

## Review article

# Worldwide Status of Insecticide Resistance of *Aedes aegypti* and *Ae. albopictus*, Vectors of Arboviruses of Chikungunya, Dengue, Zika and Yellow Fever

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## Abstract

**Background:** Controlling of *Aedes aegypti* and *Ae. albopictus*, vectors of five important mosquito-borne diseases, is known as the most effective method to prevent the transmission of arboviruses to humans, but the emergence of insecticide resistance is threat for control and prevention of vector borne diseases. A better understanding of mosquito resistance to insecticides will help to develop more effective methods to control insecticide resistance in mosquito vectors.

**Methods:** Worldwide geographical distribution of insecticide resistance in *Ae. aegypti* and *Ae. albopictus* by the available papers and map of the data for carbamates, organochlorines, organophosphates, pyrethroids, microbial and insect growth regulator insecticides were reviewed. Article data published up to December 2022 were investigated by searching the following databases: "Google Scholar", "PubMed", "Scopus", "SID" and "Web of Knowledge".

**Results:** The results showed that the susceptibility and resistance status of *Ae. aegypti* and *Ae. albopictus* to insecticides in the world is very diverse.

**Conclusion:** Due to the importance of *Ae. aegypti* and *Ae. albopictus* in the transmission of mosquito-borne arboviruses, resistance management should be given more attention worldwide to prevent insecticide resistance in the arbovirus vector and replace the new approach for vector control.

**Keywords:** Insecticide; Resistant; *Aedes*; Arboviruses; World

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## Introduction

Among arboviruses that are widespread worldwide, chikungunya, dengue, Zika and yellow fever are widely transmitted by *Aedes* spp. (1, 2). *Aedes aegypti* mosquitoes originated from Africa, but they are also found in tropical, subtropical, and temperate parts of the world (3, 4). *Aedes albopictus* has adapted to urban, suburban, and rural regions. This species is a forest species that has spread from Asia to Africa, America, and Europe through the trade of used tires (5). Dengue is the fastest mosquito transmitted disease, it has increased more than 15-fold since 2000 and has affected more than 129 countries. Because vaccines or drug treatments exist for only a small number of vector-borne

pathogens, the primary method for controlling many vector-borne diseases is direct vector control (6).

Chemical control by organic or inorganic insecticides is one of the methods of mosquito control and as part of integrated management. Insecticides used for mosquitoes, that are neurotoxic: organochlorines, organophosphates, carbamates, and pyrethroids (7). Insecticide resistance is a growing topic around the world that limits the effectiveness of control methods against vector mosquitoes. The data on insecticide resistance in *Aedes* is varying. Insecticides have an important role in the control of dengue fever, but the resistance of mosquitoes

reduces the effectiveness of these interventions in some countries (8). According to the World Health Organization (WHO), resistance to insecticides is a major risk in interventions to control vector-borne diseases. It is essential to identify the geographical regions where vector resistance to insecticides exists and can make it difficult to control the vector, and to improve the induction of innovative tools for vector control. A better identifying of resistance of insecticides helps to formulate a global measure to control insecticide resistance in disease vectors.

## Materials and Methods

Published articles were searched by terms “resistance”, “*Aedes aegypti*”, “*Aedes albopictus*”, “pyrethroid”, “organochlorines”, “organophosphate”, “carbamate”, “IGR”, and “kdr”, “P450”, “monooxygenase”, “glutathione”, or “esterase”. Data were extracted from articles published up to December 2022. The terms in the following databases: PubMed, Web of Knowledge, Scopus, Google Scholar, and SID were reviewed. The WHO guideline was considered for insecticide resistant level.

## Results

### Resistant status of *Aedes aegypti* and *Ae. albopictus* to Organochlorines insecticides

#### In Africa

Resistance of two *Aedes* species to dichlorodiphenyltrichloroethane (DDT) has been reported from each country where susceptibility testing has been performed. In Ghana (9, 10), Cape Verde, and Senegal (11) high *Ae. aegypti* resistance to DDT was reported. Experiments showed one *Ae. aegypti* population from Gabon and two populations of *Ae. albopictus* from Cameroon were resistant to DDT (12, 13). Also, in another study adult bioassays of three field populations of *Ae. albopictus* and *Ae. aegypti* from Cameroon showed different sus-

ceptibility levels from 68.75% to 100% against 4% DDT (14). In Central African Republic *Ae. aegypti* was resistant to DDT and *Ae. albopictus* had a sensitive population and the rest of the populations were tolerant (15). In Lagos State of Nigeria all populations of *Ae. aegypti* showed resistance to DDT (16), while in Kwara state, Nigeria, *Ae. aegypti* was completely susceptible to this insecticide (17). Highest resistance to 4% of DDT was observed in populations of *Ae. aegypti* from northern Nigeria, while the knockdown rate in dieldrin was very high (18). Two population types of *Ae. aegypti* (white and brown populations) examined in Cote D’ivoire, both populations were resistant to DDT (19, 20). Nine populations tested of *Ae. aegypti* from Senegal were resistant to DDT (21) (Fig. 1).

#### In Asia

In Thailand, resistance, or increased tolerance to dieldrin has been reported, and there is resistance to DDT, although DDT is not used in *Aedes* control programs. DDT has been used for agriculture in Thailand since 1934 was banned in agriculture in 1983. In health and for indoor spraying, it has been used against malaria vectors since 1949, and since 2000, its use in health has been ceased due to its destructive effects on the environment and the development of physiological resistance in other mosquitoes (22–27). In Malaysia, *Ae. aegypti* and *Ae. albopictus* showed resistance to DDT. *Aedes aegypti* was susceptible to dieldrin except in one area. Dieldrin resistance was reported in *Ae. albopictus* except in Kuala Lumpur and two other areas. The higher resistance of *Ae. albopictus* to dieldrin was due to the ecology of this species and its breeding sites, which was close to plants and in agricultural areas, and therefore exposed to dieldrin because it was still used in agriculture to control soil pests (28, 29). The adult *Ae. aegypti* from Jharia, Bihar were the first case of DDT resistance in India (30). In India DDT resistance in field collected *Ae. aegypti* has reported from

Goa (31) and Jharkhand (32). DDT and dieldrin resistance have been reported in all Indian *Ae. aegypti*. *Aedes albopictus* from western Bengal has shown resistance to DDT. *Aedes aegypti* females' exposure with 0.4% dieldrin resulted in 48% and 100% mortality, while 4% dieldrin for same exposure period showed 88% and 100% mortality (33–38). In China all *Ae. albopictus* adults tested populations showed resistance to DDT. Urban *Ae. albopictus* had a higher level of resistance to DDT than strains collected from rural areas (39–42). In Laos *Ae. albopictus* was resistant to DDT (43). There was high DDT resistance in adult of *Ae. aegypti* in Myanmar (44). In Philippines *Ae. aegypti* and *Ae. albopictus* larvae were sensitive to lindane, dieldrin, and DDT (45). Also, there was DDT resistance in Vietnam (46–48). In Japan all strains of *Ae. albopictus* were highly resistant to DDT (49). In Phnom Penh, Cambodia papers impregnated with DDT at 4% and dieldrin at 0.4 and 4% were used for the bioassays of adult *Ae. aegypti*. The mortality rates were reported 0% for 4% DDT and  $87.6 \pm 2.1\%$  and  $97.8 \pm 4.3\%$ , for 0.4% and 4% dieldrin%, respectively (50) (Fig. 1).

### In America

The development of resistance to DDT in Mexico and many parts of the Americas was due to the widespread use of this insecticide during the 1950s and 1960s (51). In the Americas *Ae. aegypti* resistance to DDT was initially found in Trinidad in 1955, and it was susceptible to dieldrin. Now, all parts of the Caribbean have *Ae. aegypti* populations that are resistant to DDT and dieldrin. From French Guiana to the Bahamas, the situation is uniform regarding this resistance (52). DDT resistance has been confirmed in *Ae. aegypti* Caribbean populations (53) and in two Florida populations and one New Jersey population (54). There were 45 dengue epidemics in Cuba in 1977, 1981, 1997 and 2002 and *Ae. aegypti* resistance to DDT has been seen in this country (55, 56). In Colombia resistance to DDT was seen in all

mosquito populations tested, although this insecticide did not use for vector control in any of the study areas (57–59). In Venezuela low mortality in larvae *Ae. aegypti* was exhibited by field strains toward DDT and confirmed the presence of high resistance to this insecticide (60). After exposure of adults of *Ae. aegypti* from Santo Domingo, Dominican Republic to discriminating concentrations of DDT, it was found that wild populations were resistant to this insecticide (61). In Brazil eradication programs from 1950 to 1970 might have led to spread of DDT resistance (62). All of populations of *Ae. aegypti* from Peru were resistant to DDT (4%), after 1 hour of exposure with papers treated (63) (Fig. 1).

