



A REVIEW ON VECTOR BORNE DISEASES AND VARIOUS STRATEGIES TO CONTROL MOSQUITO VECTORS

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ABSTRACT

Mosquito vector transmit serious infectious diseases that include dengue, chikungunya, malaria, filariasis, leishmaniasis, Japanese encephalitis, west Nile fever, yellow fever and rift valley fever. Insecticides-based control measures have historically and currently been an important control approach against major mosquito-borne diseases. Chemical pesticides, on the other hand, are non-selective and can harm other beneficial organisms. Controlling mosquitoes with entomopathogenic bacteria is a convincing, ecologically acceptable alternative to chemical pesticides. *Bacillus thuringiensis israelensis* and *Bacillus sphaericus* are insecticidal microorganisms which are spore forming and these bacteria are the most extensively utilised alternative mosquito control agents, considering the rapid development of resistance, especially to *B. sphaericus* by the larvae of *Culex* spp. Under this circumstances, it is necessary to find an alternative biological control agents from natural resources. The present review focus mainly on the various strategies to control mosquito vectors.

Key words: *Aedes aegypti*, *Culex quinquefasciatus*, *Anopheles*, vector ecology, vector borne diseases, vector control, pesticides, biological control, *Bacillus thuringiensis*, *Bacillus sphaericus*

Vectors are living organisms that can spread infection or illness among human or between animals and humans. Many of these vectors fall under arthropods which feed on disease-causing microbes while feeding on blood from infected host (animal or human) and then spread it to another victim during their next blood meal. Dengue fever, malaria, leishmaniasis, schistosomiasis, yellow fever, Chagas disease, onchocerciasis and lymphatic filariasis are vector-borne diseases caused by infection of virus, bacteria and parasites in human populations, infecting over one billion people each year and killing over one million people (WHO, 2014). Disease causing vectors include mosquitoes, ticks, flies, sandflies, fleas, beetles, and freshwater snail. Mosquitoes are the most common disease vector (WHO, 2014). It has long been known that mosquitoes are the most significant arthropods that affect human wellness (Foster and Walker, 2019). Mosquitoes are significant vectors of a variety of arboviruses, protozoa, and helminths, and their negative consequences are far reaching. Mosquitoes provide a significant public health risk by transmitting multiple tropical diseases. Mosquitoes can be found in a variety of water-related habitats. Malaria, filariasis, yellow fever, and dengue fever are mosquito-borne diseases that cause significant morbidity and

mortality, as well as a significant economic burden in disease-endemic nations (Jose, 2021). *Ae. albopictus* and *Ae. aegypti* are capable vectors of five important arboviruses (viruses of YF, Zika, RVF, DEN and CHIK) and are broadly distributed, making these species a significant contributor to the global burden of infectious diseases (Moyes et al., 2017). Malaria, yellow fever, dengue, haemorrhagic fever, and filariasis are spread by *Anopheles*, *Aedes*, and *Culex* species (WHO, 2016). As a result, managing these species of mosquitoes is critical for controlling the mosquito-borne diseases. Controlling the proliferation of vector and non-vector mosquito populations is an urgent need in order to prevent vector-borne diseases and their nuisance using appropriate management strategies. There are no vaccinations for various vector-borne diseases, and medication resistance is on the rise (WHO, 2014). Vector control is acknowledged as an effective technique to prevent all these diseases, but it is not being done to its full potential (WHO, 2014). Vector control is a critical and promising method to prevent spreading of vector-borne diseases. Every year, hundreds of millions of dollars are spent globally to protect people from being bitten by mosquitoes, which are present on all continents except Antarctica (Diagne et al., 2020).

Vector ecology

The study of disease-carrying organisms, their behaviours, and the settings in which they thrive is known as vector ecology. Climate elements such as temperature, rainfall, humidity, wind, and daylight duration have a significant impact on mosquito ecology, development, behaviour, and survival, as well as the transmission dynamics of the diseases they spread (Reiter, 2001). Except in deserts and cold places, mosquitoes can adapt to a wide range of environments (Becker et al., 2003). Climate change has raised concerns that the spread of mosquito-borne diseases would become more severe due to higher vector survival and bite rates, faster pathogen replication inside vectors, shorter reproduction rates, and longer transmission seasons (Mordecai et al., 2019). Compared to urban environments, natural and rural areas have greater levels of mosquito diversity and abundance (Ferraguti et al., 2020). There are about 3000 or more mosquito species worldwide (Hillary and Ceasar 2021). Except a few species, mosquitoes are mostly harmless to humans. Among mosquito species *Aedes*, *Anopheles*, and *Culex* are the three major mosquito vectors capable of spreading illnesses. Ecology of *Aedes*, *Anopheles* and *Culex* are given below.

