ZEAL SCIENTIFIC PUBLICATION

World Journal of
Advanced Science and Tehnology

Journal homepage: https://zealjournals.com/wjast/

(REVIEW ARTICLE)

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A review of vectors, vector borne diseases, vector control and their impact on public health

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World Journal of Advanced Science and Technology, 2022, 02(02), 001–011

Publication history: Received on 03 September 2022; revised on 10 October 2022; accepted on 13 October 2022

Article DOI: https://doi.org/10.53346/wjast.2022.2.2.0046

Abstract

Mosquitoes are most important insect vectors for human disease transmission. Dengue, yellow fever, chikungunya, and zika are all spread by *Aedes* mosquitoes in many parts of the world. The primary vector of human malaria transmission is *Anopheles. Culex* is responsible for the transmission of Japanese encephalitis, lymphatic filariasis and West Nile virus fever. Synthetic pesticides have been successfully utilized in mosquito-control programmes for several decades. However, there are a number of disadvantages to the chemical method. As a result, there has been a rise in concern in the usage of biological agents for mosquito control in recent years. Because of their highly effective mosquitocidal activity, *Bacillus sphaericus* and *Bacillus thuringiensis israelensis* have been utilized extensively. While insecticide-based interventions have successfully reduced mosquito populations for a number of years, the reliance on a few number of insecticides has now led to the evolution of resistance. So there is a need to search for novel mosquitocidal bacteria for control the mosquito species. Since soil is one of the world's most diversified environments in which bacteria and fungi are abundant, screening of soil samples for isolation of novel mosquitocidal bacteria is attempted.

Keywords: Dengue; Lymphatic filariasis; *Aedes; Culex*; *Bacillus sphaericus*; *Bacillus thuringiensis israelensis*

1 Introduction

1.1 Soil biodiversity

Diversity of bacteria and fungi are abundant in terrestrial soils [1]. Soils are important life sphere that can generate essential resources [2, 3]. One gram of soil can support billions of organisms which include thousands of bacterial and fungal species [4, 5]. Furthermore, in organic-rich soils, invertebrate species range from hundreds to thousands per square meter [6].

Microorganisms play a significant role in forming a complex relationship between plants and soil and microbial activity is very necessary to maintain soil health for optimal crop growth. Soil microorganisms are a living component of the soil system that conduct a variety of biological processes, including organic matter conversion and nitrogen fixation [7]. Soil microorganisms such as bacteria, algae, fungi, actinomycetes, protozoa, and viruses are the bodies that make up the vast array of microscopic activity [8]. The chemical and physical makeup of soil varies around the world [9]. Soil holds millions of organisms which takes part in the change of soil richness and increases plant developments [10].

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1.2 Mosquito vectors

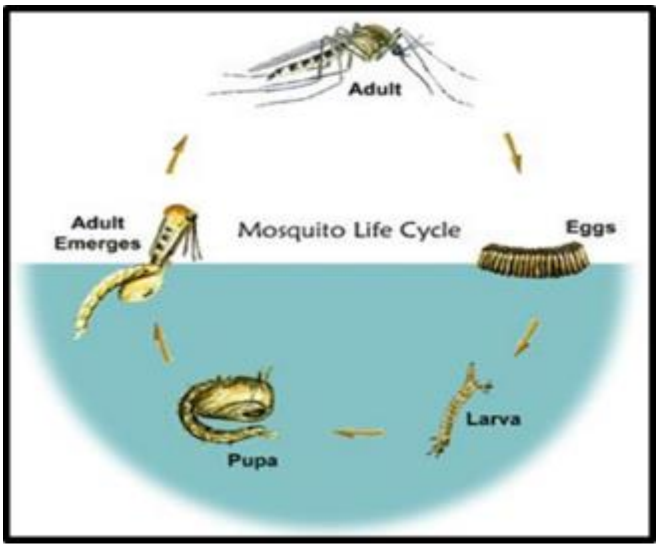
By spreading dangerous pathogens to humans and animals, mosquitoes play a significant role in the transmission of serious diseases to their hosts [11]. Mosquito breeding places have rapidly spread over the world as a result of inadequate sanitation and warm, humid weather [12]. A mosquito readily uses humans as a source of blood meal and therefore resides in high numbers in close proximity to humans over a large geographic area and in addition serves as a major vector of human pathogen. Mosquito vectors can transmit a variety of infections, including arboviruses, protozoans, and microfilariae, which cause serious infectious illnesses [13]. Mosquitoes of medical interest belong to the *Culicidae* family. There are presently 3556 recognized mosquito species in this huge family, which are divided into the subfamilies *Culicinae* and *Anophelinae*. *Anopheles*, *Aedes*, and *Culex* are the three most common mosquito vector genera [14].

