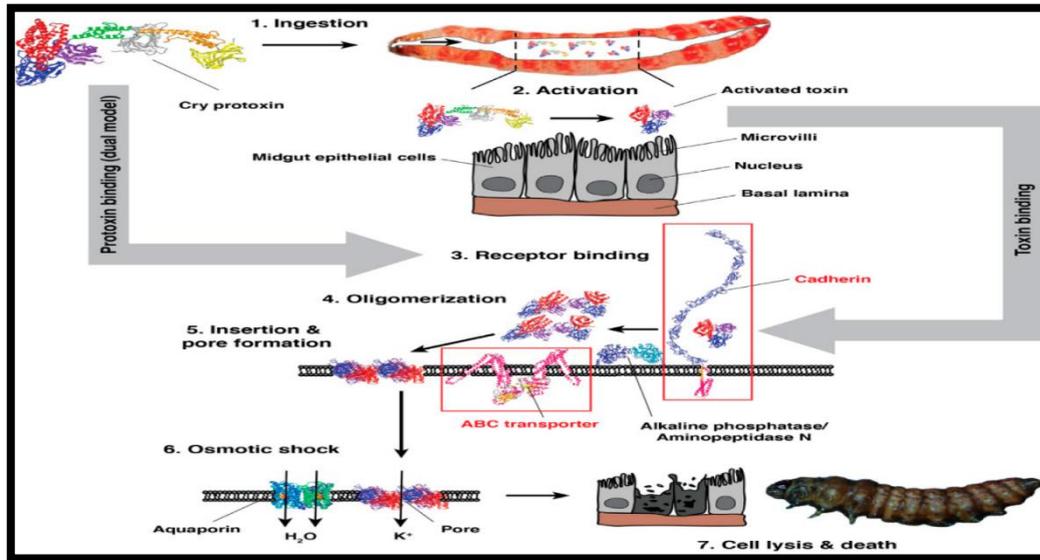


Figure 8: Mode of action of entomopathogenic bacteria

## 2.2 Entomopathogenic Viruses

Baculoviruses infect insects through ingestion of occlusion bodies. In the alkaline midgut, these occlusion bodies dissolve and release virions that invade epithelial cells. The virus multiplies systemically, causing tissue breakdown and liquefaction of the larva, thereby releasing new infectious particles into the environment (McGuire et al. 2001).

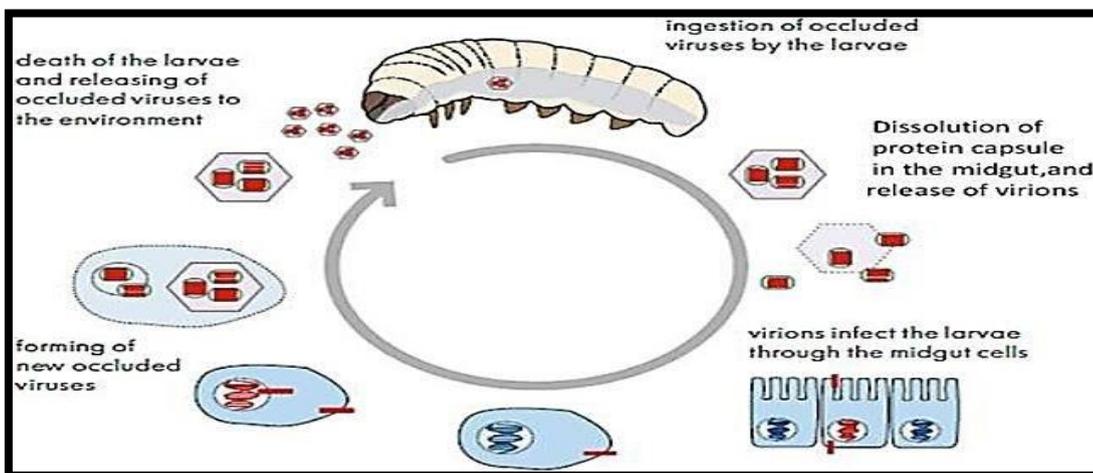


Figure 9: Mode of action of entomopathogenic virus

## 2.3 Entomopathogenic Fungi

Unlike bacteria and viruses, fungi infect insects by direct contact. Fungal conidia attach to the insect cuticle, germinate and penetrate through mechanical pressure and enzymatic degradation. Once inside the hemocoel, the fungus proliferates, produces toxins and causes host death (Rai et al. 2014).

