



Insecticide Resistance in Agricultural Insect Pests: Mechanisms, Monitoring and Management Strategies

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Insecticides are essential for managing agricultural pests, but repeated and intensive use can select resistant individuals, reducing their effectiveness and threatening sustainable pest management. Insecticide resistance is a heritable decrease in pest susceptibility that causes treatment failure despite correct insecticide use. Major mechanisms include target-site modification, metabolic detoxification, reduced cuticular penetration and behavioural avoidance. Target-site resistance involves mutations affecting proteins such as acetylcholinesterase, sodium channels, nicotinic acetylcholine receptors, GABA receptors and ryanodine receptors. Metabolic resistance commonly involves cytochrome P450 monooxygenases, esterases, glutathione S-transferases, UDP-glycosyltransferases and ABC transporters. Multiple mechanisms may occur simultaneously, resulting in cross- or multiple resistance. Effective management requires regular resistance monitoring through bioassays, biochemical tests and molecular diagnostics. Mode-of-action diversification, rotation, mixtures, synergists, biological control, resistant varieties, cultural practices and integrated pest management are essential. Sustainable resistance management therefore requires continuous surveillance and locally adapted integration of chemical and non-chemical strategies.

Keywords: biological control, cross-resistance, insecticide resistance, metabolic resistance, resistance monitoring, target-site resistance

Introduction

The continuing evolutionary conflict between insect pests and humans remains heavily dependent on synthetic insecticides, despite growing concerns about resistance, environmental contamination, human health and biodiversity (Ádám *et al.*, 2024; Wan *et al.*, 2025). Pests cause substantial losses in crops, forests, stored commodities and animal feed, while some transmit viral, bacterial and parasitic diseases (Sparks *et al.*, 2020). Global yield losses average approximately 21.5% in wheat, 30% in rice, 22.5% in maize, 17% in potato and 21% in soybean, with the greatest effects occurring in food-insecure regions (Savary *et al.*, 2019). Invasive insect pests also generate annual economic costs exceeding US\$70 billion and health-related impacts of more than US\$6.9 billion (FAO, 2023). Although organophosphates, pyrethroids and neonicotinoids have provided effective control, resistance has been documented in more than 600 arthropod species. Resistance is a heritable reduction in pest sensitivity that causes repeated control failure when insecticides are correctly applied according to label instructions (Sparks *et al.*, 2020; IRAC, 2025). Genetic variation, rapid reproduction, repeated use of identical modes of action and global trade accelerate resistance evolution and spread (Gould *et al.*, 2018). Consequently, Integrated Pest Management (IPM), combining biological, cultural, mechanical and chemical methods with monitoring, host

resistance and threshold-based decisions, is essential. Diversified IPM reduces selection pressure, protects ecosystems and biodiversity, and supports sustainable agricultural production (Rezende-Teixeira *et al.*, 2022).

Concept and Evolution of Insecticide Resistance

Insecticide resistance begins with variation in pest susceptibility, including differences in detoxification, target-site structure, penetration and behavior. Repeated insecticide use imposes directional selection, favoring individuals that survive exposure and reproduce. Short generation times and high reproductive rates can rapidly increase resistance-associated traits, especially when compounds share the same mode of action. Unnecessary applications and inadequate monitoring intensify selection, whereas threshold-based decisions reduce treatments. Resistant genotypes may spread through insect movement, infested plant material and trade. Therefore, resistance monitoring must integrate field surveillance, diagnostics and management decisions, since local patterns vary with insecticide history, cropping systems, climate and pest genetics (Haddi *et al.*, 2023).

Mechanisms of Insecticide Resistance

Insecticide resistance is mechanistically diverse. The major mechanisms are target-site resistance and metabolic resistance, while reduced penetration through the cuticle and behavioral avoidance can further reduce effective exposure. Additional mechanisms, including sequestration, non-coding RNA regulation and interactions involving the insect microbiome, are emerging areas of research. Importantly, more than one mechanism may occur in the same population, producing complex resistance phenotypes (Al Nagggar *et al.*, 2025).

