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An approach to sustainable control of mosquitoes

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Abstract
Arthropods are most dominant being, as they have highest number of species and most ancient group of animal kingdom. Mosquitoes are most diverse group of arthropods that are carriers of human diseases viz. dengue, malaria, chikungunya etc. which are not fully cured yet (in the manner of vaccinations or medications). For this purpose mosquito vector control is still the primary method of avoidance. Broad-spectrum use of conventional insecticides (larvicides along with the adulticides) during disease transmission times, are the main stays of control methods. Due to the drawbacks of conventional tactics, specifically the emergence of insecticide resistance and environmental pollution, major attempts have been made to explore new eco-friendly techniques. Therefore, biological control use as an alternative strategy that target a variety of mosquito species without causing harm to the environment or adding unnecessary risks to human health. Here in this review, we discussed biological tactics that have been used or are being tried out to control mosquito vectors.

Keywords: Mosquito, biological control, insecticide, insecticide resistance, environment

1. Introduction

Mosquitoes are significant insects that carry major human infections, such as the causative agents of encephalitis, dengue fever, yellow fever, filariasis, and malaria, in addition to being annoying biters. In order to avoid or manage these human diseases, the World Health Organization has endorsed mosquito management as the control strategy [1].

Mosquito vector control efforts achieved remarkable success with the adoption of various synthetic insecticides, after the discovery of DDT [2]. Since that period, insecticides have been widely employed to control mosquitoes and due to these causes, resistance emerged in vector species. There is worry about the harm to the environment and consequences on non-target species also because of their harmful effects on human health and the environment [3].

Insecticide substitutes that are safe, affordable, and effective for the environment are becoming more and more necessary as development of resistance has become frequent among many mosquito species [4]. To lessen the selective pressures for insecticide resistance, some eco-friendly mosquito control methods have been investigated. These diverse biocontrol techniques strive to be environment friendly and long-lasting while focusing on various stages of the mosquito lifecycle [5]. It includes natural organisms that kill mosquitoes, exploiting mosquito behaviour to improve mosquito mortality, and releasing mosquitoes that are either sterile or unable to transmit disease [6, 7]. In places where endemic mosquito-borne infections occur, environmental management (via the reduction or elimination of mosquito breeding sites) has frequently been employed in conjunction with chemical or biological ovicidal, larvicidal, and pupicidal methods [4]. Here, in this review the potential for these biological methods in mosquito control and as new tools for reducing the incidence of insecticide resistance is discussed.

2. Biological control

Biological controller is dependent on the introduction technique of living organisms that aim, aspire or otherwise decrease the abundances of the target organism. Using natural pathogens, predators, competitors, parasites and toxins produced by the microorganisms for biological control is conventionally characterized as reducing target pests and vector mosquito populations. Natural enemies of mosquito larvae are bacteria, fungi, dragonfly, naids, aquatic bugs and copepods while natural predators for adult mosquitoes include spiders, lizards, Adult dragonflies, birds and bats [8, 9]. Some of them are discussed in Table 1 [2].

