Insecticide Resistance in Insect Vectors of Human Diseases: Challenges and Management Opportunities

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Abstract

The blood-feeding arthropods are known to cause more than 60% of known human infectious diseases. Among them, insect vectors are responsible for many human deaths by causing infection. The increasing human population densities, deforestation, agricultural expansion, climate change, and international tourism are the main factors contributing to the emergence, diffusion, and success of insect-vectored zoonoses. They are very adaptive and become resistant to insecticides due to several physiological, metabolic, behavioral, and genetic mechanisms of resistance development. Several insect vector control interventions have been introduced and implemented, while the mainstay worldwide is insecticide use. The knowledge regarding insecticide resistance development, the factors driving resistance development, and integrated management alternatives for sustainable management of insect vectors of human diseases is lacking. This book chapter will focus on the introduction and associated diseases of major human disease insect vectors. The use of insecticides, insecticide resistance, and the factors driving the resistance development have been highlighted. Finally, the management challenges and studies showing effective alternative solutions have been reported. Overall, this chapter provides comprehensive information regarding human disease-causing insect vectors, insecticide resistance development and management challenges, and integrated vector management opportunities to mitigate the health hazards associated with insecticides used for disease vector management.

Keywords: Pesticides, Arthropods, Disease management, Vector control, Resistance, Biocontrol

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Introduction

The animals are known to cause more than sixty percent of known human infectious diseases, including Zika fever, Chikungunya, and Dengue fever outbreaks. During the last century, at least a quarter of all such outbreaks have been implicated by blood-feeding arthropods. Among them, insects are important vectors of several fatal diseases. The insects belonging to the order Diptera (flies) alone cause an estimated 0.7 million human deaths a year (Bellekom et al., 2021). In addition, it has been estimated that 500 million people are infected with malaria worldwide every year, following lymphatic filariasis (100 M) and dengue (25 M), which cause approximately 25,000 deaths annually (Manikandan et al., 2023). The main factors favoring the novel and existing insect-vectored zoonoses are the ever-increasing human population, movement of people to cities, movement of insects due to deforestation and habitation into new areas, the expansion of agriculture, climate change, urbanization, growing trade, and international tourism (Bellekom et al., 2021; Socha et al., 2022). Insecticides are commonly used in agriculture to control and manage insect pests. They are also used to prevent vector-borne illnesses by killing insects or preventing them from engaging in undesirable or destructive behaviors. Pesticide dependency is a potential risk to human and animal health, as well as to ecological systems. In recent decades, the resistance development in different groups of pesticides, i.e., organochlorines (OCs), organophosphates (OPs), pyrethroids, and carbamates, has also been increased. Most importantly, cross-resistance development among pyrethroids and organochlorines groups appears in malaria vector populations in Africa (van den Berg et al., 2021). Similarly, observation has been reported in the case of dengue vectors against pyrethroids and the organophosphate (temephos). Another major concern is the pyrethroid resistance in the vectors responsible for leishmaniasis and Chagas disease (van den Berg et al., 2021). Despite technological development to determine resistance mechanisms and diagnosis, their practical implementation in vector control programs remains constrained. These gaps underscore the need for more precise and comprehensive strategies to effectively mitigate resistance development in target organisms for sustainable management interventions. The GVCR (Global Vector Control Response) was launched from 2017–2030 by the World Health Organization (WHO) as a strategy for sustainable vector control. They implemented a vibrant approach to averting disease and responding to human disease vector outbreaks (van den Berg et al., 2021). Thus, several classes of vector control interventions are available or being tested, but the mainstay of these interventions for human disease vector control worldwide has been the use of insecticides. Therefore, this book chapter highlighted the important insect vectors of human diseases, investigated insecticide use for vector control, and globally reported resistant development in insect vectors. Further, some challenges are highlighted, including the integrated management solutions for the sustainable management of human disease vectors.

1. Key Insect Vectors for Human Diseases

1.1. Mosquitoes

Mosquitoes are found all over the world and are members of the *Culicidae* family. There are presently 3556 recognized species of mosquitoes in this large family, which are divided into the subfamilies *Culicinae* and *Anophelinae*. Numerous pathogens, such as arboviruses, protozoans, and filariae, which cause infectious illnesses of major public health concern, can spread through mosquito vectors (Becker et al., 2010). *Anopheles*, *Aedes*, and *Culex* are the three genera that comprise many mosquito vectors (Caglioti et al., 2013).