Target-site resistance

Target-site resistance occurs when changes in an insecticide's molecular target reduce the compound's binding or physiological effect, allowing the insect to survive despite exposure. These changes commonly result from nucleotide substitutions that alter amino acids within functional or insecticide-binding regions of target proteins (Haddi *et al.*, 2023). Important target proteins include acetylcholinesterase (AChE), voltage-gated sodium channels (VGSCs), nicotinic acetylcholine receptors (nAChRs), GABA receptors, and ryanodine receptors (RyRs). Pyrethroid resistance is often associated with knockdown resistance (kdr), caused by mutations in VGSCs, whereas organophosphate and carbamate resistance may involve alterations in AChE. In fall armyworm, the I4790K substitution in RyR is associated with reduced diamide susceptibility, while AChE substitutions such as F290V and A201S are linked with organophosphate and carbamate resistance (Al Nagggar *et al.*, 2025). Molecular assays can detect known resistance alleles and monitor their frequency, complementing phenotypic bioassays. However, mutations should be interpreted alongside phenotypic responses because not every genetic variant cause field-level resistance.

Metabolic resistance

Metabolic resistance occurs when insects increase their capacity to detoxify, transform or eliminate an insecticide before sufficient active compound reaches its physiological target. The major enzyme systems include cytochrome P450 monooxygenases, esterases and glutathione S-transferases. UDP-glycosyltransferases and ATP-binding cassette transporters can also contribute by modifying or transporting insecticide-related compounds. Increased expression, amplification or altered activity of detoxification systems can therefore broaden resistance beyond a single chemical target (Dusfour *et al.*, 2019). The importance of metabolic resistance is illustrated by fall armyworm. Al Nagggar *et al.* (2025) report that elevated CYP, GST and carboxylesterase activity contributes to resistance and that overexpression of CYP6AE43, CYP321A8 and CYP321A9 has been associated with enhanced degradation of chlorantraniliprole. Metabolic resistance is not necessarily restricted to one insecticide because detoxification enzymes can act on chemically different compounds. This helps explain why metabolic mechanisms can generate broad-spectrum resistance and why chemical rotation may fail when the products share susceptibility to the

same detoxification pathway. Biochemical assays can help identify elevated enzyme activity, while qPCR and related molecular approaches can assess expression of candidate detoxification genes. These methods are particularly valuable when combined with bioassays because they connect a measurable physiological mechanism with an observed resistance phenotype.

Reduced cuticular penetration

The insect cuticle forms an important barrier between an insecticide and its internal target. Changes in cuticle composition or structure can slow the penetration of an insecticide, thereby reducing the amount that reaches the site of action. This mechanism is sometimes described as penetration resistance or cuticular resistance. It can act together with metabolic or target-site resistance, making the overall phenotype more difficult to interpret from a single diagnostic test (Sato *et al.*, 2021). In fall armyworm, reduced cuticular penetration has been identified alongside metabolic detoxification, target-site mutations and behavioral avoidance. Such combinations are important because resistance does not always result from one dominant mechanism. A population may reduce insecticide entry, detoxify part of the chemical that enters and simultaneously carry a target-site mutation that reduces the effect of the remaining active compound (Al Naggar *et al.*, 2025).

Behavioural resistance

Behavioural resistance reduces insecticide exposure by changing how insects interact with treated plants or environments. Resistant insects may avoid treated surfaces, alter feeding or resting behaviour, or change activity patterns so that contact with the insecticide is reduced. Behavioural avoidance is therefore different from target-site resistance because the insect survives primarily by limiting exposure rather than by becoming physiologically insensitive after the chemical reaches its target. Behavioural avoidance has been reported as one component of the resistance phenotype in fall armyworm. Its importance is greatest when exposure is spatially or temporally uneven, because insects capable of avoiding treated tissues may receive doses below those required for mortality. Behavioural and penetration mechanisms can consequently reinforce one another (Al Naggar *et al.* (2025).

Emerging mechanisms and complex resistance

Emerging mechanisms include sequestration, non-coding RNAs, and insect microbiomes, which may alter insecticide availability, gene expression, or xenobiotic metabolism (Al Naggar *et al.*, 2025). Resistance can also impose fitness costs affecting fecundity or development. However, these effects vary among populations, so resistance decline after selection withdrawal cannot be assumed.

Cross-resistance and multiple resistance

Cross-resistance occurs when one resistance mechanism reduces susceptibility to multiple insecticides, whereas multiple resistance refers to the coexistence of different mechanisms that provide resistance to several insecticides. These phenomena complicate management because an apparently different product may still be compromised by an existing resistance mechanism. Al Naggar *et al.* (2025) emphasize that CYP upregulation and target-site mutations such as *kdr* can contribute to resistance across chemical classes. Consequently, rotation is most useful when the alternative insecticides have genuinely distinct modes of action and are not compromised by the same resistance mechanism.