### In Australia and Oceania

Adult bioassays detected significant resistance to dieldrin and DDT in *Ae. aegypti* population from Townsville City, despite DDT has not been used for adult control in this city for minimum 12 years, and dieldrin is not an adulticide (64). Susceptibility to DDT of *Ae. aegypti* and *Ae. albopictus* populations seems to have decreased in Papua New Guinea (65) (Fig. 1).

### Resistant status of *Aedes aegypti* and *Ae. albopictus* to Organophosphates insecticides

#### In Africa

Complete susceptibility to temephos, fenitrothion and malathion has been reported from both vectors in Cameroun, Gabon (12, 13), and Mayotte (66). In Central African Republic larvae of both species were sensitive to temephos and fenitrothion and only one population of resistant to fenitrothion was reported (15). In Cape Verde *Ae. aegypti* was sensitive to fenitrothion (11), but it shows resistant to temephos and sensitivity to malathion (67). In Dakar, Senegal also its sensibility to fenitrothion was reported (11). Organophosphates (0.8% and 5% malathion, 0.05% pirimiphos-methyl and 1% fenitrothion) were used for bioassays of *Ae. aegypti*

from Senegal. All the *Ae. aegypti* populations tested were susceptible to 5% malathion, while only two populations showed susceptibility to 0.8% malathion. Resistance in all populations were reported for 0.05% pirimiphos-methyl. Louga, Mbour and Barke'dji strains showed resistance to 1% fenitrothion (21). The *Ae. aegypti* populations in northern Nigeria were susceptible to fenitrothion in 2018 and 2019, with mortality of 98.6% and 100%, respectively. But, in 2020, mortalities of 93% observed and moderate resistance were registered (18) (Fig. 2).

### In Asia

In Thailand *Ae. aegypti* and *Ae. albopictus* resistance to temephos was demonstrated in some areas. *Aedes aegypti* showed susceptibility to malathion. All strains of *Ae. aegypti* were resistant to temephos except strains of Nakhon Ratchasima. *Aedes albopictus* was susceptible to both insecticides (68). In other study the larvae of both species were resistant to temephos and resistance or tolerance to Malathion and fenitrothion has been reported in different parts of north and south of Thailand, while in central and eastern parts of Thailand, were still susceptible to fenitrothion (24). Temephos has been used against *Ae. aegypti* larvae in Thailand since 1950, and malathion, fenitrothion, and pirimiphos methyl have been used for IRS and fogging (22–24, 26, 68, 69). In Sri Lanka *Ae. aegypti* and *Ae. albopictus* were sensitive to malathion. Although this insecticide has been widely used in the control of malaria and filariasis in endemic areas (70). Also, in 2020 reported that adult *Ae. aegypti* mosquitoes from Sri Lanka were susceptible to malathion 5%. For temephos the resistance ratios (RR50) varied between 0.69 and 3.93 (71). In one study in Malaysia, *Ae. aegypti* was sensitive to malathion and fenitrothion (29), in 2015 was sensitive to this insecticide, except in Kuala Lumpur and *Ae. albopictus* was resistant to malathion except in Kuala Lumpur. No resistance was observed in larvae to temephos, and various populations were susceptible or tolerant,

although it has been widely used since the 1970s and during the 1998 global pandemic (28). Chen et al. reported greater resistance of *Ae. aegypti* to temephos than *Ae. albopictus* (72). In India the susceptibility of two species was reported to malathion in 1993 (73). In other studies, *Ae. aegypti* adults were tolerant to fenitrothion and sensitive to malathion, also the larvae were sensitive to three tested insecticides including temephos, fenitrothion and malathion (32–34). Resistance of this species to dichlorvos was also reported (74). Results from the studies in 2015 showed that only one *Ae. aegypti* population had high levels of resistance to temephos and the rest also *Ae. albopictus* were susceptible (35, 74). In 2017 *Ae. aegypti* was reported sensitive to temephos except one population. In this study, exposure of *Ae. aegypti* with 1% fenitrothion for 30 and 60 minutes caused 40% and 100% mortality, respectively (36). In 2018, larvae of *Ae. aegypti* was susceptible to temephos (37). In a recent study in West Bengal all populations *Ae. aegypti* were reported sensitive to malathion (75). In China, resistance to malathion was clear in *Ae. aegypti* in Hainan Province but *Ae. albopictus* was susceptible (76). *Aedes albopictus* larvae were resistant to temephos and adult was sensitive to dichlorvos, with 100% mortality (41), also adult populations of *Ae. albopictus* in the four districts were all sensitive to malathion, but high resistance to temephos was registered (42). In Cambodia there is larval resistance to temephos in endemic areas. In the first study on the sensitivity of two *Ae. aegypti* populations to temephos, in one population, the larvae showed some degree of resistance to temephos and the other population was sensitive (77). In 2022, moderate *Ae. aegypti* resistance was observed for temephos in Phnom Penh, Cambodia. Also, papers impregnated with fenitrothion at 1%, malathion at 0.8% and pirimiphos-methyl at 0.2%, were used for the bioassays of adult *Ae. aegypti*. Organophosphate insecticides showed high mortality rates (50). Development of mild resistance of *Ae. ae-*

*gypti* to malathion was found in Jakarta, Indonesia. South Denpasar mosquitoes had the highest resistance to malathion, which was significantly different from the resistance reported in North Denpasar (78–80) and populations of *Ae. aegypti* in Banjarmasin, Kalimantan, Indonesia were susceptible to malathion 5% (81). In Vientiane Laos, based on larval bioassay, the wild population of *Ae. aegypti* strain was relatively resistant to temphos (82). In other study in Laos all seven population of *Ae. albopictus* but one was resistant to malathion and three of populations showed resistance to temphos and the rest were tolerant (43). In Philippines *Ae. aegypti* and *Ae. albopictus* larvae were reported sensitive to malathion (45). In Singapore, both species were reported to be sensitive to pirimiphos methyl (83). In another study, all *Ae. aegypti* populations were sensitive to pirimiphos methyl, and all populations of *Ae. albopictus* were resistant to pirimiphos methyl but southeastern populations were tolerant (84, 85). In another study, *Ae. aegypti* larvae were reported to be sensitive to temphos, although resistance was possible (86). *Aedes aegypti* from Dili, Timor-Leste was sensitive to malathion (87), also in Vietnam was sensitive to malathion (46–48). In Bangladesh *Ae. aegypti* mosquitoes varied in susceptibility to malathion (50µg/bottle) (88) (Fig. 2).

### In America

High levels of resistance to chlorpyrifos in *Ae. albopictus* has been found in Alabama and Florida (89). None of the eight populations of US *Ae. albopictus* larvae were resistant to temphos, also *Ae. albopictus* resistance to malathion was reported in Florida and New Jersey (54). Levels of malathion and temphos resistance were observed in *Ae. aegypti* Caribbean populations. Guyana, Jamaica, and Suriname *Ae. aegypti* populations showed only slight resistance to the larvicide. In most Caribbean countries, where malathion has been used sporadically for 20 to 30 years to control adults, there is little resistance to this insecti-