Mosquitoes are most important insect vectors for human disease transmission. Female mosquitoes need human blood as a source of sustenance to complete their life cycle. When they suck the blood from infected person and subsequently bite another uninfected person, they help spread infections. Human diseases are carried by several mosquito genera. Lymphatic filariasis, dengue, yellow fever, chikungunya, and zika viruses are all spread by *Aedes* mosquitoes in many location of the world. *Culex* genus is responsible for the transmission of Japanese encephalitis, lymphatic filariasis and West Nile virus [15].

Because many vector-borne diseases lack vaccines and also treatment resistance is on the rise, vector control is frequently the best and only method of preventing disease outbreaks and transmission. Controlling vectors as a means of interrupting disease transmission is one way of managing these diseases. Controlling mosquito larvae is seen to be a successful approach to integrated vector management [16]. Therefore, preventing mosquito reproduction by the use of appropriate larvicides or the application of pesticides to larval habitats and by getting rid of unnecessary containers, and educating the public are the best ways to reduce the spread of diseases [17-19]. Mosquito larvae are an attractive target for chemicals which are used to control mosquito populations. Since larvae, unlike adults, cannot alter their behaviour to elude control efforts, targeting the larval stages has the advantages of eliminating mosquitoes before they disseminate to human habitations. Besides it also reduces the overall pesticide use in adult mosquito control [20,21].

1.3 Life Cycle of Mosquitoes

Mosquitoes require a stagnant water environment to thrive. Fresh water, salt marshes, brackish water, and water found in containers, old tyres, and tree holes are all the places where they complete their life cycle On the water surface or in a flood-prone location, the female mosquito lays hundreds of eggs at a time. Unhatched eggs of some species can survive for weeks to months of desiccation and stay alive until the right conditions for hatching appear. Eggs hatch in two to three days in most species, and larvae feed on organic detritus in the water for about a week before becoming pupae. After 2 to 3 days pupae metamorphose into adult mosquitoes (Fig. 1).



(Source: EPA https://www.epa.gov/mosquitocontrol/mosquito-life-cycle)

Figure 1 Life cycle of mosquito vectors

Female mosquitoes bite animals for blood feeding while male mosquitoes dine mostly on flower nectar. The female mosquitoes need a blood meal before laying eggs and can suck more blood than their own weight in a single meal [22].

1.4 Eggs

Eggs are laid one at a time or in groups called "rafts." They float on the water surface. The eggs of *Culex* species are clumped jointly in rafts of up to 200 eggs while *Aedes* and *Anopheles* species lay their eggs separately. Many *Aedes* species deposit the eggs on moist soil that will be flooded by water, while *Anopheles*, and *Culex* lay their eggs on the water surface. Mostly these eggs develop into larvae in 48 hours or less. Water is an essential component of their environment [23] (Fig. 2).

Figure 2 Egg rafts laid by *Culex quinquefasciatus.* Colour changes from early to late stages

1.5 Larvae

The larvae are aquatic organisms that need to breathe toward surface of the water. Larvae molt 4 times before developing into the next instar. The majority of larval species breathe by syphon tubes and dangle upside down from surface of the water, while *Anopheles* larvae do not have siphon tubes, so it lies parallel to the water surface to acquire oxygen through a breathing aperture. *Coquillettidia* and *Mansonia* larvae use plants as a source of oxygen. Organic debris and Microorganisms in the water provide food for the larvae. The larva transforms into a pupa during fourth molt [23] (Fig. 3).