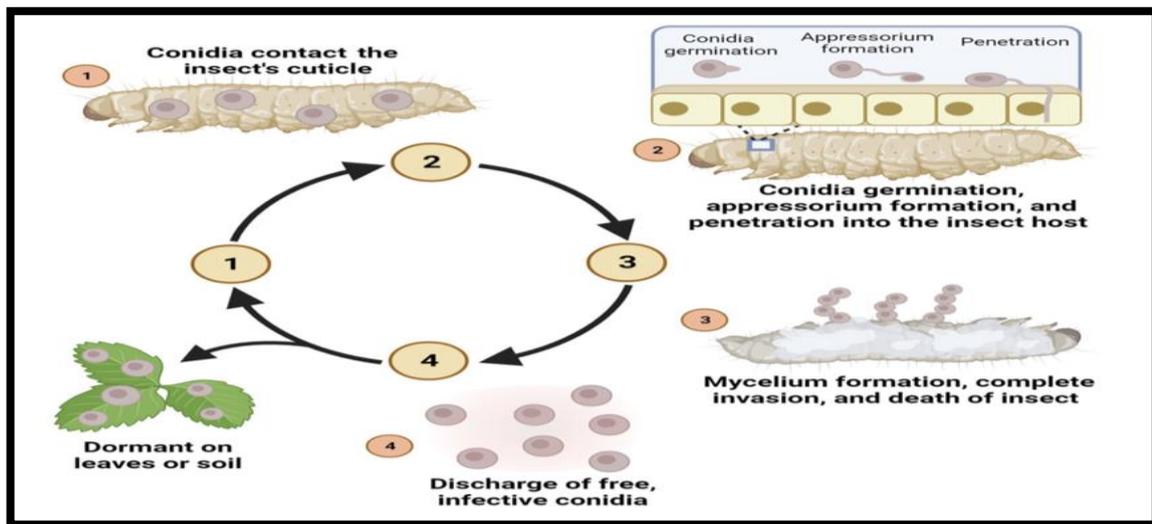


Figure 10 : Mode of action of entomopathogenic fungi

### 3. Mechanisms of Resistance to Microbial Agents

Insects possess diverse physiological and genetic mechanisms that enable survival under microbial exposure.

#### 3.1 Metabolic Resistance

Insects may enhance detoxification systems by increasing the production of proteases, cytochrome P450 monooxygenases, glutathione-S-transferases and antioxidant enzymes. In Bt-resistant populations, altered gut protease activity may prevent proper activation of Cry protoxins (Altinok et al. 2019).

#### 3.2 Altered Target-Site Resistance

Mutations or reduced expression of midgut receptor proteins such as cadherins, APN, ALP or ABC transporters can prevent effective binding of Bt toxins. Without proper binding, pore formation does not occur, allowing larvae to survive toxin ingestion.

#### 3.3 Midgut Barrier and Immune Responses

In the case of viral resistance, strengthened peritrophic matrix (PM) integrity can block viral entry into midgut cells. Insects may also activate immune pathways including RNA interference (RNAi), melanization and apoptosis of infected cells, limiting viral replication.

#### 3.4 Cuticular Modifications

For fungal pathogens, resistance may arise through increased cuticle thickness, altered surface lipids or enhanced melanization, which reduce fungal adhesion and penetration.

#### 3.5 Behavioral Resistance

Insects may avoid treated foliage, reduce feeding, or increase grooming behavior to remove fungal spores. These behavioral adaptations reduce exposure and infection probability (Altinok et al. 2019).

### **3.6 Role of Gut Microbiota**

Recent studies suggest that native gut bacteria can influence susceptibility to viral pathogens. Disruption of the gut microbial community has been shown to increase viral infection intensity, indicating that symbiotic microbes may contribute to resistance mechanisms.

## **4. Current Status of Resistance**

Field-evolved resistance to Bt toxins has been documented in several major agricultural pests, including cotton bollworm, pink bollworm, fall armyworm and diamondback moth in different regions of the world. Resistance to codling moth granulovirus (CpGV) has also been reported in Europe.

Genetic studies indicate that resistance is often autosomal and polygenic and in many cases partially recessive. However, continuous selection pressure can rapidly increase resistance allele frequency, especially in systems lacking proper resistance management strategies (Lacey and Goettel, 1995).