1.2. Sandflies

The order Diptera includes arthropods known as sand flies. Sand flies feed on blood from the nearest permissive source, depending on the availability of hosts (Gebresilassie et al., 2015). This supports the frequently asserted theory that people are typically hosts of *Leishmania* (Quinnell & Courtenay, 2009). Among 1000 species of sand flies, about 1/10 species have been identified as suspected vectors of *Leishmania spp.* parasites (Shimabukuro et al., 2017). The sandflies feed upon people, consume the appropriate reservoir hosts for zoonotic agents, and are found in nature infected with the same parasites (*Leishmania* species) that are circulating in humans. These flies also facilitate the full growth of the *Leishmania* parasites that are in circulation in humans, even after the bloodmeal leftovers have been defecated, and they can spread those parasites to vulnerable hosts when they consume blood (Dvorak et al., 2018).

1.3. Tsetse Flies

Sleeping sickness, or human African trypanosomiasis (HAT), is a parasite-borne illness. The disease is caused by an extracellular protozoan from the *Trypanosoma brucei* species. The bloodsucking tsetse fly of the species *Glossina* bites the vulnerable host, causing it to spread (Büscher et al., 2017). The two subspecies of *Trypanosoma brucei* that cause human illness are gambiense and rhodesiense. Despite sharing the same life cycle and physical characteristics, these subspecies produce separate pathogenic entities with diverse patterns of clinical and epidemiological care (WHO, 2013).

1.4. Housefly

The Housefly belongs to the order Diptera and is ubiquitous worldwide in a variety of human and animal settlements. The bulk of the public's health problems are caused by houseflies; the viruses they carry may cause diseases including cholera, typhoid fever, poliomyelitis, TB, aspergillosis, ascariasis, dysentery, and hepatitis (Graczyk et al., 2005). It has been discovered that the housefly is a carrier of pathogens like *Campylobacter jejuni* and an aggressive vector of infections like *Shigella* and *Campylobacter spp., Salmonella* species along with *Pseudomonas aeruginosa, Enterococcus*, *Staphylococcus aureus*, and other bacteria (Bahrndorff et al., 2013). In addition to contaminating food with eggs and maggots because they release saliva and feces that may contain germs, flies easily carry bacteria to our food, which can lead to digestive ailments.

1.5. Ticks

Ticks are arachnids and the second most common carriers of diseases in humans, after mosquitoes. They spread a variety of illnesses worldwide, including Lyme disease, Rocky Mountain spotted fever, ehrlichiosis, anaplasmosis, babesiosis, relapsing fever, and tick-borne encephalitis (Goddard & Goddard, 2018).

1.6. Fleas

Fleas are tiny, wingless insects that can bite people in addition to infesting animals. Since fleas primarily feed on blood, they immediately harm them. The fact that fleas are hosts to infections and so offer a natural pathway for pathogen dissemination is another, more worrisome consequence of this dietary choice. The two most well-known methods that fleas spread pathogens are by the fecal channel, which involves contaminated fecal pellets, or the oral route, which involves regurgitation of blood meals (Bitam et al., 2010).

2. Mechanisms of Insecticide Resistance

Chemical controls are considered the most effective and quickest method to keep pest populations below the economic threshold level (ETL). It played a vital role in developing pest management strategies to avoid yield loss where no sustainable substitute is available. The steady use of pesticides favors persistence, biomagnification, environmental and health issues, and, more importantly, the development of resistant populations by selection pressure (Hemingway et al., 2016; Hafeez et al., 2021), that makes plant defense more difficult to handle. Therefore, effective management strategies will require a good understanding of insecticide resistance mechanisms.

Generally, the resistance mechanisms in insects can be classified into two major types: physiological and behavioral resistance. Physiological resistance refers to the various mechanisms that insects use to defend themselves against pesticides and other harmful substances. Some insect pest species are resistant to various classes of insecticides (Table 1). The following mechanisms involved in insect vector resistance (Figure 1) are included.

- Metabolic resistance (enzyme detoxification: P450 monooxygenases, esterases, GSTs) enhances the production of metabolic enzymes that detoxify insecticides.
- Genetic mutations that alter the targeted proteins and make them less sensitive to insecticides.
- Target site insensitivity (e.g., mutations in VGSC, AChE, GABA receptor, etc.)
- Alteration of target site nerve receptors (e.g., Ace.1R, kdr, and Rdl) (Ranson et al., 2011; Panini et al., 2016).