cide (90) and low levels of temphos resistance were confirmed in Grand Cayman (53). In United States *Ae. albopictus* from Florida, California, three different North Carolina populations and *Ae. aegypti* from Texas were susceptible to malathion. Conversely, *Ae. albopictus* from North Carolina and Texas were resistant to the same malathion doses (91). Mortality of *Ae. aegypti* mosquitoes tested in Jamaica with malathion, was from 84 to 90% at 30 minutes of exposure and 100% with increasing exposure time to 45 minutes (92). In 2019, *Ae. aegypti* strains from New Mexico were susceptible to the chlorpyrifos (93). In Mexico, the *Ae. aegypti* populations showed less resistant to chlorpyrifos than to pyrethroids (94). Resistance to fenthion, fenitrothion, and temphos, has been found in Cuba (55, 56). On the Island of Martinique (Caribbean), *Ae. aegypti* populations were resistant to naled (organophosphate) that showed insecticide resistance reduced its effect when applied by ultra-low volume (ULV) thermal fogging (95). There is evident that the organophosphate insecticide resistance (malathion, fenthion and temphos) is prevalent in Trinidad and Tobago larval strains of *Ae. aegypti* (96). In Cuba, Venezuela, Costa Rica and Jamaica, *Ae. aegypti* was sensitive to malathion despite its widespread use in vector control programs in these countries (97). Resistance to organophosphates is found throughout Latin America due to its intense use to control larvae, including Colombia, Cuba, Martinique, Costa Rica, Havana, Brazil, Bolivia, French Guiana, Argentina, French Polynesia, and the Caribbean. But resistance to temphos is lower in West Africa. The susceptibility of adults and larvae of *Ae. aegypti* to insecticides from Santo Domingo, Dominican Republic, was evaluated. Hatched larvae from eggs collected from ovitraps were resistant to temphos. Adults were resistant to malathion (61). larvae of *Ae. aegypti* from Cuba and other Latin-American countries were investigated for organophosphate insecticide resistance, including malathion, pirimiphos methyl, temphos, fenthion, fenitrothion

and chlorpyrifos. All the strains showed resistance to temephos except Nicaragua strain with moderate resistance to temephos. The highest resistant ratio (RR) value to temephos was in the Havana city strain followed by Panama, Costa Rica, Peru, Jamaica, and Venezuela. *Aedes aegypti* larvae were susceptible to malathion in all of the strains, and the same results obtained for fenthion and fenitrothion, but Peru strain showed moderate resistance to fenthion, and the Havana city strain had high resistance to fenthion and moderate to fenitrothion. High resistance to pirimiphos methyl has been reported in Panama, Costa Rica and Venezuela; however, Santiago de Cuba, Jamaica and Peru showed moderate resistance to this chemical. The Santiago de Cuba strain had the highest chlorpyrifos, resistant ration of 50 followed by Costa Rica and Jamaica, with Havana city, panama, Nicaragua, and Peru showing susceptibility to chlorpyrifos. The Venezuela strain showed moderate resistance to chlorpyrifos (98). *Aedes aegypti* mosquitoes from Peru were exposed for 1 hour with malathion (5%) and pirimiphos-methyl (0.25%) papers, and for 2 hours with fenitrothion (1%) papers. The Chosica population showed resistance to fenitrothion and pirimiphos-methyl and developing resistance to malathion. While the Punchana and Piura populations were susceptible to malathion and showed resistance to other evaluated insecticides (63). In southern Ecuador *Ae. aegypti* was resistant to malathion and had a mortality rate below 80% (99). In Brazil from 1999–2000 until 2010–2011, the effectiveness of temephos on *Ae. aegypti* was high, resulting in larval mortality of more than 80% throughout Brazil. The frequency of temephos-resistant individuals in the insect population increased steadily during each biennial survey, indicating a significant reduction in the effectiveness of temephos. This trend reached high levels (less than 50% mortality) in about half of the country in early 2004–2005 (100). In Colombia mosquitoes were susceptible to malathion. A high frequency of fenitrothion resistance was reported in all *Ae.*

*aegypti* mosquitoes (58), also in 2019 no evidence of malathion resistance was found in *Ae. aegypti* (59). In Venezuela high mortality was obtained with fenitrothion and fenthion against adults and larvae *Ae. aegypti* in field strains, which suggested the absence of any appreciable amount of resistance to these insecticides, but resistance to malathion, temephos, chlorpyrifos, and pirimiphos-methyl was observed (60). Larvae of *Ae. aegypti* mosquito from the Guadeloupe and Saint Martin islands were resistant to temephos and malathion compared with the susceptible Bora Bora strain. For the first time in Guadeloupe, mosquito populations of Guadeloupe and Saint Martin were resistant (weakly) to malathion (101). *Aedes aegypti* resistance to temephos has been observed in Colombia (102), and the Caribbean (90). Result of resistance of *Ae. aegypti* in Brazil show resistance to at least one of the organophosphates (temephos, fenitrothion, malathion) tested in all populations in the states of Rio de Janeiro and Espírito Santo (103). A study in the city of Curitiba, State of Paraná in Brazil reported that temephos could be used for control larvae of *Ae. aegypti* (104). In Sao Paulo, *Ae. aegypti* was resistant to temephos and susceptible to malathion. It was suggested that malathion be used in ULV instead of cypermethrin in the dengue fever control program in Sao Peteo, and fenitrothion be used in residual spraying (105). The larvae of all studied *Ae. aegypti* populations from different Brazilian regions were resistant to temephos (106, 107). *Aedes aegypti* larvae from northeastern Brazil showed the highest levels of resistance to temephos, also adults from northeastern showed the lowest levels of susceptibility to malathion (108), and adults from Recife Brazil were susceptible to malathion (109). In Tocantins state in Brazil all evaluated populations of *Ae. aegypti* were resistant to temephos (110). Resistance to fenitrothion for the four populations of *Ae. aegypti* distributed along the French Guiana exhibited resistance to fenitrothion (111). A high level of resistance to temephos was reported from *Ae.*

*aegypti* populations in Martinique (French West Indies) (112). In this study the resistance level of Juazeiro do Norte population was much less (RR=7.2), which is only slightly lower than the 2003 level (RR=10.2), because temephos has not been used for at least seven years to control *Aedes* and has been replaced by *Bacillus thuringiensis* (Bti). The increased resistance levels to temephos in Crato and Barbalha populations, indicate that the resistance management programs in Juazeiro do Norte should be done in neighboring cities. These results also show that even if temephos was replaced in Juazeiro do Norte, the recovery of susceptibility was slow (113). The results of bioassays with temephos, that has been used for decades against *Ae. aegypti* larvae in Brazil caused all the evaluated populations to be resistant to temephos (110) (Fig. 2).

### In Europe

Exposure of *Ae. aegypti* from Pau1 do Mar (Madeira) to fenitrothion given 100% mortality that indicate mosquito susceptibility to this insecticide but *Ae. aegypti* from Funchal (Madeira) was resistant to malathion and fenitrothion (114). *Aedes albopictus* adults from the Swiss-Italian border region were susceptible malathion (109) (Fig. 2).

### In Australia and Oceania

Investigating the state of sensitivity to insecticides in *Ae. aegypti* from Townsville showed that mosquitoes were resistant to malathion and fenthion and susceptible to other organophosphates, temephos, fenitrothion and chlorpyrifos (64). *Aedes aegypti* and *Ae. albopictus* were susceptible to malathion in Papua New Guinea (65) (Fig. 2).

### Resistant status of *Aedes aegypti* and *Ae. albopictus* to Carbamates insecticides

#### In Africa

In Cameroon, resistance of *Ae. aegypti* to bendiocarb and tolerance of *Ae. albopictus* to this insecticide were reported (13). In 2021 it

was reported this species was susceptible to bendiocarb (14). In Central African Republic both vectors were sensitive to propoxur and only one resistant population to propoxur was reported (15). In Kwara state, Nigeria, mortalities from exposure of *Ae. aegypti* to bendiocarb showed that all the mosquito samples tested were resistant (17). In northern Nigeria, *Ae. aegypti* mosquitoes were resistant to 0.1% propoxur (18). In Cape Verde low sensitivity *Ae. aegypti* to propoxur was reported and in Dakar, Senegal mortality of *Ae. aegypti* with propoxur was 87.2% (11). In Cote D'ivoire white and brown populations of *Ae. aegypti* were resistant to propoxur (19, 20). In Senegal, apart from the Matam populations of *Ae. aegypti* were susceptible to 0.1% bendiocarb, and all other populations were resistant to bendiocarb and propoxur (21) (Fig. 3).