Table 1. Major mechanisms of insecticide resistance and their monitoring implications

Mechanism	Basic process	Examples	Useful monitoring approach
Target-site	Alteration of the insecticide's molecular target reduces binding or effect.	AChE, VGSC, nAChR, GABA receptor, RyR	Allele-specific PCR, sequencing, phenotypic bioassays

Metabolic	Enhanced detoxification or elimination before the insecticide reaches its target.	P450s, esterases, GSTs; UGTs and ABC transporters	Enzyme assays, qPCR/expression assays, bioassays
Cuticular	Reduced or delayed penetration through the insect cuticle.	Modified cuticle/penetration barriers	Penetration studies plus bioassay/mechanistic tests
Behavioral	Avoidance reduces contact or ingestion of the insecticide.	Avoidance of treated surfaces or altered activity	Behavioral assays plus exposure and efficacy studies

Monitoring and Detection of Insecticide Resistance

Resistance monitoring is the bridge between resistance biology and practical management. Its purpose is to detect changes in susceptibility early enough to inform insecticide selection and management decisions. Monitoring can be based on phenotype, biochemical mechanism, molecular markers, or a combination of these approaches. No single method provides a complete picture in all pest systems, particularly where several resistance mechanisms occur simultaneously.

Field surveillance and representative sampling

Monitoring begins with systematic collection of pest populations from relevant production areas and seasons. Sampling should represent the geographic and management conditions in which insecticides are being used. Repeated surveillance is important because resistance frequencies can change over time as selection pressure changes.

Phenotypic bioassays

Phenotypic bioassays measure how a pest population responds to defined concentrations of an insecticide. Dose-response assays can estimate lethal concentrations such as LC₅₀ or LC₉₀, while diagnostic-dose assays can classify individuals or populations according to susceptibility at a selected concentration. Results can be compared with a susceptible reference strain or historical baseline to calculate a resistance ratio. Bioassays remain essential because they demonstrate whether the resistance mechanism translates into reduced insecticide susceptibility (Haddi *et al.*, 2023). However, bioassays require standardized insect age, stage, diet, exposure route, temperature and other conditions. Differences in experimental design can make comparisons among studies difficult. Field efficacy should therefore be considered alongside laboratory results, particularly when environmental conditions, application coverage or insect behavior influence actual exposure.

Biochemical monitoring

Biochemical assays can identify elevated detoxification activity, particularly involving esterases, GSTs and P450-associated pathways. These assays are useful for investigating metabolic resistance and for selecting candidate mechanisms for further molecular analysis. Their limitation is that elevated enzyme activity does not always prove that a specific enzyme causes field-level resistance; it is strongest when enzyme results, gene-expression data and bioassay responses support the same interpretation (Haddi *et al.*, 2023).

Molecular monitoring

Molecular diagnostics can detect known resistance-associated mutations or changes in expression of candidate resistance genes. Allele-specific PCR and qPCR are among the approaches highlighted by Al Naggar *et al.* (2025). For example, molecular monitoring can track mutations in targets such as VGSC or RyR, while expression assays can examine candidate detoxification genes. High-throughput sequencing approaches can extend surveillance to multiple loci and help characterize complex resistance profiles. Molecular monitoring is especially valuable for early warning because a resistance allele can sometimes

be detected before a severe field-control failure becomes obvious. Nevertheless, molecular detection should be interpreted with biological context. A resistance allele may occur at low frequency, its effect may vary with genetic background and a pest may possess additional mechanisms not captured by the selected marker (Idier *et al.*, 2023).

Integrated interpretation of monitoring data

The most informative surveillance system combines phenotype, mechanism and field information. A practical sequence is: collect representative populations; conduct a standardized bioassay; investigate biochemical or molecular mechanisms when resistance is detected; estimate the frequency or intensity of resistance; and use the results to modify insecticide choice and IPM tactics. Such surveillance-driven decision thresholds are emphasized in the resistance-management framework of Al Naggar *et al.*, (2025).

Management Strategies for Insecticide Resistance

Resistance management aims to reduce selection for resistance while maintaining effective pest suppression. Because resistance is driven by interacting biological and operational factors, no single tactic is universally sufficient. The most durable approach is a multitactic system that reduces unnecessary insecticide exposure, diversifies mortality sources and uses surveillance to adapt decisions.