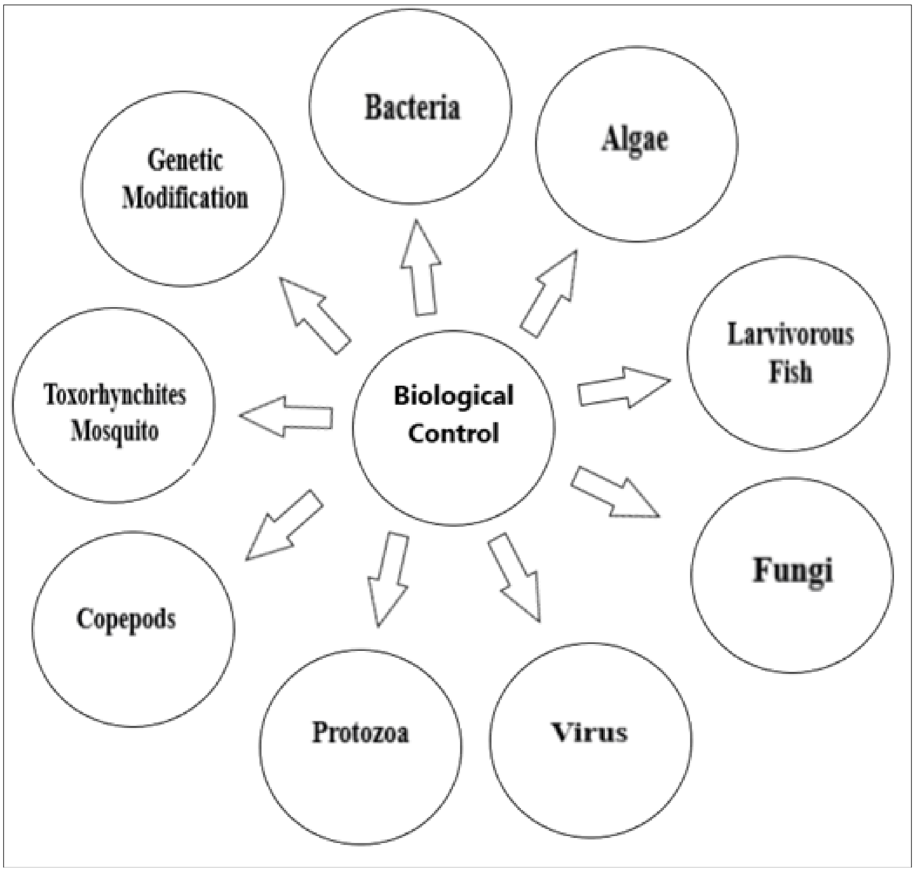

Table 1: Common mosquito predators

Order	Mosquito species
Coleoptera	*Acilius sulcatus, Colymbetes paykulli, Agabus sp., Dytiscus marginicolis, Lestes congener, Rhantus sikkimensis, Ilybius sp. Lacconectus punctipennis*
Odonata	*Aeshna flavifrons, Ischnura forcipata, Coenagrion kashmirum, Sympetrum durum, Rhinocypha ignipennis, Crocothemis servilia, Brachytron pratense, Labellula sp., Enallagma civile, Trithemis annulate, Orthemis ferruginea*
Hemiptera	*Abedus indentatus, Belostoma flumineum, Anisops sp., Corisella sp., Buenoa scimitar, Enithares indica, Diplonychus sp., Notonecta sp., Laccotrephes sp., Sphaerodema sp., Siagra hoggarica*
Diptera	*Anopheles sp., Chaoborus sp., Bezzia expolita, Culex sp., Corethrella sp., Culicoides sp., Dolichopus gratus, Culiseta longiareolata, Monohelea maya, Mochlonyx culiciformis, Toxorhynchites sp., Ochthera chalybesceens*

2.1 Virus
Viruses are first extracted from affected insects and then generated and used as bioinsecticides in the field. The pathogenic viruses of the mosquitoes relate to the four main groups: Baculoviruses (NPVs) (Baculoviridae: Nucleoplyhedrovirus), Densoviruses (DNVs) (Parvoviridae: Brevidensovirus), Cytoplasmic Polyhedrosis Viruses (CPV), (Reoviridae: Cypovirus) and Iridovirus (Iridoviridae) (MIV): Chlorovirus). *Baculoviridae*, *Pavoviridae* and *Iridoviridae* are DNA viruses and *Reoviridae* is RNA viruses those have impact on various mosquito species [10, 11]. *Aedes aegypti* densovirus (Aae DNV), the initial mosquito-specific densovirus (MDV), was discovered in *Ae. aegypti* larvae. Several other mosquito species also generated MDVs, such as *Aedes albopictus*, *Anopheles sinensis*, *Anopheles gambiae*, *and Culex pipiens* [12]. Entomopathogenic virus spreads efficiently during the first stage of development from one insect generation to the next causing paralysis and ultimately death of mosquito larvae. Since their host range is limited to insects only and they are safe to other animals and plants, baculoviruses distinguish out as a biological control agent. Additionally, baculovirus treatments don't reveal any signs of prolonged aggregation or atmospheric contamination [13].