Figure 3 *Culex quinquefasciatus* larvae (3rd instar)

1.6 Pupa

The non-feeding and resting period is known as the pupal stage. Pupae, on the other hand, are active, reacting to light changes by tumbling to the bottom or hiding spots with a flick of their tails. The mosquito transforms into an adult at this point. This process is analogous to butterfly metamorphosis, which occurs when a caterpillar transforms into an adult butterfly while in the cocoon stage. The pupal skin separates after development is complete, and the adult mosquito (imago) emerges [23] (Fig. 4).

Figure 4 *Culex quinquefasciatus* pupa

1.7 Adult

The newly emerging adult takes a brief break on the water surface to allow its body parts to harden and dry before it can fly, the wings must expand out and dry completely. After the adults emerge, mating and blood feeding do not occur for a few days. Duration of each stage is determined by temperature and species characteristics. Some species complete their life cycle in short days while others as long as a month.

The Female mosquitoes need a blood meal and bite cold and warm blooded animals as well as birds. Carbon dioxide, temperature, wetness, smell, colour, and movement are all stimuli that influence biting (blood feeding). The male mosquitoes do not bite, instead they feed on flower for nectar or other sugar sources. Although obtaining a blood meal (protein) is necessary for egg formation, most male and female mosquitoes are nectar eaters. Female *Toxorhynchites* are unable to consume blood and must rely on nectar to survive. Human blood is rarely the first choice of female mosquitoes capable of blood feeding. Horses, cattle, small mammals, and/or birds are the animals of choice [23].

1.8 Culex

Culex quinquefasciatus is found across tropics and subtropics, where it has been linked to the transfer of a variety of viruses that are harmful to humans and wildlife. *Culex quinquefasciatus* was originally from West Africa's lowlands, but human activities have spread the species to tropical and warm temperate regions. Genetic research has made great use of *Cx*. *quinquefasciatus* because of the taxonomic controversy surrounding it and its value as a vector [24].

The lymphatic filariasis is caused by nematode parasitic worms *Brugia malayi, Brugia timori* and *Wuchereria bancrofti* which are spread by *Culex* mosquitoes [25]. In many tropical regions, this illness is a serious public health concern. Although the illness is rarely deadly, the suffering of those who are infected is severe due to the disability caused by swollen extremities, acute adeno lymphangitis attacks, and the sickness itself. In rural Tamil Nadu, South India, the functional impairment caused by lymphatic filariasis was measured, and roughly 66 percent of patients indicated that the disease affected their occupation.

1.9 Anopheles

Plasmodium species, the causative agents of malaria, are transmitted by *Anopheles* mosquitoes. *An. stephensi* breeds in clean-water containers or cisterns, and the vector appears to swiftly adapt to its surroundings. Additionally, during the dry season, when malaria transmission is typically at its lowest, it can survive in extremely high temperatures. Furthermore, the new *Anopheles stephensi* genetic background appears to develop resistance to numerous insecticide classes, offering possible control issues [26]. Malaria is transmitted by *Anopheles* throughout India's rural and urban plains. *A. stephensi* thrives in walls, man-made containers, water tanks, and overhead tanks [27].

There are over 400 different species *of Anopheles* mosquitos found, with approximately 70 of them capable of transmitting malaria [28]. The life cycle of the malaria parasite starts in the vector, female *Anopheles* mosquito feeds on gametocytic forms of the parasite found in the blood of an infected vertebrate host [29].

1.10 Aedes

Human diseases such as dengue, Zika, and chikungunya can be transmitted by *Aedes* mosquitos, which are among the most frequent invasive mosquito species [30]. *Aedes* do not have the ability to travel large distances. These mosquitoes will only fly a few blocks in their lifetime [31]. Dengue fever is a viral infection spread by *Aedes* mosquitoes that causes a severe flu-like disease and, in some cases, fatal complication known as severe dengue. Dengue fever has surged by 30 times in the last 50 years [32]. One of the most effective strategies to quickly block transmission of viruses spread by *Aedes* mosquitoes is to use safe and effective insecticides against adult and larval mosquito vector populations [33].