Aedes

Some *Aedes* species breed in ground pools and marshes, such as snowmelt pools in arctic regions, particularly tropical species, numerous *Aedes* are encountered in natural habitats like leaf axils, tree holes, stumps of bamboo, rock pools, or artificial habitats such as open tin cans, tyres and water storing pots that are prone to drying out; thus, the ability of eggs to endure moisture loss is clearly helpful (Service, 2012). *Ae. aegypti* is the main vector of dengue as well as Zika, Yellow fever and Chikungunya (WHO, 2022). In Southeast Asia, the secondary dengue vector *Aedes albopictus* breeds both in wild and man-made container habitats (Service, 2012). Both *Aedes aegypti* and *Aedes albopictus* feed during the day; their prime feeding phases are early morning and before sunset (Service, 2012). They rest indoors, mostly in bedrooms and living rooms. This increases human-vector contact while minimising contact with insecticides applied outdoors, making it more challenging to manage this vector. *Aedes aegypti* is capable of breeding in dirty water or small container having little collections of water. Once a female has set her eggs, the eggs can survive in arid conditions over several months before hatching and hatch when exposed to water (WHO, 2022).

Anopheles

Anopheles mosquitoes are medically significant due to their links to malaria, filariasis, and other arbovirus diseases (WHO, 2022). Only a few of *Anopheles* species are vectors of human diseases, with 30–40 *Anopheles* species transmitting malaria in nature (Nicoletti, 2020). Adult anophelines favoured small habitats such as man-made ponds, natural ponds, drainage ditches, swamps, tyre tracks, and puddles for breeding, while increased vegetation cover lowered *Anopheles* larval counts (Hinne et al., 2021). *Anopheles* is mainly encountered in pure, pollution free streams, and is rarely seen in settings with rotting vegetation or faeces (Service, 2012). Rainfall alters the amount of breeding habitats, as more habitats are generated during the rainy season, which enhance the richness of *Anopheles* mosquitoes in all geographical areas.

Culex

In humans, the *Culex* mosquito transmits Japanese encephalitis, Lymphatic filariasis, and West Nile disease. *Culex* mosquitoes breed in a variety of stagnant water conditions. Catch basins rainwater barrels, septic tanks and storm drains are preferred oviposition habitats because they are rich in organic material (Valent Biosciences, 2022). *Culex* mosquitoes are associated with urbanisation, particularly in areas with poor drainage and sanitation. *Culex* species bite people and other hosts at night (Service, 2012).

Vector borne diseases (VBDs)

Human diseases caused by bacteria, parasites and viruses which are carried from individual to individual by vectors are known as vector-borne diseases (WHO, 2020). Each year, almost 700,000 people die from diseases like Dengue, Leishmaniasis, Malaria, Schistosomiasis, African Trypanosomiasis, Japanese Encephalitis, Chagas Disease, Onchocerciasis, and Yellow Fever (WHO, 2020). Many VBDs have been found to have expanded geographic distribution and a rise in the frequency of epidemic transmission (Muller et al., 2019). The two major mosquito-borne diseases, malaria and dengue, are reemerging in locations where they had previously receded for decades and are gradually expanding their geographic range (Watts et al., 2019). Due to an expanded geographic range and prolonged transmission season brought on by climate change, malaria and dengue transmission could increase (Messina et al., 2019; Iwamura et al., 2020). Almost 40% of the world's population is at risk from mosquito-borne diseases, including human malaria, dengue

fever, chikungunya fever, Zika virus (ZIKV) disease, and lymphatic filariasis which are a major worldwide health issue (Franklinos et al., 2019; Jones et al., 2021). More than 1 million people globally die each year from mosquito-borne diseases such malaria, dengue, Zika, chikungunya, yellow fever, and others, with the majority of these deaths occurring in undeveloped areas (Yang et al., 2021).