2.2 Protozoa
Microsporidians, or entomopathogenic protozoans, are a remarkably varied class of parasites that target a wide range of insect species. Protozoan species recognized to infect mosquitoes from Ciliophora are: *Lambornella stegomyiae, Lambornella clarki*, *Chilodonella uncinata* and *Tetrahymena pyriformis*. These all species can trigger mosquito mortality, and thus have ability as agents of biocontrol. These are single-celled eukaryotic organisms length ranging from 30-75µm and most of these described as microsporidia and ciliophora (ciliates). When cultivated *in vitro*, it displays significant levels of pathogenicity, desiccation resistance, and reproductive potential. They typically have a gradual onset and are host-specific, leading to persistent illnesses and

general host debilitation. The insect host's potential to ingest, flourish, reproduce, and survive for a long time is decreased when the infectious phase known as the spore germinates in the midgut of insect host and releases sporoplasm. *Chilodonella uncinata*, a natural protozoan pathogen, was examined in a laboratory bioassay as a promising biocontrol agent against the larvae of *Culex quinquefasciatus*, *Anopheles stephensi*, and *Aedes aegypti* [14, 15].

2.3 Algae

Most of the algal species are nutritious food for mosquito larvae but some species kill the larvae when consumed in large quantities. Cyanobacteria (blue-green algae) kill the larvae because of their toxicity. Some algal species as biocontrol agent are mention in Table 2.

Table 2: Algal species as biocontrol agent

S. No.	Genus	Reference
1	*Helicosporidium*	16
2	*Anabaena cylindrical, Anabaena sphaerica, Anabaena flosaquae, Gloeotrichiae chinulate, Plectonema boryanum, Kirchneriella irregularis, Coelastrum reticulatum, Kirchneriella cornuta, Kirchneriella irregularis, Kirchneriella contorta, Dictyosphaerium pulchellum, Dactylococcus dissociatus, Elakatothrix viridis, Scenedesmus abundans, Scenedesmus dimorphus, Scenedesmus bijugatus, Scenedesmus dispar, Scenedesmus longus, Scenedesmus quadricauda, Scenedesmus parisiensis, Tetrallantosla gerheimii* and *Tetradesmus cumbricus*	17,18
3	*Chlorella ellipsoidea* and *Rhizoclonium hieroglyphicum*	19
4	*Oscillatoria agardhii* and *Anabaena circinalis*	20
5	*Chlorella vulgaris*	21,22

2.4 Fungi

Fungi are also biocontrol vector for mosquitoes. Over 700 species from over 90 different genera have insect-pathogenic fungi reported so far [23]. The genera which include the most significant mosquito pathogens are *Coelomomyces, Beauveria bassiana, B. brongniartii, Pythium carolinianum, Entomophthora, Isaria fumosorosea, Lagenidium giganteum, Culicinomyces, Leptolegniacaudata, Metarhizium anisopliae* and *Metarhizium brunneum* [7, 24, 31]. The four species of fungi from which mycopesticides are most usually derived are *M. anisopliae, B. bassiana, I. Fumosorosea* and *B. brongniartii* [32, 33]. In an infestation based on the integument, the fungus produces hyphae to pierce the epicuticle and then spreads to the hypodermis to finish the infection. Now it replicates as blastospores, which attack the insect's vital organs by expanding across the cavity of its body through the transmission of hemolymph and ultimately kill the insect by obstructing its circulation. After the host dies, the fungus undergoes an optional feeding phase, begins to develop hyphae just outside of the integument, and releases a significant amount of spores. By releasing mycotoxins, certain entomopathogenic fungi, including *beauvericin, destruxin, desmethyl destruxin,* and *cyclodepsipeptide,* are enabled to damage the host even more swiftly [34].

It has been discovered that *Culex pipiens* can be successfully controlled by using the entomopathogenic fungus *Metarhizium anisopliae* [35] and *Aedes aegypti* can be biologically controlled by 93 isolates of entomopathogenic fungus from six species- *B. bassiana, Lecanicillium spp., M. anisopliae, Isaria flavovirescens, I. fumosorosea,* and *I. farinose* [36].

The fungus has tremendous impact on mosquito egg survival. At this time, the diapausing larvae are vulnerable to fungal infections that enter eggs through the shell of the eggs or damage larvae [37]. Implementation to areas where mosquitoes rest or must pass through, including fungus-impregnated fabrics surrounding bed nets, alluring bait locations, adult mosquito traps, and PET traps, demonstrate promising effects [3].