### In Asia

Various levels of tolerance/ resistance to propoxur and resistant to bendiocarb and propoxur in *Ae. aegypti* has been reported in parts of central and southern in Thailand (24, 26, 69). *Aedes aegypti* resistance to bendiocarb and propoxur was also reported from Malaysia as well as *Ae. albopictus* resistance (28, 29). In India, *Ae. aegypti* females were exposed to 0.1% propoxur for 30 and 60min and mortality after 24h was 96% and 100%, but in other study *Ae. aegypti* was resistant to propoxur, although this insecticide has not been used to control vectors in India. Resistance has been due to accidental exposure or to intersection resistance (36, 37), also *Ae. albopictus* from sub-Himalayan areas of West Bengal exhibit severe resistance against propoxur (38). In China, *Ae. albopictus* adult was sensitive to propoxur (41), and resistant to bendiocarb (42). In Indonesia *Ae. aegypti* was resistant to bendiocarb. Developed resistance, with about 80–90% mortality, was observed against bendiocarb 0.1% (80, 81). Papers impregnated with bendiocarb at 0.1% and propoxur at 0.1% were used for the bioassays of adult *Ae. aegypti* in Phnom Penh, Cambodia, results showed high mortality rates

with carbamate (50). Complete susceptibility to bendiocarb was reported in populations of *Ae. aegypti* from Bangladesh (88) (Fig. 3).

### In America

In the states of Alabama and Florida, propoxur cross-resistance levels were evaluated in *Ae. albopictus*. Propoxur showed the least toxicity to *Ae. albopictus*. The results showed that propoxur tolerance levels were absent or very low in all strains (89). In New Jersey, Pennsylvania, and Florida *Ae. albopictus* was sensitive to propoxur (54). In Colombia all of *Ae. aegypti* field-collected strains were susceptible to propoxur (59). In Venezuela *Ae. aegypti* resistance to propoxur was reported (60). *Aedes aegypti* adults from Santo Domingo, Dominican Republic, were resistant to propoxur (61) (Fig. 3).

### In Europe

*Aedes aegypti* from two localities in Madeira (Funchal and Pau 1 do Mar) was resistant to bendiocarb (114). After 1h exposure and 24 h holding period to bendiocarb, *Ae. albopictus* field populations from the Swiss-Italian border region were susceptible (109) (Fig. 3).

### In Australia and Oceania

In Australian 1995 strain of *Ae. aegypti* was significantly less susceptible to bendiocarb than the 1989 strain, and both strains showed high resistance to propoxur (64). *Aedes aegypti* from the Madang population, Papua New Guinea was susceptible to bendiocarb and *Ae. albopictus* also were found to be susceptible to bendiocarb (65) (Fig. 3).

### Resistant status of *Aedes aegypti* and *Ae. albopictus* to Pyrethroids insecticides

#### In Africa

Both the *Aedes* species are present in Central Africa, but *Ae. albopictus* is more influential and was first reported in 2009. A study in this area found that both vectors were resistant

to deltamethrin, and their mortality was less than 90% (15). In Ghana, *Ae. aegypti* was resistant to deltamethrin, and lambda-cyhalothrin but was sensitive to permethrin (9). In other study some populations were resistant to permethrin and some tolerant (10). In Mayotte both species had highly sensitive to deltamethrin. No resistance to deltamethrin has been recorded on the island, although deltamethrin has been used on the island since 1984 (66). In Cameroon complete susceptibility of both species was reported to deltamethrin except in Yaounde, where *Ae. albopictus* populations showed a mortality rate of about 80% (12), but in 2017 both species were resistant to deltamethrin and decreased sensitivity to permethrin was observed (13). In 2021 *Ae. aegypti* and *Ae. albopictus* mosquitoes from Cameroon were exposed to 0.05%, and 0.75% permethrin. *Aedes albopictus* populations showed full susceptibility to permethrin and deltamethrin insecticides, but *Ae. aegypti* was resistant to these insecticides (14). In a study conducted in agricultural and non-agricultural areas of Lagos State, Nigeria, all mosquitoes from both sites were susceptible to permethrin, but about deltamethrin the most populations in non-agricultural areas were resistant and mosquitoes collected from agricultural areas were reported sensitive (16). In another study, *Ae. aegypti* was completely sensitive to permethrin (17). Adult bioassays of *Ae. aegypti* in northern Nigeria were conducted by pyrethroids: 0.25% and 0.75% permethrin, 0.03% and 0.05% of deltamethrin, Lambda-cyhalothrin, and  $\alpha$ -cypermethrin, and 0.15% cyfluthrin. Populations were susceptible to cyfluthrin but highly resistant to other type I and II pyrethroids (18). In Dakar, Senegal, *Ae. aegypti* populations was susceptible permethrin. About deltamethrin mortality was 94.5% and for lambda-cyhalothrin 81.6%. In Cape Verde *Ae. aegypti* was sensitive to deltamethrin, permethrin, and lambda-cyhalothrin (11). In another study, *Ae. aegypti* was resistant to deltamethrin, and cypermethrin (67). Bioassays of pyrethroids (0.25% and 0.75% permethrin),



0.05% deltamethrin, 0.03% and 0.5% lambda-cyhalothrin, 0.05% alpha-cypermethrin), by standard WHO test kits for adults of *Ae. aegypti* from Senegal showed that susceptibility to 0.75% permethrin was observed in all populations except in three, and one population had suspected resistance to 0.25% permethrin. Only populations of the southern regions were susceptible to type II pyrethroids (21). In Dar es Salaam, Tanzania all sites showed lower susceptibility to deltamethrin, permethrin and resistance to lambda-cyhalothrin (115). In Cote D'ivoire white populations of *Ae. aegypti* were resistant to deltamethrin and brown populations were susceptible (19, 20) (Fig. 4).

### In Asia

In Japan *Ae. albopictus* in Nagasaki showed high tolerance to pyrethroids. The cause for this may be due to the widespread use of DDT in the 1950s (116). Most studies on pyrethroid resistance in *Ae. aegypti* in Southeast Asia are from Thailand. The first outbreak of dengue fever in Thailand was in 1958 (117). Since 1950, carbamates, organophosphates, and organochlorines have been used for control. Synthetic pyrethroids have been used since 1992, low price of pyrethroids, their quick knockdown effect and relative safety for humans due to low toxicity to mammals has increased their use (22). Increased tolerance or resistance to pyrethroids has been reported from *Ae. aegypti* and *Ae. albopictus* in Thailand, such as deltamethrin and permethrin, which are widespread throughout Thailand, resistance to cypermethrin in parts of northern and western Thailand, and resistance to bioallethrin, bioresmethrin, and alpha-cypermethrin in larvae and adults. Mortality of *Ae. aegypti* with lambda cyhalothrin was 100% and had tolerated to mosquito coils. *Aedes aegypti* has shown behavioral resistance and avoidance to alpha-cypermethrin, deltamethrin, permethrin, tetramethrin, cyphenothrin in Thailand (26, 68, 118–120). In Malaysia, many studies have been conducted on the resistance of the two species to insecticides. The first study on pyrethroid

resistance was in 2001. The *Ae. aegypti* urban strain had the highest resistance to permethrin, cyphenothrin, lambda-cyhalothrin, and deltamethrin. *Aedes albopictus* was sensitive to permethrin and deltamethrin (121–123). The first study on mosquito coils against *Ae. aegypti* was in 1996, that mortality was minimal (124). In 2017, in a study was reported that mosquito coils had low insecticidal activity against *Ae. aegypti* and therefore may have little protection for mosquito bites (125). In Malaysia was reported *Ae. aegypti* resistance to permethrin (29). In the other study across Malaysia, *Ae. aegypti* was resistant to permethrin and deltamethrin (28). In India, *Ae. aegypti* and *Ae. albopictus* resistance to pyrethroids such as permethrin has been reported in Delhi and Kerala (73). In 2001 *Ae. aegypti* adults was sensitive to deltamethrin, permethrin, and lambda cyhalothrin in Delhi (33). In Another study a total of five different pyrethroid compounds were tested against *Ae. aegypti* females with exposure period of 5 and 15min in Madurai West city in Tamil Nadu State, they were found invariably susceptible to all tested pyrethroid compounds. Based on the results, the efficacy in descending order of pyrethroids was cyfluthrin > permethrin > deltamethrin > lambda cyhalothrin and > etofenprox (36). In recent studies in West Bengal, all populations *Ae. aegypti* except one site were sensitive to deltamethrin and alpha-cypermethrin (75), and two *Ae. albopictus* populations, from sub-Himalayan districts were severely resistant to permethrin (38). In China, *Ae. albopictus* is resistant to deltamethrin, permethrin, cypermethrin, and beta-cypermethrin, and resistance to pyrethroids is greater than resistance to other common insecticide groups (40–42). In Cambodia, there is *Ae. aegypti* adult resistance to the two main insecticides including permethrin (nets) and deltamethrin (fumigation) in all regions (126). The pyrethroids alpha-cypermethrin at 0.03%, bifenthrin at 0.2%, cyfluthrin at 0.15%, deltamethrin at 0.03%, etofenprox at 0.5%, lambda-cyhalothrin at 0.03% and permethrin at 0.25% were used for the bioassays of