2 Major mosquito borne diseases

2.1 Malaria

Malaria remains a major public health concern, affecting many people in different countries and resulting in infections and deaths each year [17]. The most common vector-borne disease is human malaria, which is caused by protozoans (*Plasmodium spp*.). Malaria is caused by at least 4 *plasmodium* species like *Plasmodium vivax, P. falciparum, P. malariae* and *P. ovale* which are transmitted by *Anopheline* mosquitoes. There are over 400 species of *Anopheles* globally, with roughly 40 of them being major human malaria vectors [13].

Significant logistical challenges must be overcome to effectively monitor and cure malaria. An integrated strategy that combines preventive measures like indoor residual spraying and long-lasting insecticide-treated bed nets with improved access to efficient anti-malarial medications is essential to addressing the issue of lowering the prevalence of malaria. Contrarily, since many at-risk groups reside in impoverished rural regions, malaria is a disease that is brought on by and arises from poverty. Once they become infected, they are also less likely to be able to pay for treatment [34].

2.2 Filariasis

Filarial infection occurs when parasitic nematodes are transmitted to people via mosquitoes. Infection is most commonly acquired in childhood, producing concealed lymphatic damage. The parasitic nematodes (roundworms) belong to the family Filarioidea and these filarial worms look like threads. *Wuchereria bancrofti, Brugia malayi* and *Brugia timori* are the three common species causing filariasis. Lymphoma, elephantiasis, and scrotal swelling are some of the painful and disfiguring manifestations of the disease that arise later in life and can lead to permanent disability. Not only are these people physically crippled, but they also suffer mental, social, and economical losses, which contribute to stigma and poverty. It has been estimated that 863 million people in 50 countries will require preventative chemotherapy to prevent infection. The total people affected by lymphatic filariasis at the global baseline include nearly twenty-five million males with hydrocele and over fifteen million people with lymphoedema. These chronic illnesses affect at least 36 million people. Eliminating lymphatic filariasis can help to reduce poverty and minimize unnecessary suffering of the affected population [35].

2.3 Dengue

Humans are infected with dengue viruses by the infected bites of *Aedes* mosquitoes. More than 400 million people are affected by dengue fever each year. Approximately 100 million individuals are infected, and 40,000 people dying from severe dengue fever [31]. Most dengue infections are asymptomatic or produce a moderate febrile illness [36,37]. Thrombocytopenia, increased liver enzymes, and subthreshold vascular permeability are frequently present in dengue fever infections without overt signs of vascular permeability [38,39].

Dengue fever is caused by 4 different serotypes of virus like DENV-1, DENV-2, DENV-3 and DENV-4 belonging to family Flaviviridae. Subsequent infections (secondary infection) enhance the risk of severe dengue [40]. The mosquito *Aedes aegypti* is the principal DENV vector. It could breed in natural containers like tree holes and bromeliads, but it has now adapted to urban habitats and breeds in man-made containers like buckets, mud pots, discarded containers and used tyres, storm water drains, and so on, making dengue an insidious disease in densely populated urban areas [41].

2.4 Chikungunya

The Chikungunya virus is spread to humans mostly by infected *Aedes* mosquito. During epidemics, people are the principal hosts of the chikungunya virus. Mosquitoes become infected when they bite someone who harbours the virus and transmits to healthy individuals during their subsequent blood meal [42]. After an incubation period of 2 to 4 days, chikungunya usually manifests as an acute disease with an abrupt onset of fever and arthralgia, which can be incapacitating. A maculopapular rash is most evident on the facial edema and trunks are regularly formed indicators, as are headache, myalgia and pain along the spine [43]. The sickness usually starts four to eight days after an infected mosquito bite but sometimes it can range from 2 to 12 days. Joint pain can be extremely debilitating normally lasting for a few days, but it can prolong up to few weeks, months, or even years. As a result, the virus can result in acute, subacute, or chronic illness. Muscle soreness, joint swelling, headache, nausea, exhaustion, and rash are all frequent manifestations and symptoms [44].