Malaria

Malaria is a prominent vector-borne disease in tropical and subtropical areas killing significantly more people than all parasitic diseases combined (Talapko et al., 2019). Plasmodium parasites causing Malaria are spread to humans by female *Anopheles* mosquitoes that have been already infected by them (WHO, 2022). Variations in mosquito vectors and malaria parasites, as well as ecological conditions affect malaria transmission. Only 30–40 *Anopheles* species spread malaria in nature, out of approximately 530 species (Nicoletti, 2020). With more than 200 million cases in 2018, malaria remains a significant public health burden worldwide. Around 400,000 people die each year from malaria despite there being viable treatments and control measures, mostly in sub-Saharan Africa (WHO, 2019). Based on the most recent worldwide report of malaria data, there was a rise of 241 million cases of malaria in 2020 from 227 million cases in 2019. (WHO, 2022). Vector control is an important aspect of malaria control and eradication methods since it is a highly effective approach to minimise malaria transmission. In the previous year, two different initiatives—the Lancet Commission on Malaria Eradication and the World Health Organization’s Strategy Advisory Group for Malaria Eradication—analyzed potential futures and came to the conclusion that malaria eradication is possible while identifying critical priorities (Feachem et al., 2019; WHO, 2020).

Chikungunya

Chikungunya is a tropical viral illness which is caused by the Chikungunya virus, belonging to Togaviridae family (WHO, 2022). It is spread by *Aedes*, primarily *Aedes aegypti* (Cunha et al., 2017). The main vectors of chikungunya virus in the regions of Indian Ocean and Asia are *Aedes aegypti* and *Aedes albopictus*, and disease outbreaks occur during the rainy season, when vector population rises (Pialoux et al., 2007). It is believed that the virus of chikungunya originated in Africa and was first found during an outbreak in Tanganyika in 1952–1953. (Presti et al., 2014). The

first urban epidemics were noticed in 1967 in Thailand (Wimalasiri-Yapa et al., 2019). Chikungunya epidemics have been observed in India from 1963 to 1973 and 2005 to 2019. Chikungunya is indigenous in twenty-four Indian states and six union territories, showing that it is a significant public health issue in our country (Translational Research Consortia, 2021). Maharashtra, Andhra Pradesh, Gujarat, Tamil Nadu, Karnataka, Madhya Pradesh and Kerala are the states affected by chikungunya. Vaccine and drugs for chikungunya are not available to prevent or treat the infection (National Centre for Vector Borne Diseases control, 2022). Therefore, the most available efficient measures for preventing chikungunya are mosquito management and personal safeguarding from mosquito bites (Pialoux et al., 2007; National Centre for Vector Borne Diseases control, 2022).

Lymphatic filariasis

Elephantiasis is a neglected vector-borne tropical illness caused by infection with the filarial worms such as *Brugia timori* (*Brugia* spp.), *Brugia malayi* and *Wuchereria bancrofti* transmitted by mosquito species. It damages the lymphatic system and can cause hydrocele and lymphoedema (elephantiasis) in affected people (WHO, 2022). Globally, it is estimated that lymphatic filariasis affects about 15 million people with lymphoedema and 25 million men with hydrocele (WHO, 2022). Infection with parasitic nematodes (roundworms) of the family Filariodidea causes lymphatic filariasis (WHO, 2022). Lymphatic filariasis is a primary factor of long-term illness that affects people in tropical and subtropical regions of Asia, the Western Pacific, Africa, and parts of the Americas (Bockarie et al., 2008). It is spread by several mosquito species, including the *Culex*, *Anopheles*, and *Aedes* mosquitos. *Culex quinquefasciatus* is the most common filariasis vector. Around 1 billion people were at risk of contracting lymphatic filariasis (LF) from 72 nations before the World Health Organization began the Global Program to Eradicate Lymphatic Filariasis. Approximately 36 million people were affected by the related morbidity (Fang and Jang, 2019).