## **5. Impact on Sustainable Agriculture**

The development of resistance to microbial agents has significant agronomic and ecological consequences:

- Reduced effectiveness of biocontrol agents
- Increased reliance on chemical insecticides
- Disruption of Integrated Pest Management (IPM) programs
- Economic losses due to reduced yield and higher input costs
- Acceleration of resistance to other control methods
- Threat to climate-smart and sustainable agriculture goals

Failure of microbial agents may push farmers back toward heavy chemical usage, undermining environmental and human health benefits achieved through biological control.

## **6. Management Strategies for Delaying Resistance**

Sustainable use of microbial agents requires proactive resistance management.

### **6.1 Refugia Strategy**

Planting non-Bt refugia maintains susceptible insect populations that dilute resistance alleles through interbreeding.

### **6.2 Gene Pyramiding**

Incorporating multiple Bt toxins with different modes of action into a single crop variety reduces the probability of simultaneous resistance development (Zahiri et al. 2002).

### 6.3 Integration with IPM

Combining microbial agents with cultural practices, biological control and limited chemical use reduces selection pressure and prolongs effectiveness.

### 6.4 Genetic and Molecular Innovations

Recombinant microbial strains, RNAi-based approaches and improved formulations offer promising avenues for enhancing virulence and overcoming resistance (Zahiri et al. 2002).

### 6.5 Regular Monitoring

Surveillance programs and bioassays are essential for early detection of resistance and timely corrective measures (Sarwar, 2015).

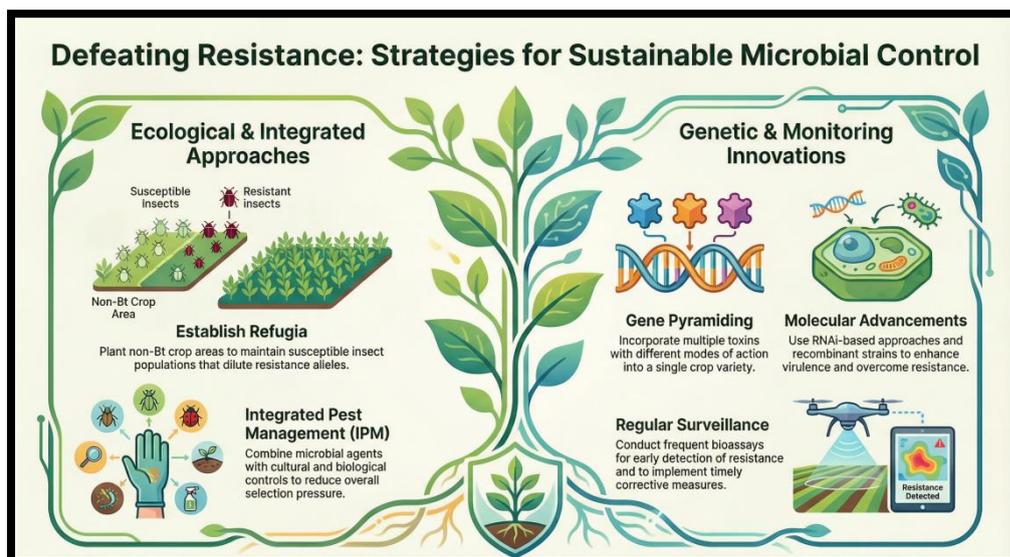


Figure 11: Strategies for Sustainable Microbial Control

## 7. Future Perspectives

Understanding host–pathogen interactions, genetic basis of resistance and microbiome-mediated defense mechanisms will be critical for developing next-generation strategies. Advances in molecular biology, nanotechnology and microbial strain improvement may enhance the durability of biocontrol agents.

For long-term sustainability, microbial agents must be deployed within diversified and adaptive management frameworks rather than as standalone solutions.

## 8. Conclusion

Microbial biocontrol agents remain vital tools in environmentally sustainable pest management. However, insect pests possess remarkable adaptive capacity, enabling them to evolve resistance through metabolic, genetic, structural, immunological and behavioral mechanisms.

To safeguard the efficacy of microbial agents, integrated resistance management strategies such as refugia, gene pyramiding, IPM integration and continuous monitoring are essential. A balanced and science-based approach will ensure that microbial biocontrol continues to contribute to resilient and sustainable agricultural systems.

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