2.5 Japanese Encephalitis

JEV causes Japanese encephalitis, which is the most common cause of viral encephalitis in Asia. It is a flavivirus that is transmitted by mosquitoes. Humans are infected with JEV via mosquito bites from infected *Culex* species (mainly *Culex tritaeniorhynchus*). Mosquitoes, pigs, and waterfowl are all part of a virus transmission cycle (enzootic cycle). The disease is especially prevalent in rural and periurban areas, where people live in close proximity to vertebrate hosts. In most temperate areas of Asia, JEV is predominantly distributed during the summer, when large outbreaks can occur. In the tropics and subtropics, transmission occurs all year, although it is most vigorous during the rainy season and the pre-harvest period in rice-growing countries [45]. The ecology of JE virus has been widely studied. Mosquitoes, bats, pigs, and water birds belonging to the *Ardeidae* family have a zoonotic transmission cycle [46].

2.6 Zika

Aedes mosquitoes, which bite throughout the day, are the main carriers of the Zika virus. Headache, fever, conjunctivitis, joint and muscle stiffness are the most common symptoms which endure for two to seven days. Most of the Zika virus infected patients show no signs or symptoms. On the island of Yap, the first Zika virus sickness epidemic was observed in 2007 (Federated States of Micronesia). In 2013, French Polynesia and other Pacific countries and territories saw a significant Zika virus infection outbreak. In March 2015, Brazil experienced a significant rash illness outbreak that was quickly identified as a Zika virus infection and then linked to Guillain-Barre syndrome in July 2015 [47].

During pregnancy, ZIKV is transmitted from infected mothers to the foetus through the placenta. Another theory is that viruses travel through holes created by damage or inflammation. ZIKV also has the unusual capacity to hide inside a host cell and pass the placental barrier. Pathology findings demonstrating that the virus affects placental cells prompted this hypothesis [48].

3 Mosquito control measures

Vector control has a proven track record of controlling vector-borne diseases. Synthetic pesticides have been successfully utilized in mosquito-control programmes for several decades. However, the chemical approach has a number of drawbacks, including the development of pesticide resistance, pollution, and biological amplification of food chain contamination. As a result, there has been a rise in concern in the usage of biological agents for mosquito control in recent years [49].

3.1 Chemical Control

Following the discovery of DDT and its insecticidal capabilities in the twentieth century, numerous other insecticides (organophosphorus compounds) such as Malathion, Folithion, and Temephose were also produced at the same time. Other insecticides used to control mosquitoes include BHC, Carbamate, Organophosphorus, and Pyrethroid, despite the fact that their usage often results in the emergence of resistance in mosquitoes [50].

Folithion, Malathion, and Temephose are three Organophosphorus substances, while Alphamethrin and Deltamethrin are two synthetic pyrethroids that were used to control the larvae and adults of six species of vector mosquitoes: *Aedes albopictus* (Skuse), *Aedes aegypti, Anopheles culicifacies*, *Anopheles*, *Culex tritaeniorhynchus* and *Culex quinquefasciatus* in India [51].

3.2 Indoor Residual Spraying (IRS)

IRS is a highly effective technique for combating dengue and malaria, and it has the potential to have a long-term impact in places where transmission is high. Unfortunately, due to increased mosquito resistance and insufficient development of novel compounds over the last 20 years, the availability of low-risk and cost-effective pesticides is dwindling. WHO Pesticide Evaluation Scheme (WHOPES) now recommends twelve pesticides from 4 chemical classes (Carbamates, Organophosphates, Organochlorines, and Pyrethroids) for IRS, with Pyrethroids being endorsed for use on long-lasting insecticidal nets. Regulation of voltage-gated sodium channels and inhibition of acetylcholinesterase are two sole mechanisms of action for these four chemical classes [52].

3.3 Biological Control

Since there are so many ecological, environmental, social, and economic issues, Integrated Vector Management (IVM) initiatives are now concentrated on eliminating *Aedes* at the larval and/or adult stages using diverse biological control strategies [53]. There is no evidence of environmental pollution or *Aedes* resistance when biological agents are used. Their negative effects on humans, domestic animals, and the environment are minimal. The functional diversity of biological control agents also reflects the significance of biological vector control. Additionally, a lot of current and future proposals center on employing genetically modified microbes to either stop the dengue virus from developing inside the *Aedes* vector or to attack the vector itself [54].