Dengue

The most typical arthropod-borne viral disease with severe public health effects is dengue fever. Dengue is a disease that can affect over 2.5 billion people and is present in over 100 nations (Fonseca et al., 2002). *Ae. aegypti* and *Ae. albopictus* mosquitoes both spread the virus that causes it (WHO, 2022). Humans are the

primary host. The disease is prevalent in the warm temperate and tropics regions (Chan et al., 2006). Humans contact the virus by bites from infected female mosquitos. Dengue haemorrhagic fever and dengue fever are two well-known clinical manifestations. There are 4 different dengue viruses (serotypes) namely, Dengue virus-1, Dengue virus-2, Dengue virus-3, and Dengue virus-4 that are antigenically related (WHO, 2022). The Americas, Southeast Asia, and the Western Pacific regions are severely affected, with Asia accounting for 70% of the worldwide disease load (WHO, 2022). Globally, in the year 2019, the highest number of dengue cases was reported. All regions were affected, for the first time, Afghanistan was affected by dengue (WHO, 2023). Dengue fever has been endemic throughout Southeast Asia since the 1950s, when DHF/DSS was first identified (Fonseca et al., 2002). Dengue fever and its severe version, DHF or DSS, became one of the world's leading infectious diseases as the mosquito, *Aedes aegypti*, rapidly colonised urban areas in tropical countries (Halstead, 2002). Sanofi-dengue Pasteur's vaccine (Dengvaxia) has received approval in a number of nations, although there are safety concerns for mass delivery (Aguiar et al., 2016). Although dengue vaccine has been developed, WHO recommends nationwide dengue control programmes that use environmental management methods and pesticides (WHO, 2016).

Yellow fever

Because it is transferred among vertebrate hosts by arthropods, yellow fever virus is called as 'arbovirus'. YF is an acute severe sickness in humans that causes vomiting, hepatitis with jaundice, shock, epigastric pain, fever, nausea, renal failure, bleeding, and death in 20–60% of cases (Monath, 2015). YF is caused by the genus *Flavivirus*, which encompasses roughly 70 positive-strands, single-strand RNA viruses, most of which are spread by mosquitoes and ticks (Monath, 2015). Female *Aedes aegypti* is the principal yellow fever vector. The virus is spread from one host to another, primarily between monkeys, people and monkeys and humans (WHO, 2014). From the 18th century to the early twentieth century, YF was a major hazard to public health, with epidemics recurring after introductions to coastal towns and cities far from endemic areas in the Caribbean, Europe and North America. (Monath, 2015). Yellow fever is prevented by an effective vaccine, which is safe and affordable (WHO, 2023). One of the first viral vaccines, the yellow fever vaccine, has proven to be safe and convincing (WHO, 1998). The virus employed in this vaccination study was virus 17 D. In 1951, the Nobel Prize of

Physiology or Medicine had been given to Max Theiler for the discovery of a convincing vaccine against yellow fever (Norrby, 2007). The best yellow fever treatment is prevention through a vaccine (WHO, 2022). A total of 203 confirmed cases, 252 probable cases, 40 deaths (a case fatality ratio of 9%), and 13 countries in the WHO African Area reported cases to WHO between January 1 and December 7, 2022 (WHO, 2023).

Japanese encephalitis

The Japanese encephalitis virus is a zoonotic flavivirus infecting a huge spectrum of vertebrate animals, especially large waterfowl birds and swine, in an enzootic cycle (Endy et al., 2002). The Japanese encephalitis virus is a flaviviridae virus that is spread between animals and humans via *Culex* mosquitoes. Although Japanese encephalitis virus has been isolated from over 30 species, the virus is primarily transmitted by mosquitoes breeding in paddy fields of the *Cx. vishnui* subgroup, especially *Cx. tritaeniorhynchus* (Van den Hurk et al., 2009). Temperature and abundant bodies of water, such as those found in paddy fields across most of Asia, provide an excellent habitat for vectors and viral multiplication within the mosquito hosts (Endy et al., 2002). Historical perspective epidemics of Japanese encephalitis was documented in Japan since 1871 (Erlanger et al., 2009), but the first big epidemic occurred in 1924 (Endy et al., 2002), including approximately 6000 patients (Endy et al., 2002; Van den Hurk et al., 2009). Children and young people are the most vulnerable to this disease. JE epidemics have been documented in various places of India, and it is considered a major paediatric issue (Tiwari et al., 2012).