2.5 Bacteria

Most of the attention of pest control scientists focuses on bacterial agents targeting both aquatic and adult stages [3]. Such bacteria generate protein crystals or some toxins with an insecticide effect during the sporulation process [11]. Bacteria's crystal proteins are very labile to temperature, and crude proteins are more successful than slightly purified exclusions to larvae of mosquitoes [38]. These bacterial toxins and other pathogenic substances disturb the host insect's midgut epithelium after consumption, and then proliferate in the nutrient-rich hemocoel, causing septicemia and the insect host's demise [39]. Cell death is caused by osmotic stress via the pore structure that is created by toxin monomer oligomerisation [11]. Within bacteria, there are currently records of Bacillus sphericus, Bacillus thuringiensis var. krustaki, Bacillus thuringiensis var. jegathesan, Bacillus thuringiensis var. kenyae, Bacillus thuringiensis var. entomocidus, Bacillus popilliae, Bacilus subtilis, Bacillus circulans, Bacillus laterosporus, Clostridium bifermentans and Brevibacillus laterosporus with possibilities for exercising control over insect dipterans [11, 40, 42]. The bulk of commercially accessible microbial products are built on gram-positive bacteria belonging to the genus Bacillus due to their long-term reliability. The crystal and vegetative toxins of *Bacillus thuringiensis* are created transgenically, making it the most powerful microbial pesticide to date. Bti kills mosquito larvae by accumulating crystal and cytolytic proteins throughout the bacteria's sporulation process [43]. Highest selling mosquito dunks and bits, marketed under the brand names Aquabac©, Bactimos©, Teknar©, and Vectobac©, contain Bti as their main ingredient. To prevent the growth of a parasite well before vector host turns infectious, the genus *Asaia* disrupts the cycle inside that vector. Wolbachia, an additional microbe, is an endosymbiotic bacterium that infects mosquito species spontaneously and causes cytoplasmic incompatibility, a reproduction phenotype in mosquito species [44].

2.6 Larvivouros fish

The usage of larvivorous fish is the oldest and most important way to regulate mosquitoes biologically and seen as greater active system in contrast with chemical regulation[45]. *Gambusia affinis, Gambusia holbrooki, Esomus dandricus, Fundulus, Rasbora daniconius, Rivulus* (killifish), *Tilapia mossambica, Poecilia reticulata, Trichogaster lalia, Trichogaster fasciata,* and *Sarotherodonni loticus* are mainly used for the management of the larval mosquitoes. *Gambusia affinis*, the mosquito fish, was first discovered more than 100 years ago and was highly consistent with the simultaneous use of certain chemical or biological control substances [7, 45, 47]. This is the most efficient attacker of *Aedes aegypti* and *Anopheles stephensi* larvae that mostly preys on third instar larvae. A distinct study found that *Aphanius dipar* (killifish) can replicate in both artificial and natural environment situations and are especially good mosquito predators in their third, fourth larval, and pupal phases, and defending surrounding population from a variety of mosquito-borne illnesses such as dengue, malaria, encephalitis, and others [48]. There are additional species that can feed on mosquito larvae, including *Clarias fuscus* (edible catfish) and carp (*Ctenopharyngo donidella* and *Cyprinus carpio*) [49]. Larvivorous fishes can be chosen as they show least threat of resistance in mosquitoes, inexpensive development, comfortably reared, safe to both animals and human beings and used at narrow quantities [45].

2.7 *Toxorhynchites* mosquito species

Traditionally, larvae of the genus *Toxorhynchites* have been identified as predators for larvae of clinically significant mosquitoes and frequently exhibit cannibalism. They may eat up to 400 mosquito larvae while they are still larvae, especially if they are placed into enclosed confined areas [50]. *Toxorhynchites* can be released in environment because they are autogenous, and absence the urge for blood meals, making this mosquito species suitable for biological regulation, without raising the possibility of spreading of infection. Most species include in biocontrol are: *Toxorhynchites splendens, Tx. moctezuma, Tx. brevipalpis, Tx. Amboinensis* and *Tx. rutilus*. When *Tx. splendens* larvae were introduced in *Aedes aegypti, Aedes albopictus,* and *Culex quinquefasciatus* breeding grounds, it was reported that these mosquito larvae were completely or nearly eradicated in 3–4 days [7, 51].