Mode-of-action diversification and rotation

Mode-of-action (MoA) rotation is a central insecticide-resistance management principle. Insecticides should be differentiated according to their biochemical target rather than simply by trade name or active-ingredient identity. Rotating among genuinely distinct modes of action can reduce continuous selection for the same resistance mechanism. However, rotation is not automatically effective: it is weakened when cross-resistance exists or when resistant individuals are already common. Al Naggar *et al.*, (2025) therefore emphasize mechanism-informed rotation supported by surveillance.

Mixtures and synergists

Mixtures can reduce the probability that an individual carrying resistance to one component survives exposure to both components, provided that the components have appropriate independence of action and are used according to evidence-based recommendations. Synergists can also suppress detoxification pathways and restore activity against populations in which metabolic resistance is important. Piperonyl butoxide, for example, can inhibit P450-mediated detoxification in suitable systems. However, mixtures and synergists should not be treated as universal solutions because pre-existing cross-resistance or shared detoxification mechanisms can compromise their effectiveness (Haddi *et al.*, 2023).

Refuges and preservation of susceptible genotypes

Refuges are used in particular resistance-management systems to maintain susceptible insects that can mate with resistant survivors, thereby diluting resistance alleles. They are especially important in transgenic crop systems where insecticidal traits create strong and persistent selection. Al Naggar *et al.*, (2025) describe structured non-Bt plantings as a strategy for preserving susceptible genotypes in Bt crop systems. Refuge design and compliance must be appropriate to the crop, pest, trait and regulatory framework.

Biological control and biopesticides

Biological control diversifies pest mortality away from synthetic insecticides and can therefore reduce chemical selection pressure. Predators, parasitoids and entomopathogens can be incorporated into IPM where ecological conditions permit. Al Naggar *et al.*, (2025) highlight parasitoids, entomopathogenic fungi and viruses as components of sustainable pest suppression. Biological control can be especially useful when combined with selective insecticides that conserve natural enemies. Pegalepo *et al.*, (2025) provide practical examples from rice systems in Sub-Saharan Africa. The review reports the use of parasitoids, predators, *Beauveria bassiana*, *Bacillus thuringiensis*, neem-based products and pheromone traps against different rice pests. In Tanzania, neem-based IPM reduced reliance on synthetic pesticides, while farmer field schools in Zambia supported farmer knowledge of

environmentally friendly management. These examples demonstrate how non-chemical tactics can be adapted to local farming systems and integrated with other controls.

Host-plant resistance

Host-plant resistance reduces pest fitness or preference through plant traits and therefore provides pest suppression without direct insecticide selection. The rice review documents resistant or tolerant rice varieties as an important component of sustainable pest management. Examples include Bph3 and Bph14-associated resistance to brown planthopper and resistant rice materials used against African rice gall midge (**Zeng *et al.*, (2023)**). Such traits can reduce pest pressure and complement biological and chemical tactics. Host resistance is particularly valuable in resistance management because it attacks pest populations through a mechanism different from insecticide toxicity. However, resistance traits themselves can impose selection on pests, so durable deployment should be combined with other tactics and monitored for changes in pest adaptation.

Cultural and mechanical practices

Cultural practices can reduce pest abundance, exposure and habitat without selecting directly for insecticide resistance. The weed and alternative-host management, destruction of volunteer plants, intercropping, sanitation and other practices as components of sustainable pest management. Such approaches are especially useful when they are integrated before pest populations reach damaging levels **Pegalepo *et al.*, (2025)**.

Monitoring-based IPM

Integrated Pest Management provides the overall framework in which resistance management can operate. IPM begins with correct pest identification, monitoring and understanding of pest biology. Management decisions are then based on pest density, crop stage, expected damage and available tactics rather than routine calendar spraying. The rice review emphasizes that limited awareness, extension access and pest-control resources can restrict IPM adoption; therefore, farmer education and locally appropriate recommendations are important components of resistance management (**Kinyanjui *et al.*, (2025)**).

Mechanism-informed and adaptive management

The strongest resistance-management programs are adaptive. When surveillance indicates metabolic resistance, management may prioritize compounds less vulnerable to the identified detoxification pathway and strengthen non-chemical controls. When a target-site mutation becomes frequent, products relying on that target should be reassessed. Where fitness costs are demonstrated, temporary withdrawal of the affected insecticide may allow susceptible genotypes to increase, although this strategy must be supported by population-specific evidence. **Al Naggar *et al.*, (2025)** propose a dynamic model that combines molecular diagnostics, synergist-enhanced formulations, ecological management, biological control and knowledge of fitness costs.