Although JE remains a main public health issue in Asia, the number of cases reported is reducing, with only 10,426 cases reported in 2011. This is thought to be caused by JE immunisation (particularly in China and India), agricultural pattern changes, urbanisation, and advanced living environment (Wang and Liang, 2015). Estimation of the real global burden of disease and development of effective JE-control approaches must be strengthened in Japanese encephalitis endemic region of India in order to avoid JE-related morbidity, mortality, and sequelae. JEV transmission can be prevented and controlled by one of the three tactics, each of which targets a different stage of the transmission cycle: (a) human vaccination, (b) control of increasing hosts via swine immunisation or changing livestock breeding style, or (c) vector management (Van den Hurk et al., 2009). Mosquito repellents, insecticide-impregnated mosquito bed nets, and clothing that cover the full

body and prevents from bug bites are all used in vector management.

Mosquito vector control measures

Vector control is crucial in the fight against pandemic vector-borne diseases. In many cases, vector control is the only method to avoid disease epidemics (WHO, 2014). Vector control measures aim to limit disease transmission by reducing the quantity of disease vectors or interactions between animals and disease vectors, as well as people (WHO, 2016). Indoor Residual spraying, insecticide-treated nets, or self-protection measures, depending on the parasite-vector species, may help to protect individuals from infection (WHO, 2022). Classically, mosquito control efforts have centred on killing mosquitoes with a range of insecticides. Insecticide-based vector control is crucial for the prevention and treatment of infectious diseases like malaria, dengue fever, and filariasis (Gillbert and Gills, 2010). Controlling mosquitoes can be achieved using different measures.

Chemical control

Chemical techniques have been promising in limiting disease spread to endemic regions (Demirak and Canpolat, 2022). Chemical insecticides were once the main method of controlling mosquitoes, however in recent years, mosquitoes have developed widespread chemical resistance (Peng et al., 2022). Arsenicals, which are stomach poisons, are among the first generation of insecticides. The second generation consists of contact insecticides including chlorinated hydrocarbons, carbamates, organophosphates and pyrethroids (Becker et al., 2003). Organophosphates (OPs), Organochlorines (OCs), Carbamates (Cs), and Pyrethroids (PYs) are the most common insecticides. They work by damaging the neurological system of insects. Insecticides may harm nontargeted organisms, due to similarities in nervous system components that make it nearly impossible to find insecticides that exclusively impact insect pests (Prasad et al., 2013). There are three types of insecticides: natural organic, inorganic and synthetic organic. The majority of pesticides used to control mosquito vectors are synthetic compounds (Becker et al., 2003). To stop the spread of mosquito-borne diseases, man-made insecticides are used widely due to the appearance or re-emergence of mosquitoes in endemic, non-endemic, and new areas of the world (Demirak and Canpolat, 2022). The widespread usage of insecticides in recent decades has had a negative impact on the environment

and public health (Tembhare, 2016). Some insecticides degrade water quality or have other negative effects on organisms (Prasad et al., 2013). Majority of synthetic pesticides are neurotoxic to the pests (Olson et al., 2015). The emergence of physiological resistant in vectors, environmental degradation that causes bio-magnification of food chain contamination, and deleterious effects on beneficial animals have all made the use of chemical insecticides difficult (Poopathi et al., 2010). A sustained and high selection pressure as a result of repeated applications of a mono class of insecticide (or another with the same mechanism of action) is the primary source of resistance development in insects in the field (Gillbert and Gill, 2010). Alternatives to conventional mosquito control methods that are safer, biodegradable, and target-specific have been researched due to the emergence of resistant mosquitoes and worries about toxicity to both target and beneficial organisms. (Demirak and Canpolat, 2022). Insecticide resistance has been observed in various mosquito species of Anopheles. The emergence of mosquito resistance to extensively used pesticides in dengue and malaria control has a significant negative impact on the management of these disease mosquito vectors (Poopathi et al., 2010). Current mosquito control research is aimed at better understanding of mosquito resistance to synthetic insecticides and devising new tactics to combat resistance (Demirak and Canpolat, 2022).