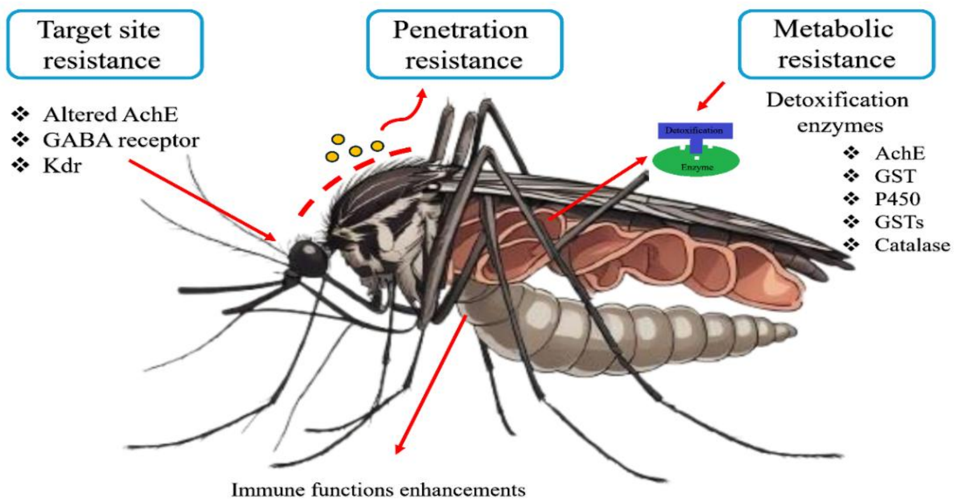

Fig. 1: An illustration shows metabolic resistance in mosquito spp. against different pesticides. Several mechanisms of resistance have been defined in insects, such as metabolic resistance, penetration resistance, and target site resistance (Modified from Siddiqui et al., 2023; the mosquito picture was drawn from https://leonardo.ai/).

Table 1: Key insect vectors causing several diseases in the human population. They belong to different families, including different orders.

Disease Name	Disease vector				Reference
	Common name	Technical name	Family	Order	
Dengue	Mosquitoes	*Aedes aegypti* and *Aedes albopictus*	Culicidae	Diptera	Yousuf et al., 2024
Zika virus		*Aedes aegypti*			Duffy et al., 2009
Chickenganya		*Aedes aegypti* and *Aedes albopictus*			Morrison, 2014
Malaria		*Anopheles stephensi*			Cowman et al., 2016
West Nile Virus		*Culex pipiens*			Haba & McBride, 2022
Leishmaniasis	Sandflies	Phlebotomus spp	Psychodidae		Shimabukuro et al., 2017
Sleeping Sickness	Tsetse Flies	*Glossina morsitans*	Glossinidae		Büscher et al., 2017
Anthrax	Housefly	*Musca domestica*	Muscidae		Graczyk et al., 2005
Cholera					
Shigellosis					
Ascariasis					
Lyme disease	Ticks	*Ixodes scapularis*	Ixodidae	Siphonaptera	Goddard & Goddard, 2018
Rocky Mountain spotted fever					
Tick-borne encephalitis					
Plague	Fleas	*Xenopsylla cheopis*	Pulicidae	Siphonaptera	Rajamannar et al., 2022
Murine typhus					Gillespie et al., 2009

3. Global Distribution and Case Studies of Insecticide Resistance in Disease Vectors

A major obstacle to global vector-borne disease management initiatives is insecticide resistance in disease vectors.

- *Anopheles gambiae* is a known vector of malaria in sub-Saharan Africa. It has been reported that mosquito resistance to pyrethroids has increased. The factors that are responsible for this resistance development are target-site mutations (knockdown resistance, kdr), and cytochrome P450 enzymes. The phenotypic resistance to insecticides was also attributed to the low levels of the L1014S kdr point mutation found in coastal Kenya (Munywoki et al., 2021)
- The increased use of insecticides in South America and Southeast Asia's including urbanization, has been linked to pyrethroids and organophosphates in *Aedes aegypti* (Moyes et al., 2017). The use of *Bacillus thuringiensis* israelensis (*Bti*) as a biological control strategy has become popular in Brazil. This is because of widespread resistance to a larvicide named Tempos. Similarly, high levels of deltamethrin resistance in Thailand have been reported due to kdr mutations in *Aedes aegypti*. This highlights the importance of integrated vector management (IVM) strategies (Kasai et al., 2014).

- The sand flies are responsible for the spread of leishmaniasis. The parts of the Middle East, South Asia, and South America have been reported to be affected due to sand flies (*Phlebotomus* spp.). Pyrethroid and organophosphate resistance have been reported in these regions.

