

International Journal of Advanced Biochemistry Research



ISSN Print: 2617-4693
ISSN Online: 2617-4707
NAAS Rating (2026): 5.29
IJABR 2026; SP-10(8): 1749-1755
www.biochemjournal.com
Received: 08-06-2026
Accepted: 12-07-2026

KS Kolhe

M.Sc. (Agri.) Student,
Department of Entomology,
Mahatma Phule Krishi
Vidyapeeth, Government
College of Agriculture, Dhule,
Maharashtra, India

AS Mahale

Assistant Professor,
Department of Entomology,
Mahatma Phule Krishi
Vidyapeeth, Government
College of Agriculture, Dhule,
Maharashtra, India

PB Toradmal

M.Sc. (Agri.) Student,
Department of Entomology,
Mahatma Phule Krishi
Vidyapeeth, Government
College of Agriculture, Dhule,
Maharashtra, India

AK Mali

Assistant Professor,
Department of Entomology,
Mahatma Phule Krishi
Vidyapeeth, Government
College of Agriculture, Dhule,
Maharashtra, India

PS Magdum

M.Sc. (Agri.) Student,
Department of Entomology,
Mahatma Phule Krishi
Vidyapeeth, Government
College of Agriculture, Dhule,
Maharashtra, India

Corresponding Author:**KS Kolhe**

M.Sc. (Agri.) Student,
Department of Entomology,
Mahatma Phule Krishi
Vidyapeeth, Government
College of Agriculture, Dhule,
Maharashtra, India

Genomic changes in insect body resistance against insecticides

KS Kolhe, AS Mahale, PB Toradmal, AK Mali and PS Magdum

DOI: <https://www.doi.org/10.33545/26174693.2026.v10.i8Ss.9665>

Abstract

Insecticide resistance has emerged as one of the most critical challenges threatening sustainable agriculture, food security, and ecosystem stability worldwide. The extensive and repeated use of synthetic insecticides has imposed strong selection pressure on insect populations, resulting in the rapid evolution and spread of resistant pest strains. This review highlights the major factors responsible for insecticide resistance development under field conditions, including biological characteristics, genetic variability, operational practices, agricultural management systems, and ecological and environmental influences. The molecular and biochemical mechanisms underlying resistance are discussed, with emphasis on target-site resistance involving mutations in voltage-gated sodium channels, acetylcholinesterase, and GABA receptors, along with metabolic resistance mediated by detoxification enzymes such as cytochrome P450 monooxygenases, glutathione S-transferases, and esterases. Behavioural and penetration resistance mechanisms, as well as cross-resistance and multiple resistance phenomena, further complicate effective pest management. The consequences of insecticide resistance include reduced efficacy of control measures, increased production costs, pest resurgence, environmental contamination, loss of biodiversity, and threats to global food security. Sustainable resistance management approaches, including integrated pest management (IPM), insecticide rotation, biological control, biopesticides, host plant resistance, resistance monitoring, and judicious insecticide use, are essential for delaying resistance evolution. Future strategies involving genomic technologies, CRISPR-based approaches, RNA interference (RNAi), artificial intelligence, precision agriculture, and climate-smart pest management offer promising opportunities for sustainable pest suppression. Effective collaboration among researchers, farmers, industries, and policymakers is crucial to develop innovative and environmentally responsible strategies for managing insecticide resistance and ensuring long-term agricultural sustainability.

Keywords: Insecticide resistance; Target-site resistance; metabolic resistance; Genomic mechanisms; integrated pest management; Sustainable agriculture.

Introduction

The continuous struggle between humans and insect pests has relied heavily on synthetic insecticides as the principal means of pest management. However, the increasing occurrence of insecticide resistance, together with growing concerns regarding environmental degradation, biodiversity loss, and risks to human health, has challenged the long-term sustainability of this approach (Adam *et al.*, 2024; Wan *et al.*, 2025) ^[1, 67]. Prolonged and often excessive application of insecticides has imposed intense selection pressure on insect populations, accelerating the evolution of resistant strains and creating serious challenges for modern agriculture, public health, and ecosystem stability.

Insect pests cause substantial losses in agricultural crops, forests, stored products, and livestock feed, while numerous species act as vectors of viruses, bacteria, protozoa, and parasitic pathogens that threaten human and animal health (World Health Organization [WHO], 2024). Beyond direct crop damage, insect infestations compromise global food security, disrupt ecosystem functioning, and impose significant economic losses, particularly in low- and middle-income countries. Recent evidence suggests that climate change, agricultural intensification, and global trade are accelerating the spread, establishment, and persistence of insect pests by expanding their geographic distribution, increasing the number of generations per year, and enhancing their capacity to damage crops. Under a 2°C global warming scenario, insect pest-induced yield losses are projected to increase by