3.4 *Bacillus thuringiensis* var *israelensis*

Because of their powerful mosquitocidal action, *Bacillus sphaericus* and *Bacillus thuringiensis* subspecies *israelensis* have been utilized extensively among other *Bacillus* species as bio-control agents [55].

Since its discovery in 1976, *Bacillus thuringiensis* subsp. *israelensis* has been the subject of intense research into its particular toxicity to mosquito larvae. At least 4 main insecticidal crystal proteins (Cry11Aa, Cyt1Aa, Cry4Ba, and Cry4Aa) are found in the parasporal inclusion body of *Bti*, with others present in smaller levels [56,57]. Despite the fact that *Bti* toxins are effectively commercialized for mosquito control, screening activities to find and characterize additional mosquitocidal *Bt* isolates and toxin genes have persisted around the world [58]. Blackflies and mosquitoes, dipteran pest insects and disease vectors, are frequently managed with *Bacillus thuringiensis* subsp. *israelensis*. These bacteria have a long history of safe usage, with no reports of insect resistance in the field [59].

The presence of proteinaceous inclusions, which can be detected as crystals of a unique shape under the phase contrast microscope, is the main cause of the insect pathogenic activity of this bacterium. Insecticidal crystal proteins (Cry proteins) or δ- endotoxins are the proteins that make up these inclusions [60].

3.5 Bacillus sphaericus

A mesophilic, aerobic gram-positive bacteria known as *Bacillus sphaericus* (*Bs*) is widely distributed in water and soil. It produces a distinctive spherical spore at one end, a trait that distinguishes it from other *Bacillus* species [61]. Because of its good biological properties, *Bacillus sphaericus* was used as mosquito biolarvicide and taken into industrial manufacturing [62].

The mosquito midgut protease can activate crystal proteins in the target insect species, transform them into toxic polypeptides, and then attach those polypeptides to receptors on the midgut epithelial cells, perforating the cells and killing the larvae [63,64]. *Bs* has various advantages over other biological insecticides, including minimal environmental toxicity, high specificity, high potency, and environmental durability [65,66]. Furthermore, *Bs* was found to be effective in reducing the transmission of mosquito-borne infections in epidemic areas [67,68].

3.6 Larval control

Larval control is an excellent strategy for reducing adult mosquito emergence from breeding sites. Larval control is the best cost-effective strategy that is particularly well suited to areas with few and well-defined breeding sites [69,70]. When carried out systematically, larval management is successful in highlands, desert fringes, urban settings, epidemic-prone areas, and rural areas [71,72].

4 Insecticide resistance

Aedes mosquito populations have been successfully reduced by insecticide-based interventions for a number of years, but resistance has now developed as a result of the reliance on a few number of active ingredients that have been approved for use in public health [73]. In most cases, the insecticide is either detoxified or sequestered before it reaches its target site due to changes in detoxification enzymes or changes in the pesticide target sensitivity as a result of mutations that reduce the insecticide's affinity for its target [74]. The use of chemical, mechanical, and biological treatments to regulate vector populations is primarily responsible for the prevention of mosquito borne illnesses which have a negative impact on quality of life and tourist development [13].

5 Conclusion

Adult mosquito biocides, such as pyrethroid, are also available and can be used indoor as well as outdoor residential places where adult mosquitoes gather. Biocides is an important tool for disease prevention, however pesticide resistance is a serious issue connected with their widespread use. Furthermore, many biocides share the same active ingredient like pyrethroid as agricultural insecticides, increasing the pressure for insecticide resistance since vectors are exposed to agricultural chemicals through contamination of neighboring breeding sites [75]

When handled incorrectly, chemical pesticides can be hazardous and cause environmental issues. This problem is becoming more prevalent as insects develop resistance to certain pesticides. As a result, interest in using alternative pest control techniques, such as *Bacillus thuringiensis* toxins, has gained importance [76].

Compliance with ethical standards

Acknowledgments

To PhD guide (Dr. S. Poopathi, Scientist-G) by the first author. Authors also acknowledged to the Director of ICMR-Vector Control Research Centre in Pondicherry for providing the facilities.

Disclosure of conflict of interest

The authors declare no conflict of interest.

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