Biological control

Biopesticides are non-toxic, environment friendly pesticides made from living organisms including microorganisms, animals and plants that can control severe plant destructing insect pests and diseases causing vectors. They are becoming increasingly important around the world. Biological control has emerged as the most viable alternative pest control strategy for controlling vectors while avoiding negative consequences for the environment and non-target organisms. Fungus spores were first utilised as a biopesticide in the late 1800s to manage insect infestations. One of the earliest documented uses of a biopesticide is when Agostine Bassi, an Italian entomologist showed in 1835 that the white-muscadine fungus spores (*Beauveria bassiana*) could infect silkworms and kill them by causing white muscardine disease. Since then, the use of biopesticides has persisted uninterrupted throughout the history of modern agriculture, but it has only ever represented a minor industry in comparison to traditional crop

protection. The mode of action, which includes mating disruption, anti-feeding, asphyxia, and desiccation, is what distinguishes biopesticides from synthetic pesticides (Olson et al., 2015). It is hoped that in the future, in addition to parasites and predators, more focus will be placed on biological control through introducing microbial agents (Tembhare, 2016). Natural molecules that are more effective and less hazardous than man-made compounds continue to gain popularity among scientists (Demirak and Canpolat, 2022). Compared to traditional synthetic pesticides, crude bacterial extracts are far less likely to lead to the development of mosquito resistance because they almost always contain numerous compounds with insecticidal activity (Engdahl et al., 2022). To lessen the selection pressure for pesticide resistance, environmentally friendly alternatives have been investigated. These numerous biocontrol strategies aim to target distinct stages of the mosquito lifecycle in an environment friendly and long-lasting way.

As effective treatments for diseases like dengue and Zika are not yet broadly available, conventional insecticide-based vector control methods continue to be a majorstay (Namias et al., 2021). Contrary to pesticides, bio-control agents are host-specific, environmentally safe, easier to implement in the field, more affordable to manufacture, non-pathogenic to mammals, including humans (Prasad et al., 2013). Microbes are one of the current natural sources being investigated for the development of novel mosquitocidal treatments (Caragata et al., 2020; Dahmana et al., 2020). Organisms including fungi, viruses, bacteria, nematodes, protozoa, invertebrate predators and fish have been investigated for controlling mosquito vectors. However, copepods, some spore-forming bacteria and fish have been successfully tested in the wild (Poopathi et al., 2010). Although while research into natural sources for novel compounds with mosquitocidal action has resurged, relatively few natural products have succeeded in becoming approved vector control agents (Marrone, 2019). Typically, one or more issues with toxicity, strict regulatory requirements, efficacy, prices and availability are the cause of this failure. In addition to that, a new product must be outstanding to the ones that are already on the market from a marketing perspective (Demarque & Espindola, 2021).

Biopesticides and other insecticides have been developed, mostly for the control of mosquito larvae. Apart from being safe for the environment and non-target creatures such as humans, these microorganisms

have certain significant advantages over traditional insecticides in mosquito control operations (Poopathi et al., 2010). *Bacillus thuringiensis* (Brühl et al., 2020) and *Bacillus sphaericus* are already utilised as effective pesticide alternatives. They have been quite efficient against *Anopheles*, *Culex*, and *Aedes* species for the past two decades, though *Bacillus sphaericus* is particularly powerful against *Culex* (Prasad et al., 2013). Despite the fact that few mosquito species (such as *Culex quinquefasciatus* in the lab and *Culex pipiens* in the field) have developed resistance to *Bt* and *Bs*, other species, such as *Aedes vexans*, never had developed resistance despite being exposed to the pesticide for more than 25 years. Hence, in the field of microbial pesticides, *Bt* and *Bs* are still maintaining their reliability (Hegazy et al., 2022).

Bacillus thuringiensis

Bacillus thuringiensis is a naturally occurring, spore forming bacterium. During the sporulation phase, this bacterial species produces insecticidal proteins concentrating in a parasporal body (PSB) termed the protein crystal, which mostly consists of more than one protein named Cry and Cyt toxins (Gilbert and Gill, 2010). When consumed by vectors, *Bacillus thuringiensis* (*Bt*) damages the insect gut (Olson et al., 2015). The entomopathogenic features of *Bt* separate it from other members of the *B. cereus* group, and *Bt* entomopathogenic activity is mostly attributable to Cry toxins (Gilbert and Gill, 2010).

The parasporal body (PSB) of *B. thuringiensis israelensis* is responsible for the insecticidal impact. The PSB comprises of four main toxin proteins with various molecular weights: Cry4A (125kDa), Cry4B (135kDa), Cry10A (58kDa), and Cry11A (68kDa) (Delecluse et al., 1996). This bacterial bio-pesticide seems to remain longer in the environment, especially in dirty water, and hence could be a suitable choice for long-term mosquito control (Prasad et al., 2013).