Table 2. Resistance-management tactics and their role

Tactic	Main purpose	Key consideration
MoA rotation	Reduce repeated selection on the same biochemical target.	Use genuinely different MoAs and account for cross-resistance.
Mixtures/synergists	Reduce survival of insects carrying single resistance mechanisms or inhibit detoxification.	Use only where compatibility and resistance patterns support the approach.
Refuges	Maintain susceptible genotypes and dilute resistance alleles.	Requires appropriate design and compliance.
Biological control	Add non-chemical sources of mortality.	Conserve natural enemies and avoid disruptive broad-spectrum sprays.

Tactic	Main purpose	Key consideration
Host resistance	Reduce pest establishment, feeding or development.	Combine with other tactics to reduce selection on the resistance trait.
Cultural/mechanical control	Lower pest density and reduce reliance on chemicals.	Adapt to crop and local farming conditions.
Monitoring-based IPM	Match control decisions to pest density and resistance status.	Requires regular surveillance and farmer/extension capacity.

Emerging Technologies and Future Directions

Future resistance management will increasingly rely on rapid diagnostics, molecular surveillance, and data-informed decisions. qPCR-based expression assays and allele-specific PCR can support real-time monitoring of detoxification genes and target-site mutations, while high-throughput sequencing can characterize multiple resistance loci (Al Nagggar *et al.*, 2025). Shared resistance databases may improve comparison of resistance patterns across regions. RNA interference (RNAi), including transgenic and sprayable approaches, offers an alternative to conventional insecticides by targeting essential insect genes, but requires appropriate resistance-management strategies rather than repeated reliance on a single technology (Haddi *et al.*, 2023). New insecticidal chemistries can further diversify available modes of action. Fluxametamide, an isoxazoline (Group 30), showed a relatively small increase in LC50 and fitness costs in a selected fall armyworm strain, although continued monitoring remains necessary (Lv *et al.*, 2024). Biotechnology, molecular diagnostics, and precision agriculture also offer opportunities in rice pest management. Their successful adoption requires farmer training, policy support, infrastructure, and region-specific research, particularly in smallholder systems (Pegalepo *et al.*, 2025).

Major Challenges in Resistance Management

One major challenge is the speed with which resistance can evolve relative to the development and registration of new insecticides. Once a resistance mechanism becomes common, switching products may provide only temporary relief if cross-resistance is present. Another challenge is incomplete surveillance. Without repeated sampling and standardized bioassays, resistance may be detected only after field failure has become widespread (Dusfour *et al.*, 2019) (Al Nagggar *et al.*, 2025). Mechanistic complexity is another obstacle. A pest population may carry target-site and metabolic resistance simultaneously, while reduced penetration or behavioral avoidance further changes effective exposure. This makes single-marker diagnostics insufficient in some systems. Monitoring must therefore evolve from simple susceptibility measurements toward integrated resistance profiling (Al Nagggar *et al.*, 2025). Implementation constraints are equally important. Farmers may have limited access to alternative products, diagnostic services, biological control agents or extension advice. In such situations, recommendations that require frequent changes in inputs may be difficult to implement (Pegalepo *et al.*, 2025). Finally, resistance management requires coordination among researchers, diagnostic laboratories, extension systems, regulators, agrochemical stakeholders and farmers. The objective is not merely to identify resistant insects but to ensure that the information changes management before control options are lost (Pegalepo *et al.*, 2025).

Conclusions

Insecticide resistance is an evolutionary response to selection pressure and a major constraint on chemical pest management. Resistance can develop through target-site modification, enhanced metabolic detoxification, reduced penetration, and behavioral avoidance, with multiple mechanisms sometimes occurring together and producing cross- or multiple resistance (Haddi *et al.*, 2023). Regional variation in resistance, including that observed in

fall armyworm, highlights the importance of local and continuous surveillance. Effective management should therefore move from reactive product replacement toward proactive, surveillance-driven strategies. Standardized bioassays, biochemical assays, and molecular diagnostics can collectively characterize resistance phenotypes, detoxification processes, and resistance-associated mutations. Management should diversify pest-control tactics through mode-of-action rotation, appropriate mixtures or synergists, refuges where relevant, host-plant resistance, cultural practices, biological control, biopesticides, and monitoring-based IPM. Evidence from rice systems in Sub-Saharan Africa demonstrates the value of integrating resistant varieties, natural enemies, biopesticides, cultural practices, and farmer training. Strategic insecticide use can slow resistance evolution while maintaining effective crop protection (Al Nagggar et al., 2025).

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