approximately 46 per cent in wheat, 19 per cent in rice, and 31 per cent in maize compared with current levels, highlighting the escalating challenge of sustainable crop protection and global food security (Ma *et al.*, 2025; FAO, 2025). Among the most destructive invasive pests, the tomato leaf miner (*T. absoluta*), native to South America, has spread to more than 100 countries across Europe, Africa, Asia, and the Middle East since its introduction. Under severe infestations, it can cause yield losses of up to 80–100% in tomato if left unmanaged, resulting in substantial economic damage and increased reliance on chemical insecticides. Moreover, the rapid evolution of resistance to multiple insecticide classes has further complicated its management, increased production costs and reducing the effectiveness of available control measures, thereby making *T. absoluta* one of the most economically important invasive agricultural pests worldwide (Desneux *et al.*, 2010; Biondi *et al.*, 2018)^[13, 24]. The global dependence on chemical insecticides remains substantial owing to their indispensable role in safeguarding agricultural productivity and public health. According to the latest FAOSTAT statistics, global agricultural pesticide use reached 3.73 million tonnes of active ingredients in 2023, representing a two-fold increase since 1990 despite a slight decline compared with 2022. Herbicides accounted for the largest share of pesticide consumption (51%), followed by insecticides (22%), fungicides and bactericides (22%), and other pesticide classes (5%). Brazil was the largest pesticide-consuming country (800.65 thousand tonnes), followed by the United States (429.50 thousand tonnes), Indonesia (294.94 thousand tonnes), Argentina (262.51 thousand tonnes), and China (229.03 thousand tonnes), while India ranked 17th globally with an estimated pesticide consumption of 40.09 thousand tonnes (FAO, 2025). Insecticides primarily disrupt essential physiological processes in insects, particularly neural transmission and cellular energy metabolism, and have contributed significantly to increased agricultural productivity since the Green Revolution. Several major classes of insecticides, including organophosphates, carbamates, pyrethroids, neonicotinoids, diamides, and spinosyns, have played a pivotal role in the management of agricultural and public health pests. However, their intensive and repeated use has imposed strong selection pressure on insect populations, resulting in the evolution of insecticide resistance in more

than 600 arthropod species, with thousands of documented resistance records reported worldwide. Consequently, the efficacy of many conventional insecticides has declined substantially, posing a major threat to sustainable pest management, agricultural productivity, and global food security (Sparks & Nauen, 2015; Bass *et al.*, 2015; Arthropod Pesticide Resistance Database [APRD], 2025)^[12, 48]. Insecticide resistance develops when heritable genetic changes reduce the susceptibility of pest populations, ultimately resulting in repeated control failures despite the correct application of insecticides according to recommended practices. The Insecticide Resistance Action Committee (IRAC, 2025) defines insecticide resistance as, "A heritable change in the sensitivity of a pest population that is reflected in the repeated failure of a product to achieve the expected level of control when used according to the label recommendation for that pest species." The continued evolution of insecticide resistance has substantially reduced the efficacy of many conventional insecticides, making the management of economically important insect pests increasingly difficult. As resistance becomes more widespread, growers often respond by increasing application frequency, applying higher doses, or shifting to alternative insecticides, thereby intensifying selection pressure and accelerating the evolution of resistant populations. Excessive reliance on insecticides also contributes to environmental contamination, disrupts beneficial arthropods and biodiversity and poses risks to human and animal health. The evolution of resistance is driven by multiple biological and operational factors including pre-existing genetic variation, high reproductive capacity, short generation times, gene flow, and the repeated use of insecticides with the same mode of action, which promote the rapid selection and spread of resistance-conferring alleles within pest populations. Consequently, sustainable insecticide resistance management (IRM) strategies including insecticide rotation based on mode of action, integrated pest management (IPM), regular resistance monitoring and the development of innovative pest control approaches are essential to delay resistance evolution, preserve insecticide efficacy and ensure long-term agricultural productivity and environmental sustainability (IRAC, 2025; FAO, 2025; Bass and Field, 2025; Ma *et al.*, 2025; Sparks *et al.*, 2025)^[11].

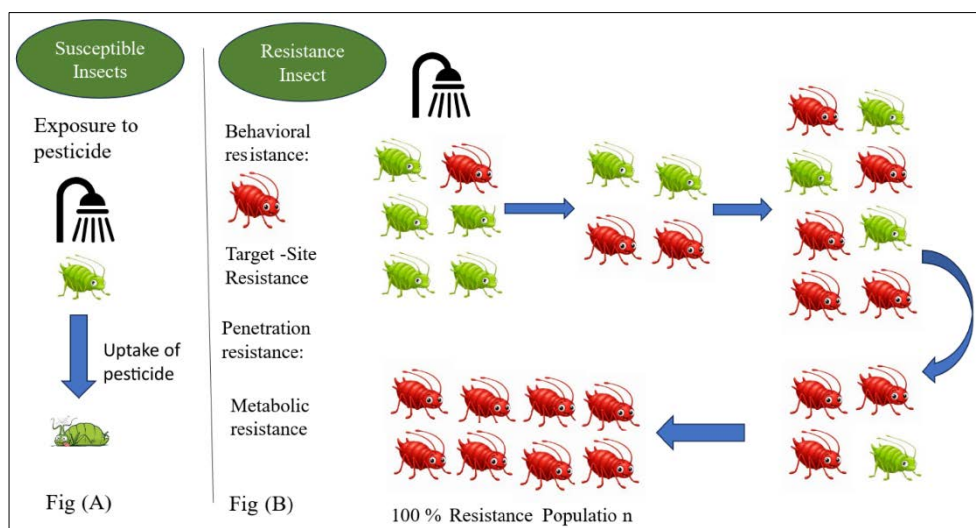


Fig 1: Process of Resistance development in Insect Body.