adult *Ae. aegypti*. The adult mortalities were 0% for etofenprox,  $1\pm 1.9\%$  for permethrin,  $3.1\pm 4.1\%$  for bifenthrin,  $4.2\pm 8.3\%$  for lambda-cyhalothrin,  $10.2\pm 7.1\%$  for deltamethrin,  $11\pm 4.5\%$  for alpha-cypermethrin and  $35\pm 11\%$  for cyfluthrin and there were low mortality rates with all the tested pyrethroid insecticides (50). In Indonesia, *Ae. aegypti* larvae were sensitive to pyrethroids (78, 127). *Aedes aegypti* adult resistance was reported to more than one pyrethroids of cypermethrin, permethrin and D-allethrin (78). In other study, adult *Ae. aegypti* resistance to permethrin and deltamethrin and high levels of resistance to alpha-cypermethrin and lambda cyhalothrin has been reported (128). In 2017, all *Ae. aegypti* adults tested in Jakarta were resistant to deltamethrin, permethrin, and lambda cyhalothrin, with a mortality rate of less than 90%. Resistance to permethrin was higher than the others (79). Also, resistance of *Ae. aegypti* to deltamethrin, permethrin, lambda cyhalothrin, cyfluthrin in Denpasar, Bali has been reported (80). In Banjarmasin, Kalimantan, Indonesia, all *Ae. aegypti* populations showed different degree of resistance to 0.15% cyfluthrin 0.05% deltamethrin, 0.05% Lambda-cyhalothrin, and 0.75% permethrin, with mortalities less than 90% (81). In Laos high level of resistance against permethrin, and high susceptibility to deltamethrin was reported in *Ae. aegypti* (129). In the other study seven populations of *Ae. albopictus* were sensitive to permethrin and deltamethrin (43). In Myanmar high pyrethroid resistance (permethrin and deltamethrin) has been reported in the larvae and adult of *Ae. aegypti* (44). In Singapore, *Ae. aegypti* is the primary vector of Dengue Virus. The first case was reported in the 1960s (130). *Aedes aegypti* resistance to permethrin, cypermethrin, and deltamethrin has been demonstrated in Singapore (83-85). In other two studies, *Ae. aegypti* larvae were resistant to permethrin and etofenprox (86), and *Ae. aegypti* adult with PermaNet® had less than 80% mortality (131). *Aedes aegypti* from Dili, Timor-Leste, has become resistant to perme-

thrin, lambda-cyhalothrin and resmethrin (87). In the first insecticide resistance investigation of *Ae. aegypti* in several locations of Central Highlands and Nam Bo in Vietnam, the mosquitoes were susceptible to pyrethroids such as deltamethrin in the central and northern regions. In the southern and central mountainous regions *Ae. aegypti* was resistant to deltamethrin, permethrin, lambda-cyhalothrin and alpha-cypermethrin. This is due to the long use of pyrethroids in the control of malaria and dengue fever and its use in agriculture, especially in the southern and central regions (46). In the next study, *Ae. aegypti*'s sensitivity to permethrin, lambda-cyhalothrin, deltamethrin, and alpha-cypermethrin was reported in many parts of the north and center but was resistant to these insecticides in southern and central Vietnam (47). In 2009, it was reported that, *Ae. aegypti* sensitivity to D-allethrin has decreased. Mosquitoes were sensitive to pyrethroids in northern and central Vietnam but were resistant in southern and central Vietnam (132). In 2016 and 2003 also, *Ae. aegypti* resistance was reported to permethrin and lambda-cyhalothrin (48, 133). Also, populations of *Ae. albopictus* tested from Vietnam exhibited high-level resistance to permethrin (134). In 2010, study of pyrethroid susceptibility of larvae *Ae. albopictus* collected from Nagasaki City, Japan, indicated populations of *Ae. albopictus* tolerant to pyrethroids spread widely in Nagasaki (116). In other study in this city insecticide susceptibility tests were performed on *Ae. albopictus* adults and larvae of F1 colonies collected from Nagasaki City, Japan. The results were compared with those of several such colonies collected from other locations in Japan. The larvae collected from Nagasaki City, also from other locations in Japan were resistant to *d*-T80-allethrin and more than half of the adults of the Nagasaki and Fukuoka colonies showed resistance to permethrin (135). Susceptibility of adult *Ae. aegypti* mosquitoes from Sri Lanka to deltamethrin 0.05%, permethrin 0.75% were evaluated by the standard WHO mosquito bi-

bioassay protocol. Results revealed resistance in all *Ae. aegypti* populations for both permethrin (10–89%) and deltamethrin (40–92%) (71). In Bangladesh *Ae. aegypti* mosquitoes were exposed to diagnostic dose of 15µg/ bottle for permethrin, and 10µg/bottle for deltamethrin. High levels of resistance to permethrin were reported in *Ae. aegypti*, while sensitivity to deltamethrin was different between populations (88) (Fig. 4).

### In America

High resistance to pyrethroids were observed in *Ae. aegypti*. All Grand Cayman *Ae. aegypti* populations survived after one hour of exposure to pyrethroid-impregnated papers (53). In the USA adult mortality after a 24h exposure to the pyrethroid insecticides (deltamethrin, prallethrin, and phenothrin) at discriminating doses showed that, all the field populations tested were susceptible (99–100% mortality) (54). In Florida, California, North Carolina, and Texas, vectors were resistant to low doses of etofenprox. *Ae. aegypti* was also resistant to high doses in Texas. Six populations of *Ae. albopictus* showed susceptibility to bifenthrin and two populations *Ae. aegypti* and *Ae. albopictus* were resistant and possible resistance was shown in one *Ae. albopictus* population. Seven *Aedes* spp. populations were susceptible (100%) to permethrin and one population was resistant. Possible resistance was shown in one *Ae. albopictus* population. All tested *Ae. albopictus* were susceptible (100%) to phenothrin and one population of *Ae. aegypti* was resistant. Six *Ae. albopictus* populations were susceptible to the low dose of deltamethrin. At the high deltamethrin dose, seven *Ae. albopictus* populations were susceptible and two *Ae. albopictus* and *Ae. aegypti* populations showed possibility of resistance (91). *Aedes aegypti* from New Mexico showed high pyrethroid resistance and kdr mutation F1534C in the para gene (93). In Texas/Mexico border cities all populations of *Ae. aegypti* showed resistance to permethrin, deltamethrin and sumithrin, although none of these

insecticides are commonly used for vector control activities in this region (136). All *Ae. aegypti* mosquitoes tested in Jamaica were resistant to permethrin (92). Laboratory bioassay on the Island of Martinique (Caribbean) showed that *Ae. aegypti* populations were strongly resistant to pyrethrins and deltamethrin therefore insecticide resistance decreased the efficacy of space sprays for adult mosquito and dengue control (95, 137). There is evidence of resistance to permethrin in populations in Baja California North, South and in Quintana Roo, south of Mexico and some states of northeast Mexico due to use for more than 10 years in Mexico for control of *Ae. aegypti* (138-140). The results obtained from Veracruz State Mexico showed that the field strains of *Ae. aegypti* were resistant to most of the pyrethroids analyzed including cypermethrin, deltamethrin, δ-phenothrin, α-cypermethrin, *d*-phenothrin, *z*-cypermethrin, λ-cyhalothrin, bifenthrin, and permethrin and suggested that populations in the state of Veracruz were under the strong selection pressure, causing from the continuous use of permethrin for more than a decade (141). In Cuba, *Ae. aegypti* resistance was reported to deltamethrin, lambda cyhalothrin, beta-cypermethrin, cypermethrin, and cyfluthrin (55, 56). *Aedes aegypti* from Jamaica was resistant to permethrin with types of the mode of mechanism (92). One study on mosquitoes collected from eight Latin American countries showed that larvae from the Havana city strain were resistant to all the pyrethroids, the highest RR50 was to deltamethrin, as well as lambda cyhalothrin, betacypermethrin and cyfluthrin showed high resistance. Larvae from Santiago De Cuba, Peru and Venezuela showed high deltamethrin RR50 values as well as Havana City (98). Populations of *Ae. aegypti* from Peru were exposed for 1h to papers treated with alpha-cypermethrin (0.05%), cypermethrin (0.05%), deltamethrin (0.05%), etofenprox (0.5%), lambda-cyhalothrin (0.05%), and permethrin (0.75%). Results showed *Ae. aegypti* from Chosica was resistant to alpha-cypermethrin, cypermethrin, etofenprox, also developing resistance