4. Challenges in Managing Insecticide Resistance

- Limited availability of new insecticide classes: The high developmental cost with uncertain results, regulatory challenges, and a relatively small market (vector control as compared to agricultural pest control), making the entrepreneur less interested in investing in it (Mnzava et al., 2015).
- Ineffective implementation of vector control programs: Operational inefficiencies (poor community engagement, weak monitoring, and evaluation) may be due to inadequate training (insecticide application and equipment calibration), logistical issues (delay in procurement and distribution), and resource limitations (Wilson et al., 2020). Weak monitoring and evaluation results in incomplete or outdated data, causing ineffectiveness of the control strategy.
- Gaps in resistance monitoring and surveillance: There are many gaps in resistance monitoring, such as insufficient geographical coverage, inadequate infrastructure, lack of standardized protocol, and infrequent monitoring (Fournet et al., 2018).
- Economic and logistical constraints in developing regions: Economic constraints include limited funding for vector control, high cost of insecticide and equipment, and economic limitations towards innovations. Priorities shift of the government or overreliance on foreign funding from the international organizations and donors are the main factors of the limited funding for management of vectors.
- Public health risks due to failed vector control strategies: Failed vector control programs can increase disease transmission, outbreaks of epidemics, economic concerns, and global health security threats. Failed vector management in one region can be a greater threat to global health security by spreading these species to other parts of the world by transportation and trade.

5. Management Opportunities and Solutions

The Global Vector Control Response 2017-2030 was initiated by the World Health Organization (WHO), and integrated vector management (IVM) is described by the WHO as a systematic decision-making framework aimed at the most effective use of resources for vector control. The primary objective is to apply vector control strategies effectively to improve public health by preventing, mitigating, or eliminating vector-borne diseases. Vector control initiatives have significantly contributed to the prevention, management, and regulation of various vector-borne diseases (Wilson et al., 2020). This framework promotes the integration of chemical, biological, and environmental controls, leading to the consideration of a sustainable, effective, and multidisciplinary approach for managing vector-borne diseases.

a. Chemical Control

Recently, multiple vector control solutions have been introduced such as microencapsulated formulations of pirimiphos-methyl, clothianidin (neonicotinoids), and deltamethrin designed for indoor residual spraying (IRS). The pyrethroid-PBO nets and dual insecticide nets have also been developed (World Health Organization, 2021). Outdoor insecticide applications are also employed in larval habitats and near mosquito resting areas and are periodically applied for dengue control (Bowman et al., 2016).

b. Biological Control

A diverse range of predators and pathogens (Table 2) is effectively used to manage the immature stage of mosquitoes such as fish (Subramaniam et al., 2015), amphibians (Bowatte et al., 2013), copepods (Pauly et al., 2022), odonate young instars (Choo et al., 2021), water bugs (Das & Maity, 2023) and even larvae of other mosquito species use as predators to reduce mosquito population. Ghosh & Dash (2007) reported that 315 fish species distributed across genera showed larvivorous properties and were significantly used in controlling malaria.

c. Environmental Control

Effective water sanitation and hygiene practices, particularly in rural areas, can significantly reduce breeding sites for vectors. Management of water reservoirs, irrigation systems, and domestic water storage, along with interventions such as intermittent irrigation, can reduce malaria and other vector-borne disease risks (Alirol et al., 2011; Jones et al., 2023), e.g., malaria transmission increased with Amazon deforestation. Conclusively, environmental management can have a significant impact on addressing the causes of vector proliferation.

d. Enhanced Monitoring and Surveillance

The biological assays are often the primary assessment applied to identify the prevalence of resistance. These dose-response bioassays provide more accurate assessments. However, some effective testing tools have also been developed for kdr mutations in *Ae. aegypti* (Moyes et al., 2017). They are often integrated into resistance monitoring programs for sustainable management.

e. Genetic and Biological Tools

The sterile insect technique (SIT) is a strategy for the management of insect populations and is frequently used for mosquito and tsetse fly control (Vreysen et al., 2014; Lees et al., 2021). The other strategies include the Incompatible Insect Technique (IIT), RIDL (Release of Insects Carrying a Dominant Lethal Gene), and Precision-Guided Sterile Insect Technique (PgSIT). The implementation of the above-mentioned techniques can be very effective for integrated vector management efforts on a sustainable basis.

f. Community Engagement and Education

The participation of community members is crucial for the success of any vector control program. The educational campaigns and community mapping to increase awareness can play a very important role in vector control.

Table 2: Studies on biological control agents, including predators, entomopathogenic fungi, and various bacterial strains from 2023–2025, against targeted insect vectors of human diseases.