The figure illustrates the process of insecticide resistance development in an insect population through repeated exposure to pesticides and the subsequent selection of resistant individuals over successive generations. It is divided into two sections: Figure A, which represents a susceptible insect population, and Figure B, which depicts the gradual evolution of a resistant population. In Figure A, the initial population consists entirely of susceptible insects (shown in green) that lack any resistance mechanisms. When these insects are exposed to an insecticide, the toxic compound penetrates their cuticle and is absorbed into their body. The insecticide then reaches its target site, such as the nervous system where it disrupts normal physiological functions, ultimately causing paralysis and death. This demonstrates the high effectiveness of insecticides against susceptible populations before resistance evolves.

Factors Responsible for development of Insecticide Resistance in field condition.

Resistance is driven by various factors, including genetic variability, high reproductive rates, and operational practices such as repeated use of similar chemical classes. These factors facilitate rapid selection of resistant phenotypes and increase the likelihood of resistance allele fixation within populations.

- **1. Biological Factors:** Biological factors are generation time, number of offspring per generation migration and emigration insect species strongly affect their potential to develop and maintain insecticide resistance (Carriere *et al.*, 2010) [16].

- **2. Genetic Factors:** Genetic factors are frequency and dominance of the resistance gene, fitness of resistance genotype and number of different resistance alleles. (Hawkins *et al.*, 2019) [34].
- **3. Operational Factors:** Treatment, persistence and insecticide chemistry, all of which may and therefore timing and dosage of insecticide application should be operational factors (Sparks *et al.* 2021, Nauen, *et al.* 2019) [48]. Low-dose insecticides application is a major cause of development of resistance (IRAC, International 60th Meeting 2026).
- **4. Management Practices:** Management practices have a major impact on the development of insecticide resistance in agroecosystems (Thrall *et al.*, 2011) [64]. Monoculture-based production systems create optimum conditions for pest outbreaks, leading to increased dependence on insecticides and increased selection pressure for resistance.
- **5 Ecological and environmental factors** influence insecticide resistance development by affecting pest population dynamics and selection pressure. Intensive monoculture systems provide continuous host availability, increasing pest abundance and resistance evolution. Temperature, humidity, rainfall affect insect growth, metabolism and insecticide persistence. Limited refuges reduce susceptible insect survival, promoting rapid spread of resistance alleles in populations. (Hawkins *et al* 2019, Carriere *et al* 2010) [16, 34].

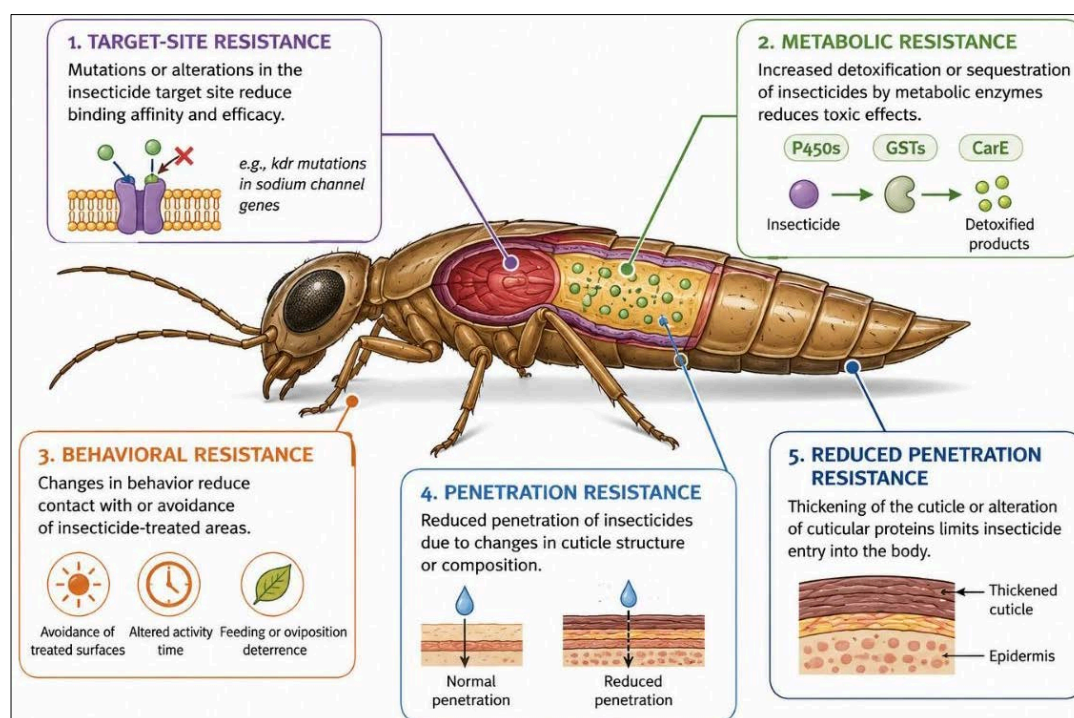


Fig 2: Genetic mechanisms underlying insecticide resistance

2.1. Target-Site Resistance

Target-site resistance arises when specific mutations alter the molecular conformation of an insecticide's binding site, diminishing or abolishing its affinity (He *et al.*, 2025). This can prevent the compound from exerting its intended neurotoxic and biochemical effect. Resistance mechanism can be classified into four broad categories based on the nature of target sight: (1) Neurological targets (e.g., AChE,

nAChR, sodium channel, chloride channel, etc.) (Davies *et al.*, 2007) [21] (Mutero *et al.*, 1994) [47]. (2) Physiological and metabolic targets (e.g., chitin synthase, ryanodine receptor, mitochondrial respiratory chain, etc.) (Hemingway *et al.*, 2004), (Liu *et al.*, 2011) [36, 43]. (3) Growth and developmental targets (e.g., juvenile hormone receptors, ecdysteroid receptors, etc.) (Ononamadu *et al.* 2021) [50].