2.8 Copepods

Copepods, primarily Mesocyclops and species of Macrocyclops, are crustaceans used for biological control of mosquitoes by feeding primarily on first instar larva. There have been reports of several copepod species actively targeting mosquito early instars, including *Cyclops vernalis, Megacyclops aspericornis, Mesocyclops formosanus, Mesocyclops guangxiensis, Mesocyclops edax, Mesocyclops thermocyclopoides,* and *Mesocyclop slongisetus*. Cyclopoids are self-replicating, wasteful predators that can damage greater larvae than they actually consume, which is advantageous [52]. Without any established adverse impacts on human welfare, cyclopoid copepod became an effective approach for mosquito control following initial effective reduction of mosquito populations. The associations among copepods and the reservoir's size at breeding sites for mosquitoes are another important factor for the predation behaviour. The improvement in predatory performance correlated with reduced container size has been exhibited by a greater larval mortality [7].

2.9 Nematodes

The use of 14 families and 5 orders of nematodes to combat insects has been found to be successful [53]. It has been observed that the Mermithidae family has the greatest success in lowering mosquito numbers in their natural habitat [54]. However, eight additional major nematode families, including the Diplogasteridae, Allantonematidae, Heterorhabditidae, Rhabditidae, Neotylenchidae, Steinernematidae, Sphaerulariidae, and Tetradonematidae, are recognized to sterilization or insect elimination along with alteration in host progression. Mermithids are a more resilient and well-liked nematode species for suppressing mosquito larvae because they influence a host growth stage, demonstrate host selectivity, and have enormous multiplicative power. Being free swimmers, they may be spread easily to manage mosquitoes when they are in the infectious state. There are a number of newly found mermithid species that control about 63 different types of mosquito's larvae [55]. The species attacks its host by penetrating the spiracles, cuticle, or anus, or after the host insect has ingested it [53].

2.10 Genetically modified mosquitoes and vector control

Since before the strategies of stably modifying mosquitoes became operational, biological control for arboviral diseases by genetically modified mosquitoes was introduced. This idea is dependent on the purpose of swapping competent mosquito organism in the environment with modified mosquitoes. There are two main techniques that were being studied as biological control mechanisms for genetically modified mosquitoes.

2.11 Sterile insect technique (SIT)

SIT depleted the community at embryonal stage by lethality. Traditional SIT sterilizes mosquito males at pupae stage by using radiation. The emergence of irradiated sterile males, which bear chromosomal disruption to sperm, struggle with wild males to mate with females but are unable to inseminate them and no viable offspring produced, this may eventually lead the species to abolished [6-7, 56].

2.12 Release of insect carrying a dominant lethal gene (RIDL)

This is a genetic upgrade or modern updated version of excellently-established sterile insect technique (SIT) [7, 57]. The method is focused on "release of insects with dominant lethality" (RIDL) that incorporates superior fatal gene expression in vector species by introducing male transgenic mosquitoes containing the dominant lethal gene [7]. The RIDL mosquitoes were stated to be more fit and competent, because RIDL utilizes genetic approaches to obtain sterility, rather than radiation [58].

3. Conclusion

Mosquito biological control is not only environmentally friendly, but also a way to produce more lasting and effective control. In comparison to merely using synthetic insecticides, that are not being produced quickly enough to prevent resistance, employing aquatic insect predators is a practical alternative. The insect predators must demonstrate positive preference for mosquitoes over a variety of alternative prey in order to be efficient as a biological mosquito control agent. Eliminating aquatic larval phases is a preventative intervention, but controlling adult mosquitoes that may be infectious is a response that is forced by insufficient management. Predators should be taken seriously in this situation because they have the benefit of being able to acclimatize to the numerous water sources that are incredibly dispersed around human population. Predators can efficiently suppress mosquito populations once they are settled and auto-replicating to a level that no drug can hope to equal.

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