to lambda-cyhalothrin, and susceptibility to deltamethrin were reported. But the Punchana and Piura populations were resistant to all insecticides (63). In Tocantins state in Brazil the data showed different resistance to deltamethrin among the samples of *Ae. aegypti* (110). In southern Ecuador *Ae. aegypti* was resistant to deltamethrin and alpha-cypermethrin (99). In study of insecticide resistance status of *Ae. aegypti* from Colombia, susceptibility to deltamethrin and cyfluthrin was reported in all mosquito populations studied. Six populations were resistant to lambda-cyhalothrin. Four field populations showed resistance to permethrin, two populations were also resistant to lambda-cyhalothrin. Pyrethroid resistance was not found in populations from the state of Antioquia. Resistance to etofenprox was reported in all mosquito populations, however, there is no record of using this insecticide for dengue control programs at any of the study sites (58). In other study the most of field populations were resistant to permethrin. The resistance to deltamethrin was observed only in one site and lambda cyhalothrin resistance in three sites (59). The lambda cyhalothrin resistance has been commonly detected in Colombia (142). In Venezuela *Ae. aegypti* moderate levels of resistance to permethrin and lambda cyhalothrin was reported (60). *Aedes aegypti* in different Brazilian regions were resistant to deltamethrin, cypermethrin, permethrin (104–108, 113, 143). In Brazil *Ae. albopictus* adult mortality rates with permethrin and  $\lambda$ -cyhalothrin were close to 100% (109). Evaluation of insecticide resistance in *Ae. aegypti* populations the case of Tocantins state in Brazil showed different state of resistance to deltamethrin among the samples (110). In one study, severe resistance to deltamethrin with weak knockdown effect and low mortality was observed in French Guiana *Ae. aegypti* populations (111). *Aedes aegypti* adults from Santo Domingo, Dominican Republic, were reported resistant to permethrin and deltamethrin (61). Tests done with adult mosquitoes of *Ae. aegypti* reported moderate resistance status to deltamethrin

from Guadeloupe and Saint Martin islands (101) (Fig. 4).

### In Europe

In Italy resistance to  $\alpha$ -cypermethrin and permethrin in adult *Ae. albopictus* has been reported. Resistance to permethrin was seen from Ferrara Province in Emilia-Romagna and from Bari Province in Puglia while the field-population from Athens (Greece) showed possibility of resistance. Resistance to  $\alpha$ -cypermethrin was reported for the mosquitoes in Ferrara Province Venezia Province and Rome but four Italian populations were susceptible. Eight Italian populations, and the Albanian one, showed susceptibility to deltamethrin but the Greek laboratory colony was resistant (144). In the Swiss-Italian border region *Ae. albopictus* adult mortality rates with permethrin and  $\lambda$ -cyhalothrin were close to 100% (109). In Spain, 5 populations of *Ae. albopictus* were studied, four populations were sensitive to deltamethrin and permethrin. In the case of cypermethrin, two populations of *Ae. albopictus* were sensitive to this toxin and two populations were tolerant and one population was reported to be resistant (145). *Aedes aegypti* from Funchal was reported to be resistant to cyfluthrin and permethrin. Resistance to pyrethroids was also seen in the Pau 1 do Mar population. Pyrethroids mortality rates were between 2% (permethrin), and 88% (cyfluthrin) (114). Populations of *Ae. albopictus* tested from Italy exhibited high-level resistance to permethrin (134) (Fig. 4).

### In Australia and Oceania

Results a study in 1999 showed that there was no evidence of resistance to synthetic pyrethroids (deltamethrin and permethrin) (64). Experiments on Queensland mosquitoes with pyrethroids (bifenthrin, deltamethrin and lambda-cyhalothrin) did not show *Ae. aegypti* resistant, and bioassays showed only weak tolerance. There was no evidence of kdr mutations in Queensland *Ae. aegypti*. In Cairns South, a low resistance to lambda-cyhalothrin was re-

ported in a sample of *Ae. aegypti* at 24h after exposure. Obvious resistance to bifenthrin has not been detected in field populations of *Ae. aegypti* from northern Queensland (146). Study of resistance of *Ae. aegypti* and *Ae. albopictus* in Papua New Guinea clearly show high pyrethroid resistance: deltamethrin and lambda cyhalothrin in both Madang and Port Moresby *Ae. aegypti* populations. The *Ae. aegypti* population in Port Moresby show a higher level of deltamethrin resistance than Madang where susceptibility to lambda-cyhalothrin has been greatly reduced (65) (Fig. 4).

### **Resistant status of *Aedes aegypti* and *Ae. albopictus* to Insect growth regulator (IGRs) and microbial insecticides**

#### **In Africa**

In Cameroon, Gabon (12) and Central African Republic (15) larvae of both species were susceptible to *Bacillus thuringiensis israelensis* (Bti). In Mayotte complete susceptibility to Bti, and IGRs including spinosad, diflubenzuron, pyriproxyfen, and methoprene was reported (66). In Cape Verde also was observed sensitivity to diflubenzuron and Bti (67) (Fig. 5).

#### **In Asia**

In China, *Ae. albopictus* larvae from all studied areas were sensitive to Bti and hexafluoromoron, but in one population showed high resistance to pyriproxyfen and moderate resistance to pyriproxyfen (42). In Singapore, larval mortality due to Bti was 100% (86). In Malaysia susceptibility of field *Ae. aegypti* larvae to Bti was reported (147), but *Ae. aegypti* and *Ae. albopictus* populations from 12 states in Malaysia showed a different state of resistance to five IGRs (pyriproxyfen, methoprene, cyromazine, novaluron and diflubenzuron). *Aedes albopictus* was susceptible against cyromazine, pyriproxyfen, and methoprene. Field-collected *Ae. aegypti* showed high susceptibility to diflubenzuron, cyromazine, and novaluron (148). Susceptibility of a wild larval population of *Ae.*

*aegypti* against Bti, diflubenzuron, pyriproxyfen and spinosad was tested in Vientiane Laos. With bioassays of larvae was found that the wild *Ae. aegypti* strain was moderately resistant to spinosad and susceptible to the other insecticides. Based on field bioassays, all tested insecticides remained above the WHO acceptable larvicidal threshold after 28 weeks (82). In Cambodia for larvae, moderate *Ae. aegypti* resistance was reported for spinosad ( $RR_{90} < 5.6$ ) but, there was no resistance against Bti ( $RR_{90} < 1.6$ ) (50) (Fig. 5).

#### **In America**

The susceptibility *Ae. albopictus* to imidacloprid, spinosad, and Bti was investigated in Alabama and Florida. These results reported that mosquitoes collected from field were much more susceptible to spinosad than to the other insecticides tested in the study (89). Of the eight USA populations of *Ae. albopictus*, none were resistant to the larvicides tested (Bti, spinosad, methoprene, and pyriproxyfen) but reduced susceptibility *Ae. albopictus* to the IGRs pyriproxyfen and methoprene was observed in Florida and New Jersey (54). The larvae of all studied *Ae. aegypti* populations from different Brazilian regions were susceptible to diflubenzuron and Bti (106, 107, 109). A tolerance to IGRs and full susceptibility to spinosad and Bti was reported in Martinique. In experiments pyriproxyfen and Bti had 28- and 37-weeks activities in permanent breeding containers, whereas under field conditions they could not control *Ae. Aegypti* populations after four weeks. But diflubenzuron and spinosad were effective for 16 weeks, therefore these chemicals can be alternatives to Bti and temephos to control resistant *Ae. aegypti* (112, 149). In French Guiana, ULV spraying with BT was caused 100% mortality in *Ae. aegypti* populations (111) (Fig. 5).