(4) Other novel or rare targets (e.g., octopamine receptor (Verlinden *et.al* 2010, Roeder T. 2020) ^[55, 65], midgut cell membranes (Wang, *et.al.* 2016) ^[68], oxidative phosphorylation and decoupling agents, etc.)

I. Voltage-gated sodium channels: Mutations in these channels can confer resistance to pyrethroids and DDT, a phenomenon known as “knockdown resistance” or “kdr”. kdr (Knockdown Resistance) Mutations The term kdr refers to mutations in the voltage-gated sodium channel gene that confer resistance to pyrethroids and DDT. This mutation, such as L1014F in mosquitoes, alter the sodium channel structure, reducing the insecticide ability to induce paralysis and death of mosquitoes. kdr mutations are widespread in many insect species and are a major focus of resistance monitoring efforts (Ranson *et al.*, 2000) ^[53].

II. Acetylcholinesterase (AChE): Changes in AChE can be preventing organophosphate and carbamate from effectively inhibiting this enzyme, leading to formation of resistance. Ace-1 Mutations in the ace-1 gene, which encodes acetylcholinesterase, are responsible for resistance to organophosphates and carbamates. The G119S mutation in *Anopheles* mosquitoes, for example, reduces the binding affinity of acetylcholinesterase, organophosphates diminishing to their effectiveness in controlling malaria vectors (Weill *et al.*, 2003) ^[69].

III. GABA receptors: Mutations in GABA-gated chloride channels reduce susceptibility to cyclodiene insecticides (Remnant *et. al.*, 2014, Gassel *et. al.*, 2014) ^[28, 54]. Target-site resistance occurs when mutations in the genes encoding the target proteins of insecticides reduce the chemical's ability to bind and exert its toxic effects. For example, mutation in the voltage-gated sodium channel gene is responsible for resistance to pyrethroids, a widely used class of insecticides. These mutations alter the structure of the sodium channel, preventing pyrethroids from disrupting nerve function (Davies *et al.*, 2007) ^[21].

2 Metabolic resistances

- Resistant insects may detoxify and destroy the toxin faster rate than susceptible insects, and quickly rid their bodies of the toxic molecule.
- Most common mechanism and often presents the greatest challenge (Pu *et al.*, 2024).
- Insect use their internal enzyme systems to break down the insecticides.
- Resistant strains may possess high levels or more efficient forms of this enzyme.
- In addition to being more efficient, this enzyme system also may have a broad spectrum of activity (i.e., they can degrade many different insecticide).
- The normal enzymatic metabolism of this insect is modified to increase insecticide detoxification or prevent activation of insecticides.
- The enzymes responsible for detoxification of xenobiotics in living organisms are transcribed by members of large multigene families of esterases, oxidases, Glutathione transferases (GSTs) (Casida *et al.*, 2017) ^[18].
- In Dipteran insects, they occur as a gene cluster on the same chromosome. Individual member of the gene clusters may be modified in instances of insecticide

resistance, by changing a single amino acid that converts the specificity of an esterase to an insecticide hydrolase or by existing as multiple-gene copies that are amplified in resistant insects (the best studied examples are the B1 and A2-B2 amplicons in *Culex pipien* and *C. quinque* (Brogdon and McAllister, 1998) ^[15].

3. Behavioural resistance

Behavioural resistance is one of the earliest adaptive mechanisms by which insects respond to insecticide exposure. It occurs when insects modify their behaviour to minimize or avoid contact with insecticides, thereby reducing exposure to toxic compounds without developing physiological or biochemical tolerance (Sparks *et al.*, 1989; Lockwood *et al.*, 1984) ^[44].

- Resistant insect may detect or recognize a danger and avoid the toxin (Lockwood *et al.*, 1984; Sparks *et al.*, 1989) ^[44].
- This mechanism of resistance has been reported for various classes of insecticides, including organochlorine, organophosphate, carbamate and pyrethroid (Sparks *et al.*, 1989; Georgiou *et al.*, 1990) ^[29].
- Insects may simply stop feeding if they come across certain insecticide, or leave the area where spraying occurred (for instance, they may move to the underside of a sprayed leaf, move deeper in the crop canopy or fly away from the targeted area) (Hoy *et al.*, 1998; Sparks *et al.*, 1989) ^[37].
- E.g. *Plutella xylostella* (Diamond back moth): Reduced oviposition on sprayed crops (Talekar and Shelton, 1993; Furlong *et al.*, 2013) ^[27, 62].