Bacillus sphaericus

This bacterium produces either terminal or sub-terminal endospores and is an aerobic, gram-positive, rod-shaped spore-forming bacterium. It is found in both soil and aquatic habitats. It produces binary toxic proteins during sporulation with molecular weights of 51.4kDa and 41.9kDa that are harmful to mosquito larvae (Becker et al., 2003). *Anopheles* and *Culex* species are highly susceptible to the binary toxin of *Bs* strains, however most *Aedes* species are less susceptible

(Poopathi et al., 2004). When these poisonous proteins are consumed, they destroy the intestinal epithelial cells of the larvae, resulting in death. *Bs* is fully safe for humans, animals, wildlife, and the environment, and they are excellent for community use (Bendary, 2005). Contrary to *Bti*, for which there have been no cases of known field resistance, *Bacillus sphaericus* crystal toxin resistance has been noted in *Culex* larvae (Gilbert and Gill, 2010). As a result, the recent emergence of resistance has hampered mosquito control efforts.

Because these bacteria are safe for animals, the environment, humans, numerous formulations in the form of Granules (G), Flowable concentrate (FC), Water Dispersible Concentrate (WDC), Emulsifiable Concentrate (EC), Wettable Powder (WP) and Dust (D) have been developed to control a variety of mosquito species. Tests have been conducted extensively for these formulations in the United States, Zaire, Brazil, France, India, and Bangladesh (Poopathi et al., 2004).

Physical control

Physical control, in its broadest definition, aims to reduce mosquito breeding sources by improving sanitation, water management, changing the water-air interface, and limiting human-mosquito interaction (Becker et al., 2003). Water supply management can limit the growth of mosquito vector populations and hence can reduce the transmission of mosquito-borne diseases. Scarcity of water can increase public health issues including vector-borne infections. Water scarcity may allow non-indigenous mosquito vector incursions, increase the number and quality of mosquito habitats, and prolong the “mosquito season” by providing a perfect habitat year-round during normally dry season (Akanda et al., 2020).

Personal protection

Personal protection from mosquito vectors is considered to be a significant strategy of avoiding infection from any mosquito-borne diseases, in addition to all of the above-mentioned mosquito vector control methods. Insecticide-impregnated bed nets, for example, were successfully used in Thailand, China, Latin America, and certain African nations to combat malaria and other vector-borne infections (WHO, 1996). Additionally, repellents on the skin or clothing, mosquito coils, vapourising mats, and liquid vapourisers all play important roles in personal protection against blood-sucking mosquito vectors and the transmission of vector-borne diseases.

CONCLUSIONS

The importance of mosquitoes as disease carriers in medical field has put them at the centre of entomological research (Becker et al., 2003). Even though chemical insecticides were effective for decades to control mosquitoes, the occurrence of resistant mosquitoes (Peng et al., 2022), as well as an understanding of the long-term negative effects of chemicals on beneficial living things and concerns about chemical accumulation in the environment, has hastened the need to develop alternatives (Deng et al., 2019). As a result, finding more sustainable, environmentally friendly, and low-cost alternative biological control strategies became a necessity (Deng et al., 2023).

Controlling mosquitoes with entomopathogenic bacteria has become a convincing, ecologically acceptable alternative to synthetic pesticides (Park and Federici, 2009). *Bacillus thuringiensis israelensis* and *Bacillus sphaericus* are insecticidal spore-forming microorganisms which are the most extensively utilised alternative mosquito control agents (Park et al., 2010). Considering the development of resistance, especially by *B. sphaericus* against *Culex* larvae (Gilbert and Gill, 2010), isolating new indigenous and more potent mosquitocidal bacterial strains is necessary. Every natural ecosystem contains bacteria and other microorganisms, and soil is no exception. An attempt can be made to find a novel mosquito larvicidal bacteria to control mosquito vectors from soil samples of different places.

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KG has prepared the manuscript, collected literatures and has contributed in compilation of the manuscript, BB, SM, YA,KA, SM, JL and PH have contributed in literature search, reference work and assisted in compiling the manuscript. AM and KV have contributed in interpretation of background work by the various

authors in the subject. SP has given the background ideas, conception of the studies, reviewing the literatures revision and modification of the manuscript. KG has written the manuscript. All authors have read and approved the manuscript.

CONFLICT OF INTEREST

No conflict of interest.

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