#### **In Europe**

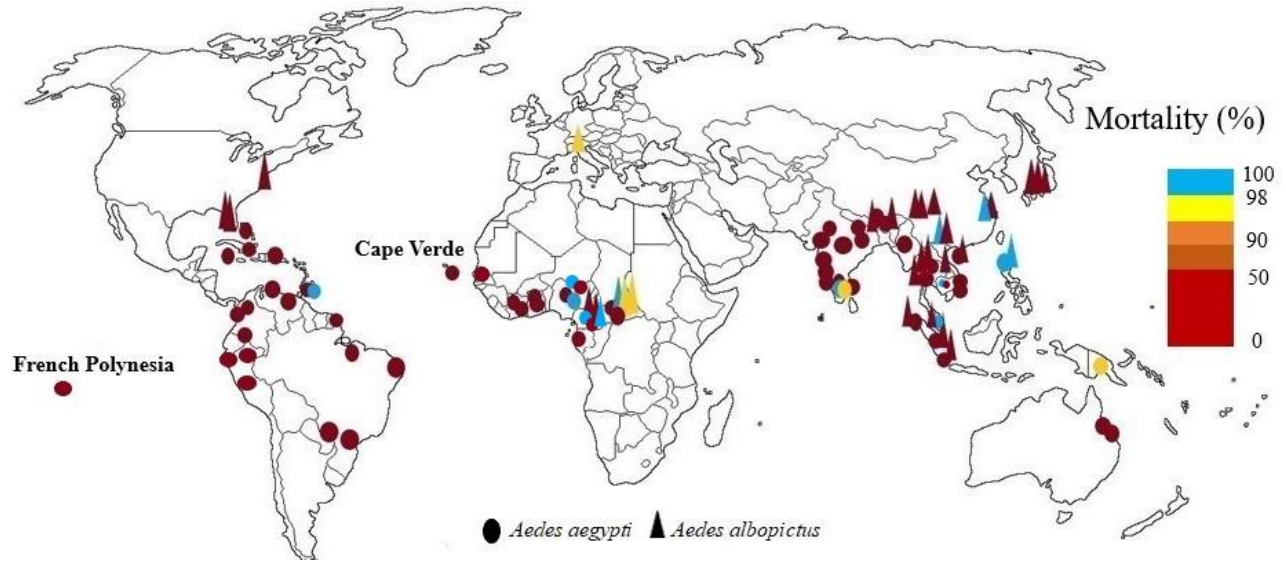
The *Ae. albopictus* populations from the Canton of Ticino in southern Switzerland, and the Como area in northern Italy were all sus-

ceptible to Bti. The efficacy of *Lysinibacillus sphaericus*, another entomopathogenic bacterium, was tested against *Ae. albopictus* and showed good activity. The activity a mixture of Bti and *L. sphaericus* crystals “Vectomax®”, was also studied to determine if these insecticidal components are effective for controlling *Ae. albopictus*. In this study *Ae. albopictus* was also susceptible to diflubenzuron (109) (Fig. 5).

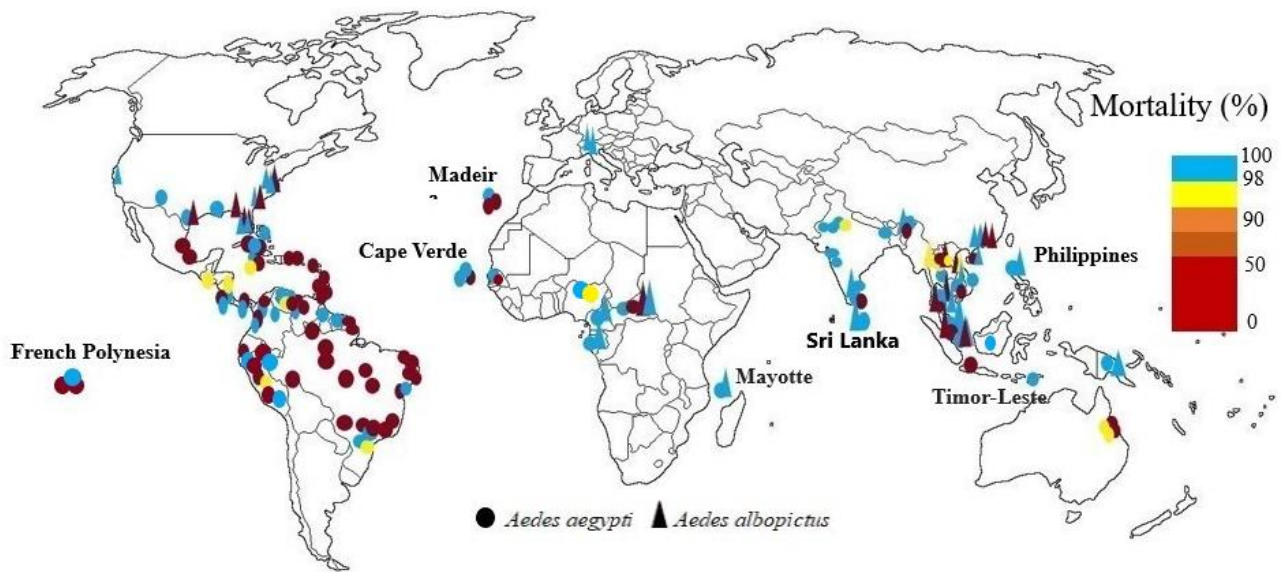
### **Mechanisms of insecticide resistance in *Aedes aegypti* and *Ae. albopictus***

The mode of action of insecticides is mostly on the nervous system of insects. Target-site mutations and metabolic resistance are two main resistance mechanisms in *Ae. aegypti* and *Ae. albopictus*. In the mutation at the target site, which is one of the worst resistance mechanisms in insects, the insect makes the insecticides ineffective by changing the structure of the targets of the insecticides. Pyrethroids and DDT act on voltage-gated sodium channels, and the mutation in the amino acid sequence of this gene causes the sensitivity of the channels to prevent the binding of pyrethroids and DDT to decrease. The use of pyrethroids with cross-resistance mechanisms (especially *kdr* mutations) existing in DDT caused to the rapid rise of pyrethroid resistance. Also, resistance to acetylcholinesterase (AChE) is current in *Aedes* and is related to organophosphate and carbamate insecticides. Mutations in the gene coding for the neurotransmitter acetylcholinesterase number one (*ace-1*) decrease the inhibition effect of the insecticide on the enzyme. Metabolic resistance is very current in mosquitoes and has been observed against all insecticides used for vector control. Mosquitoes have enzyme systems that protect them from foreign compounds, and some of these enzymes can break down insecticides before they reach their site of action. In metabolic resistance, the enzymes that detoxify the insecticide are overexpressed or the enzyme's affinity for the insecticide is altered by amino acid substitution. Three of the most important of these enzymes are cytochrome P450 monoox-