4. Penetration resistance

- Resistant insects may absorb the toxin slower than susceptible insect (Oppenoorth *et al.*, 1985; Feyereisen *et al.*, 2015) ^[26, 51].
- Penetration resistance occurs when the insect's outer cuticle develops barriers which can slow absorption of the chemical into their body (Bass and Field, 2025; Balabanidou *et al.*, 2018) ^[10, 11].
- This can protect insects from a wide range of insecticides (Balabanidou *et al.*, 2018; Feyereisen, 2015) ^[10, 26].
- Penetration resistance is frequently present among the other forms of resistance, and reduced penetration intensifies the effects of those other mechanisms (Sparks and Nauen, 2015; Balabanidou *et al.*, 2018) ^[10, 48].
- *Helicoverpa armigera*: Reduced deltamethrin penetration through enhanced cuticular esterases (Ahmad *et al.*, 2006) ^[2].

Cross-resistance and multiple resistance: While not a standalone mechanism, cross-resistance and multiple resistance amplify the challenges posed by resistance.

Cross-resistance: Occurs when a single resistance mechanism provides tolerance to multiple pesticides with similar modes of action. For example, enhanced cytochrome P450 activity can confer resistance to both organophosphates and pyrethroids. (Hall *et al.*, 1994, Quintela, *et. al.*, 2025, Thiesen, *et.al.* 2025) ^[33]

Multiple resistance: Occurs when a pest population exhibits more than one resistance mechanism, making it resistant to multiple classes of pesticides. (Tang *et al.* 2025; Kiuru *et al.* 2025)^[40]

Impacts of insecticide resistance in Agriculture -

- Increased pest population
- Increased costs for farmers (Bass *et al.*, 2015)^[12].
- Threat to food security (Wan *et al.*, 2025)^[67].
- Loss of profitability (Ali *et al.*, 2023)^[4]
- Reduce Effectiveness of Control measures (Sparks and Nauen, 2015)^[48].
- Pest resurgence and secondary pest outbreak (Guedes *et al.*, 2016)^[31]
- Higher pesticide residues in agricultural products (Carvalho, 2006)^[17].
- Environmental Pollution (Gill *et al.*, 2014; Aktar *et al.*, 2009)^[3, 30].
- Destruction of natural enemies (Chagnon *et al.*, 2015; Desneux *et al.*, 2007)^[19, 22].
- Human and Animal Health risks (Carvalho *et al.*, 2006)^[17].
- Reduce crop yield and quality
- Development of cross resistance (Mir Washim *et al.* 2024)^[46]

6. Strategies for Managing Resistance to Insecticides:

Chemical, Biological, and Integrated Approaches The escalating threat of resistance to insecticides in pest populations necessitates a paradigm shift in pest control strategies. Traditional reliance on chemical insecticides has proven insufficient and environmentally detrimental in the long term (Kansman, *et al.* 2023, Villavicencio-Vasquez *et al.* 2025)^[39, 66]. Therefore, modern pest management strategies emphasize integrated pest management approaches that combine biological, chemical, and ecological tactics to delay development of resistance evolution and minimize ecological impacts.

1. Integrated Pest Management (IPM) (Desneux *et al.*, 2022).^[22].
2. Rotation and combination of pesticides (Zhao *et al.*, 2010; Sparks *et al.*, 2020)^[71].
3. Sequential Application Strategies (Sarwar *et al.*, 2015)^[56]
4. Use of biopesticides (Ngegba *et al.*, 2022)^[49]
5. Role of biological control (Haase *et al.* 2025) (Lacey *et al.*, 2015; Arthurs *et al.*, 2023)^[9, 32, 42].
6. Adoption of Genetically Modified (GM) crops (Kumar *et al.*, 2008)^[41].
7. Host Plant Resistance / use of resistance plant varieties (Dara, 2022)^[20].
8. Epigenetic Regulation of Insecticide Resistance (Biswas, 2025)^[14]
9. Use of recommended insecticide doses and proper application practices (Sparks *et al.*, 2020; Nauen *et al.*, 2022)^[48].
10. Conservation of natural enemies (Desneux *et al.*, 2022)^[22].

Future Strategies

- Apply CRISPR and RNAi technologies to study and manage resistance mechanisms (Yadav *et al.*, 2025; Joga *et al.*, 2021)^[38, 70].

- Develop new insecticides targeting novel molecular sites to prevent cross-resistance (Sparks *et al.*, 2020).
- Promote insecticide rotation and gene-based resistance management strategies.
- Integrate genomic approaches with Integrated Pest Management (IPM) for sustainable control.
- Application of Artificial Intelligence technology and precision farming tools (Li *et al.*, 2024; (Benelli *et al.*, 2023).
- Precision agriculture and smart pest management (Dara *et al.*, 2022)^[20].
- Expansion of biological control and biopesticides (Lacey *et al.*, 2022)^[42].
- Climate-smart pest management approaches (Deutsch *et al.*, 2018)^[25].

Conclusion

Insecticide resistance has emerged as a critical challenge affecting agricultural sustainability, global food security, and ecosystem health. The continuous and indiscriminate use of insecticides has accelerated the evolution of resistant insect populations through genetic adaptation, strong selection pressure, and the accumulation of diverse resistance mechanisms, including target-site modification, metabolic detoxification, behavioural adaptation, and reduced penetration. These resistance mechanisms have significantly reduced the effectiveness of conventional insecticides, leading to increased production costs, pest resurgence, environmental contamination, and threats to beneficial organisms and human health.