Sr. No	Biological Agents	Target Vectors	Geographical location	References
1	*Rhantus elevatus* (Diving beetle)	*Mosquito (Culex pipiens*)	North Africa	Rashed et al., 2025
2	Molly Fish (*Poecilia sphenops*) Mosquito fish (*Gambusia affinis*)	*Mosquito (Aedes* species)	Southeast Asia	Syifa et al., 2024
3	*Channa punctata* (Native Murrel) *Channa stewartii* (Native Murrel) *Poecilia reticulate* (Exotic Guppy)	Mosquito *(Aedes* spp. and *Culex pipiens)*	Southeast Asia	Gogoi & Biswas, 2024
4	*Lantana camara* essential oil (LECO) and its nano emulsion (LCNE)	Mosquito (*Anopheles culicifacies*)	South Asia	Sonter et al., 2024
5	*Bacillus thuringiensis israelensis* (Bti)	Mosquito *(Anopheles gambiae sensu lat*)	Central Africa	Munyakanage et al., 2024
6	*Metarhizium anisopliae* strain LCM S01 *Beauveria bassiana* strain LCM S19	Mosquito *(Aedes aegypti*)	South America	Rocha et al., 2024
7	*Metarhizium anisopliae* strain CG 153	Mosquito (*Aedes aegypti*)	South America	Ribeiro et al., 2024
8	*Copper Nano-particles synthesis from Metarhizium robertsii Biogenic* CuNPs	Mosquito (*Aedes albopictus*)	Southeast Asia	Vivekanandhan et al., 2024
9	*Metarhizium robertsii* strain CEP 423 and ARSEF 2575	Mosquito (*Aedes aegypti*)	South America	Paixao et al., 2024
10	Beneficial bacterial phage cocktails including *Klebsiella* and *Enterobacter,* Harmful bacterial phage cocktails including *Providencia, Pseudomonas,* and *Morganella*	*Housefly (Musca domestica)*	East Asia	Zhang et al., 2024
11	Entomopathogenic bacterial strains including *Serratia marcescens, Pseudomonas protegensa* and *Photorhabdus temperata*	*Housefly* (*Musca domestica*)	North America	Johnson et al., 2024
13	*Bacillus thuringiensis* (Btcps)	Ticks (Hyalomma spp)	South Asia	Noor et al., 2024
14	*Heterorhabditis bacteriophora* HP88	Tick (*Rhipicephalus sanguineus*)	North Africa	Abdel-Ghany et al., 2024
15	*Bacillus thuringiensis* (Bt)	Flea (*Ctenocephalides canis*)	Southeast Asia	Gaur & Gautam, 2024
18	*Chromobacterium anophlis IRSSSOUMB001*	*Mosquito (Anopheles coluzzii)*	West Africa	Gnambani et al., 2023
19	Dragonfly/Damselfly Naiad	*Mosquito (Aedes, Anopheles, Culex)*	Southeast Asia	Priyadarshana & Slade, 2023
20	*Bacillus sphaericus* synthesized into nickel nanoparticles (BS@NiNPs)	*Mosquito (Anopheles subpictus* and *Culex quinquefasci)*	South Asia	Santhoshkumar et al., 2023
	Brassicaceae seed	Mosquito (*Aedes aegypti*)	North America	Flor-Weiler et al., 2023
21	*Beauveria bassiana* strain Bb-NBAIR and Bb5a	*Mosquito (Anopheles stephensi)*	South Asia	Renuka et al., 2023
22	*Utricularia australis*	*Mosquito* (*Aedes albopictus*)	Southern Europe	Casini et al., 2023

Conclusion

Insect vectors are causing life losses to human beings due to the transmission of several pathogens. Therefore, insecticide exposure and resistance evidence indicate an increase in the risk of pathogen transmission and may increase the infectivity potential of vectors. These changes may result from altered gene expression, particularly in genes linked to blood-feeding and immune responses in insect disease vectors. Therefore, for the sustainable management of insect vectors of human diseases, comprehensive integrated vector management programs need to be designed and implemented on a large scale, involving all the stakeholders. The components may integrated vector management may include effective monitoring and surveillance, public awareness, resistance diagnosis, rational use of insecticides, cultural control, mechanical control, biological control, genetic control, and the development of novel insecticides. The current review also reported several biocontrol studies indicating the potential for vector management. In addition, more refined studies can now be undertaken to fill knowledge gaps. Therefore, we need more in-depth research to create sustainable interventions to manage insect vectors that spread human diseases, helping to safeguard current and future generations.

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