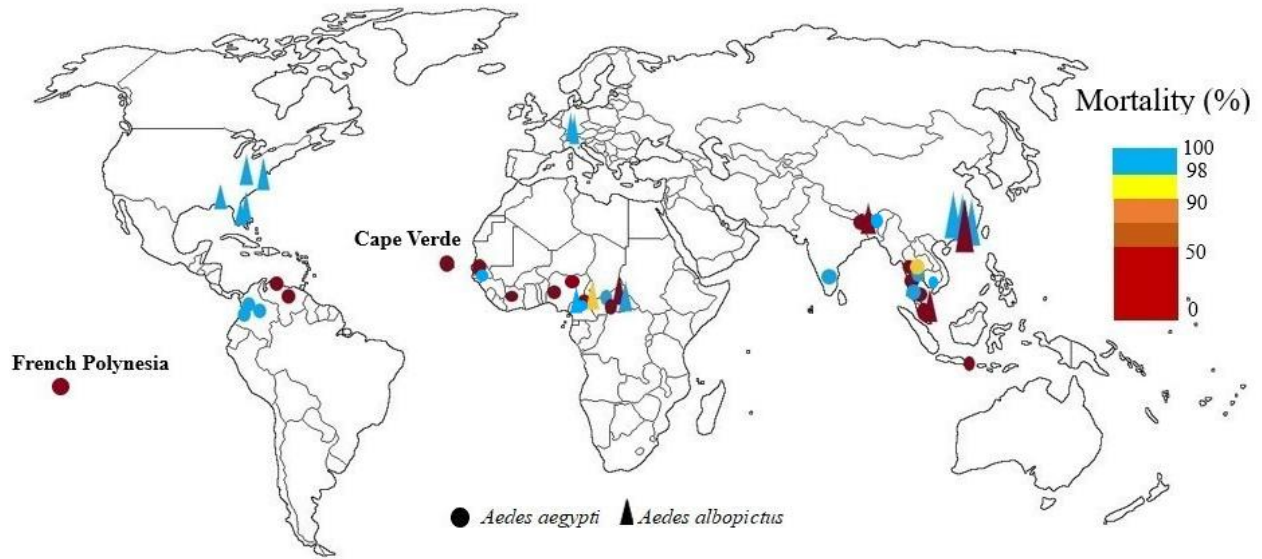
xygenases, glutathione S-transferases (GSTs) and esterases (62, 150, 151). Bti bacterial larvicide due to the presence of an intact endotoxin complex and synergy among individual toxins, especially the presence of Cyt1A, it has the lowest risk of developing resistance. Bti plays an important role in reducing the development of resistance and maintaining sensitivity in other biolarvicids. Binary toxins from *Bacillus sphaericus* have many advantages in controlling mosquito larvae. Laboratory data and field studies worldwide showed that a combination of Bti with *B. sphaericus*, the best way to increase larvicidal activity is to prevent resistance and restore susceptibility to *B. sphaericus*. In the case of IGR insecticides, the risk of developing resistance is low. Late 4th instar larvae and pupae with lower internal juvenile hormone titers are more susceptible to juvenile hormone analogs such as methoprene and pyriproxyfen in the transfer from late 4th instar larvae to pupae and adults. In aquatic habitats, different ages of mosquito larvae coexist, with very different levels of internal rejuvenation hormones. This phenomenon leads to sublethal exposures, tolerance and even the development of resistance (152).



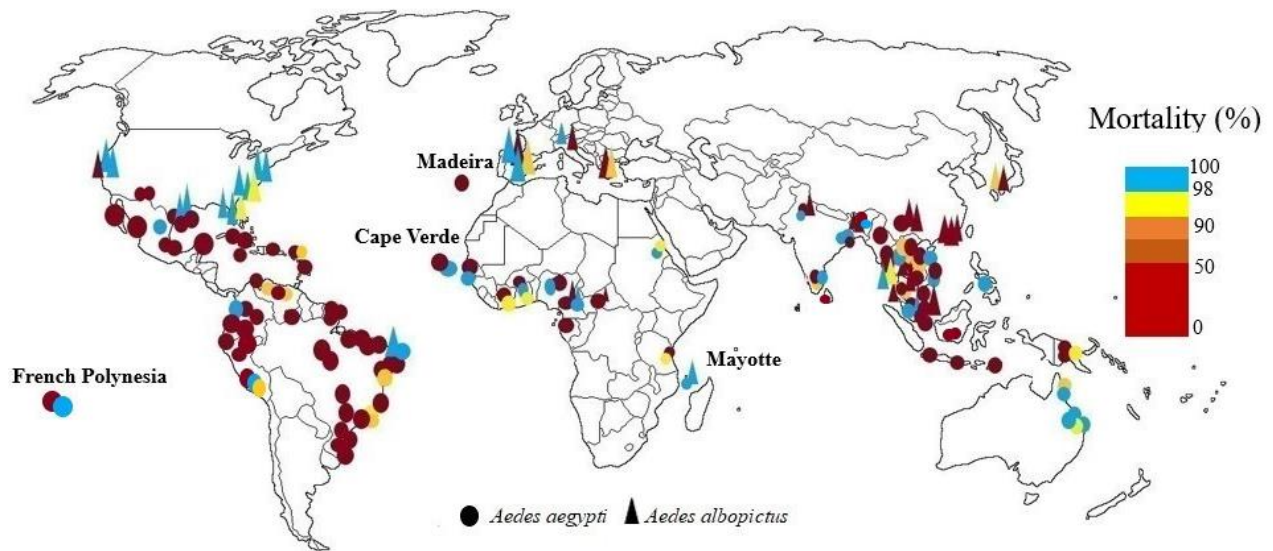
**Fig. 1.** World mapping of organochlorine insecticide resistance in *Aedes aegypti* and *Aedes albopictus* up to December 2022



**Fig. 2.** World mapping of organophosphates insecticide resistance in *Aedes aegypti* and *Aedes albopictus* up to December 2022

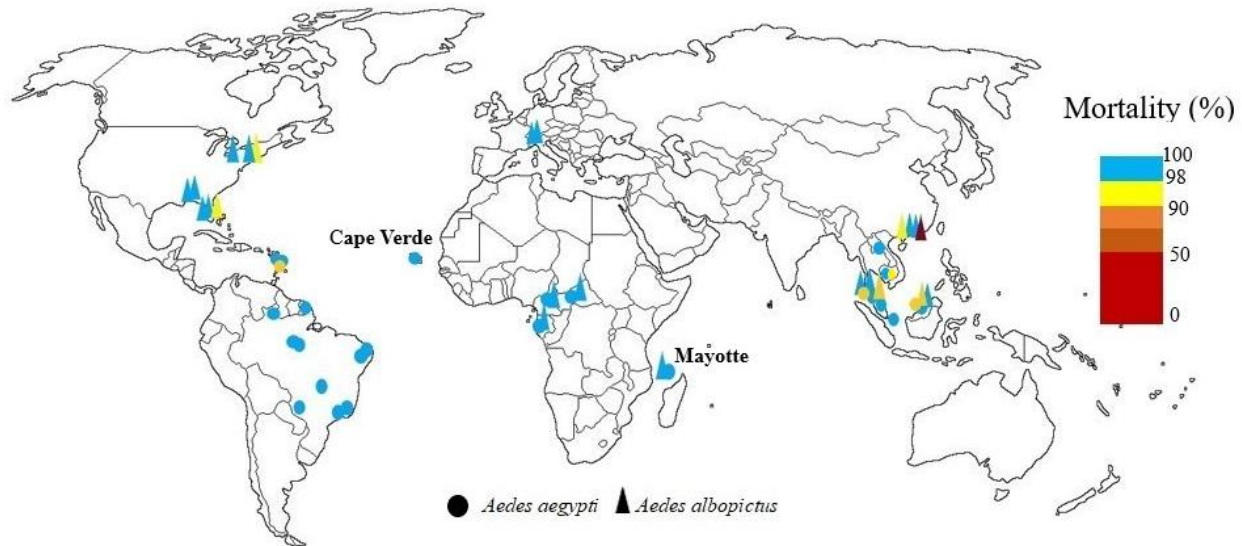


**Fig. 3.** World mapping of carbamates insecticide resistance in *Aedes aegypti* and *Aedes albopictus* up to December 2022



**Fig. 4.** World mapping of pyrethroids insecticide resistance in *Aedes aegypti* and *Aedes albopictus* up to December 2022





**Fig. 5.** World mapping of Insect growth regulator (IGRs) and microbial insecticides insecticide resistance in *Aedes aegypti* and *Aedes albopictus* up to December 2022

## Conclusions

WHO recommended bendiocarb, propoxur, DDT, fenitrothion, malathion, pirimiphos-methyl,  $\alpha$ -cypermethrin, bifenthrin, cyfluthrin, deltamethrin, etofenprox, lambda cyhalothrin has been recommend as indoor residual spraying for mosquito control. Alpha-cypermethrin, cyfluthrin, deltamethrin, deltamethrin, etofenprox, lambda cyhalothrin, permethrin are being used for impregnation of bednets. Fenitrothion, malathion, pirimiphos-methyl, bioresmethrin, cyfluthrin, cypermethrin, cyphenothrin, d,d-trans-cyphenothrin, deltamethrin, d-phenothrin, etofenprox, lambda cyhalothrin, permethrin, resmethrin for thermal fog and space spraying. Fuel oil, *B. thurigiensis*, chlorpyrifos, diflubenzuron, fenthion, methoprene, novaluron, pyriproxyfen, pirimiphos-methyl, and temephos are recommended as larvicides.

Because of importance of *Ae. aegypti* and *Ae. albopictus* in transmission mosquito-borne arboviruses, resistance management programs and strategies should be further considered in worldwide to prevention from insecticide resistance in arbovirus vectors.

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## Conflict of interest statement

The authors declare there is no conflict of interests.

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