Effective management of insecticide resistance requires a transition from sole dependence on chemical control toward integrated and sustainable pest management approaches. Strategies such as insecticide rotation, mode-of-action diversification, resistance monitoring, biological control, biopesticides, host plant resistance, and conservation of natural enemies are essential for delaying resistance evolution. Emerging technologies, including genomics, CRISPR-based approaches, RNA interference (RNAi), artificial intelligence, and precision agriculture, provide promising opportunities for understanding resistance mechanisms and developing innovative pest management solutions. A coordinated approach involving researchers, farmers, industries, and policymakers is necessary to implement effective insecticide resistance management programs. Sustainable agricultural practices, rational insecticide use, and integration of advanced technologies will be crucial for preserving insecticide efficacy, maintaining ecological balance, and ensuring long-term crop productivity and food security under changing climatic conditions.

References

1. Adam B, Cocco P, Godderis L. Hazardous effects of pesticides on human health. *Toxics*. 2024;12(3):186.
2. Ahmad M, Arif MI, Ahmad Z. Occurrence of insecticide resistance in field populations of *Helicoverpa armigera* (Lepidoptera: Noctuidae) in Pakistan. *Crop Prot*. 2006;25(8):809-817.
3. Aktar MW, Sengupta D, Chowdhury A. Impact of pesticides use in agriculture: their benefits and hazards. *Interdiscip Toxicol*. 2009;2(1):1-12.
4. Ali MA, Abdellah IM, Eletmany MR. Towards sustainable management of insect pests: protecting food

- security through ecological intensification. *Int J Chem Biochem Sci.* 2023;24(4):386-394.
5. Anonymous. Annual meeting on the implementation of the FAO Global Action for Fall Armyworm (FAW) control in Africa: report. FAO; 2023.
 6. Anonymous. FAOSTAT analytical brief No. 109: pesticides use and trade: 1990-2023. FAO; 2025.
 7. Anonymous. Prevention and management of insecticide resistance. IRAC; 2025.
 8. Anonymous. Arthropod Pesticide Resistance Database (APRD) [Internet]. Michigan State University; 2025 [cited 2026 Aug 21]. Available from: <https://www.pesticideresistance.org/>
 9. Arthurs SP, Dara SK, Lacey LA. Microbial control of insect pests: advances and challenges for sustainable pest management. *Biol Control.* 2023;177:105112.
 10. Balabanidou V, Grigoraki L, Vontas J. Insect cuticle: a critical determinant of insecticide resistance. *Curr Opin Insect Sci.* 2018;27:68-74.
 11. Bass C, Field LM. Molecular mechanisms of insecticide resistance in insects. *Annu Rev Entomol.* 2025.
 12. Bass C, Denholm I, Williamson MS, Nauen R. The global status of insect resistance to neonicotinoid insecticides. *Pestic Biochem Physiol.* 2015;121:78-87.
 13. Biondi A, Guedes RNC, Wan FH, Desneux N. Ecology, worldwide spread, and management of the invasive South American tomato pinworm, *Tuta absoluta*: past, present, and future. *Annu Rev Entomol.* 2018;63:239-258.
 14. Biswas AP, Das SC, Rahman MM. Epigenetic mechanisms driving insecticide resistance: implications of DNA methylation and histone modification for sustainable pest management. *Discov Sustain.* 2025;6:1138.
 15. Brogdon WG, McAllister JC. Insecticide resistance and vector control. *Emerg Infect Dis.* 1998;4(4):605-613.
 16. Carriere Y, Crowder DW, Tabashnik BE. Evolutionary ecology of insect adaptation to Bt crops. *Evol Appl.* 2010;3(5-6):561-573.
 17. Carvalho FP. Agriculture, pesticides, food security and food safety. *Environ Sci Policy.* 2006;9(7-8):685-692.
 18. Casida JE, Bryant RJ. The ABCs of pesticide toxicology: amounts, biology, and chemistry. *Toxicol Res.* 2017;6(6):755-763.
 19. Chagnon M, Kreutzweiser D, Mitchell EAD, Morrissey CA, Noome DA, Van der Sluijs JP. Risks of large-scale use of systemic insecticides to ecosystem functioning and services. *Environ Sci Pollut Res.* 2015;22(1):119-134.
 20. Dara SK. The new integrated pest management paradigm for the modern age. *J Integr Pest Manag.* 2022;13(1):12.
 21. Davies TGE, Field LM, Usherwood PNR, Williamson MS. DDT, pyrethrins, pyrethroids, and insect sodium channels. *IUBMB Life.* 2007;59(3):151-162.
 22. Desneux N, Decourtye A, Delpuech JM. The sublethal effects of pesticides on beneficial arthropods. *Annu Rev Entomol.* 2007;52:81-106.
 23. Desneux N, Han P, Mansour R, Arno J, Breault T, Campos MR, *et al.* Integrated pest management of invasive pests: current challenges and future directions. *Annu Rev Entomol.* 2022;67:511-536.
 24. Desneux N, Wajnberg E, Wyckhuys KAG, Burgio G, Arpaia S, Narváez-Vasquez CA, *et al.* Biological invasion of European tomato crops by *Tuta absoluta*: ecology, geographic expansion and prospects for biological control. *J Pest Sci.* 2010;83(3):197-215.
 25. Deutsch CA, Tewksbury JJ, Tigchelaar M, Battisti DS, Merrill SC, Huey RB, *et al.* Increase in crop losses due to climate change and insect pests. *Science.* 2018;361(6405):916-919.
 26. Feyereisen R. Insect P450 enzymes. *Annu Rev Entomol.* 2015;60:507-525.
 27. Furlong MJ, Wright DJ, Dosdall LM. Diamondback moth ecology and management: problems, progress, and prospects. *Annu Rev Entomol.* 2013;58:517-541.
 28. Gassel M, Wolf C, Noack S, Williams H, Ilg T. The novel isoxazoline ectoparasiticide fluralaner: selective inhibition of arthropod γ -aminobutyric acid- and L-glutamate-gated chloride channels and insecticidal/acaricidal activity. *Insect Biochem Mol Biol.* 2014;45:111-124.
 29. Georgiou GP. Overview of insecticide resistance. In: Green MB, LeBaron HM, Moberg WK, editors. *Managing resistance to agrochemicals: from fundamental research to practical strategies.* Washington (DC): American Chemical Society; 1990. p. 18-41.
 30. Gill HK, Garg H. Pesticides: environmental impacts and management strategies. In: Larramendy ML, Soloneski S, editors. *Pesticides: toxic aspects.* London: IntechOpen; 2014.
 31. Guedes RNC, Smagghe G, Stark JD, Desneux N. Pesticide-induced stress in arthropod pests for optimized integrated pest management programs. *Annu Rev Entomol.* 2016;61:43-62.
 32. Haase S, Sciocco-Cap A, Romanowski V. Baculovirus insecticides in Latin America: historical overview, current status and future perspectives. *Viruses.* 2015;7(5):2230-2267.
 33. Hall LM, Holtum JAM, Powles SB. Mechanisms responsible for cross resistance and multiple resistance. In: Powles SB, Holtum JAM, editors. *Herbicide resistance in plants: biology and biochemistry.* Boca Raton: CRC Press; 1994. p. 243-262.
 34. Hawkins NJ, Bass C, Dixon A, Neve P. The evolutionary origins of pesticide resistance. *Biol Rev.* 2019;94(1):135-155.
 35. He Z, Wang D, Kou Y, Liu Y, Zhao D, Yang C, *et al.* Insecticide resistance and the role of target-site insensitivity mutations among malaria vectors in China: a systematic review and meta-analysis. *Parasit Vectors.* 2025;18:374.
 36. Hemingway J, Hawkes NJ, McCarroll L, Ranson H. The molecular basis of insecticide resistance in mosquitoes. *Insect Biochem Mol Biol.* 2004;34(7):653-665.
 37. Hoy MA. Myths, models and mitigation of resistance to pesticides. *Philos Trans R Soc Lond B Biol Sci.* 1998;353(1376):1787-1795.
 38. Joga MR, Zotti MJ, Smagghe G, Christiaens O. RNA interference technology in pest management: current status and future perspectives. *Pest Manag Sci.* 2021;77:2195-2207.
 39. Kansman JT, Jaramillo JL, Ali JG, Hermann SL. Chemical ecology in conservation biocontrol: new perspectives for plant protection. *Trends Plant Sci.* 2023;28(12):1166-1177.

40. Kiuru C, Constantino L, Cole G, Karisa J, Wanjiku C, Okoko M, *et al.* Multiple insecticide resistance in *Anopheles funestus* from Mopeia, central Mozambique. *Malar J.* 2025;24:81.
41. Kumar S, Chandra A, Pandey KC. *Bacillus thuringiensis* (Bt) transgenic crop: an environment-friendly insect-pest management strategy. *J Environ Biol.* 2008;29(5):641-653.
42. Lacey LA, Grzywacz D, Shapiro-Ilan DI, Frutos R, Brownbridge M, Goettel MS. Insect pathogens as biological control agents: back to the future. *J Invertebr Pathol.* 2022;190:107737.
43. Liu N, Xu Q, Zhu F, Zhang L. Insecticide resistance in mosquitoes: impact, mechanisms, and research directions. *Annu Rev Entomol.* 2011;56:307-328.
44. Lockwood JA, Sparks TC, Story RN. Evolution of insect resistance to insecticides: a revaluation of the roles of physiology and behaviour. *Bull Entomol Soc Am.* 1984;30(4):41-51.
45. Ma CS, Wang BX, Wang XJ, *et al.* Crop pest responses to global changes in climate and land management. *Nat Rev Earth Environ.* 2025;6:264-283.
46. Mir Washim, Manda P, Das R. Pesticide resistance in insects: challenges and sustainable solutions for modern agriculture. *Int J Agric Food Sci.* 2024;6(2):121-127.
47. Mutero A, Pralavorio M, Bride JM, Fournier D. Resistance-mediating mutations in acetylcholinesterase, the target site of organophosphates and carbamates, in insect species. *Pestic Biochem Physiol.* 1994;48(2):63-77.
48. Nauen R, Bass C, Feyereisen R, Vontas J. The role of cytochrome P450 monooxygenases in insecticide resistance. *Annu Rev Entomol.* 2022;67:347-370.
49. Ngegba PM, Cui G, Khalid MZ, Zhong G. Use of botanical pesticides in agriculture as an alternative to synthetic pesticides. *Agriculture.* 2022;12(5):600.
50. Ononamadu CJ, Abdalla M, Ihegboro GO, Li J, Owolarafe TA, John TD, *et al.* *In silico* identification and study of potential anti-mosquito juvenile hormone binding protein (MJHBP) compounds as candidates for dengue virus-vector insecticides. *Biochem Biophys Rep.* 2021;28:101178.
51. Oppenoorth FJ. Biochemistry and genetics of insecticide resistance. In: Kerkut GA, Gilbert LI, editors. *Comprehensive insect physiology, biochemistry and pharmacology.* Vol. 12. Oxford: Pergamon Press; 1985. p. 731-773.
52. Pu J, Chung H. New and emerging mechanisms of insecticide resistance. *Curr Opin Insect Sci.* 2024;63:101184.
53. Ranson H, Jensen B, Vulule JM, Wang X, Hemingway J, Collins FH. Pyrethroid resistance in African anopheline mosquitoes: what are the implications for malaria control? *Trends Parasitol.* 2000;16(8):343-350.
54. Remnant EJ, Morton CJ, Daborn PJ, Lumb C, Yang YT, Ng HL, *et al.* The role of *Rdl* in resistance to phenylpyrazoles in *Drosophila melanogaster*. *Insect Biochem Mol Biol.* 2014;54:11-21.
55. Roeder T. The control of metabolic traits by octopamine and tyramine in invertebrates. *J Exp Biol.* 2020;223:jeb194282.
56. Sarwar M, Salman M. Insecticides resistance in insect pests or vectors and development of novel strategies to combat its evolution. *Int J Bioinform Biomed Eng.* 2015;1(3):344-351.
57. Sparks TC, Nauen R. IRAC: mode of action classification and insecticide resistance management. *Pestic Biochem Physiol.* 2015;121:122-128.
58. Sparks TC, Lorschach BA, Sparks JM, Duke SO. Origins of new modes of action for fungicides, herbicides and insecticides: a review and analysis. *Pest Manag Sci.* 2025;81(10):6019-6028.
59. Sparks TC, Crossthwaite AJ, Nauen R, Banba S, Cordova D, Earley F, *et al.* Insecticides, biologics and nematicides: updates to IRAC's mode of action classification—a tool for resistance management. *Pestic Biochem Physiol.* 2020;167:104587.
60. Sparks TC, Lockwood JA, Byford RL, Graves JB, Leonard BR. The role of behavior in insecticide resistance. *Pestic Sci.* 1989;26(4):383-399.
61. Sparks TC, Storer N, Porter A, Slater R, Nauen R. Insecticide resistance management and industry: the origins and evolution of the Insecticide Resistance Action Committee (IRAC) and the mode of action classification scheme. *Pest Manag Sci.* 2021;77(6):2609-2619.
62. Talekar NS, Shelton AM. Biology, ecology, and management of the diamondback moth. *Annu Rev Entomol.* 1993;38:275-301.
63. Thang J, Nauen R, Bass C. Multiple insecticide resistance in agricultural insect pests: mechanisms, monitoring and management strategies. *Pest Manag Sci.* 2025;81(12):7345-7362.
64. Thrall PH, Oakeshott JG, Fitt G, Southerton S, Burdon JJ, Sheppard A, *et al.* Evolution in agriculture: the application of evolutionary approaches to the management of biotic interactions in agro-ecosystems. *Evol Appl.* 2011;4(2):200-215.
65. Verlinden H, Vleugels R, Marchal E, Badisco L, Pflüger HJ, Blenau W, *et al.* The role of octopamine in locusts and other arthropods. *J Insect Physiol.* 2010;56:854-867.
66. Villavicencio-Vasquez M, Espinoza-Lozano F, Espinoza-Lozano L, Coronel-Leon J. Biological control agents: mechanisms of action, selection, formulation and challenges in agriculture. *Front Agron.* 2025;7:1578915.
67. Wan NF, Fu L, Dainese M, Kiær LP, Hu YQ, Xin F, *et al.* Pesticides have negative effects on non-target organisms. *Nat Commun.* 2025;16:1360.
68. Wang Y, Qi Z, Qi M, Hu Z, Wu W. Effects of periplocoside P from *Periploca sepium* on the midgut transmembrane potential of *Mythimna separata* larvae. *Sci Rep.* 2016;6:36982.
69. Weill M, Malcolm C, Chandre F, Mogensen K, Berthomieu A, Marquie M, *et al.* The unique mutation in *ace-1* giving high insecticide resistance is easily detectable in mosquito vectors. *Insect Mol Biol.* 2003;12(6):593-598.
70. Yadav AK, Tiwari S, Kumar V, Soni S, Yadav P, Bharati P, *et al.* Precision molecular entomology: CRISPR, RNAi and multi-omics paradigms for next-generation pest management. *J Adv Biol Biotechnol.* 2025;28(9):537-546.
71. Zhao JZ, Collins HL, Shelton AM. Testing insecticide resistance management strategies: mosaic versus rotations. *Pest Manag Sci.* 2010;66(10):1101-1105.