



How a sub-lethal effect of natural mosquitocides contribute in control of mosquito borne diseases in view of ecofriendly bioinsecticides: A review article

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Abstract

Mosquitoes are more threaten human and other veterinary animals, than any other arthropod or even another macrocarnivorous animals, which are vectors of pathogenic agents of many serious diseases as malaria, lymphatic filaria, and arboviruses such as; yellow fever, Nile fever, dengue, Zika, Japanese encephalitis, and, chikungunya, Zika, and dengue. Moreover, host annoyances within taking up blood meal by female piercing mouth parts. In spite of forests are mosquito niche, but now are consider as urbane insect inhabitate brackish and polluted water and modulated their habit into anthropophilic behavior. To raise awareness about the dangers of mosquito-borne diseases, now public health organizations are annually celebrated by World Mosquito Day in 20th august since 1937, the day commemorates the discovery made by Sir Ronald Ross in 1897, who established that female *Anopheles* mosquitoes transmit malaria. Mosquito control programs were mainly emphasized on immature stages, by application with synthetic insecticides. But, after appearances of ecological problems and insecticide-resistance, mosquito control tends to sublethal doses to minimize environmental effect and preserve on biological diversity.

The sublethal effect of bioinsecticides as plant secondary metabolites resources (as juvenoids and phytoecdysosteroids) and non-consumption by the mosquito predators kairomones, which are interfere with the mosquito natural hormones and other metabolic activities. This effectiveness less than mortality, will not allow the generation fitness. Today, literature body about mosquito program control mainly focusing on sublethal activity of the bioinsecticides, therefore, in this review, we shall evaluate the effectivity of biological insecticides as plant extracts and predators with sublethal doses and non-consumptive effectiveness of mosquito predators.

Keywords: Mosquitoes, Sublethal effect, Bioinsecticides, Biological control

1. Introduction

According to taxonomic literature, the culicid family had been divided into two subfamilies; Anophelinae and Culicinae [1]. Recent studies had been reported that 113 genera and 3726 species of mosquitoes have been recorded globally [2], and among them, the three genera (*Anopheles*, *Aedes* and *Culex*) comprise significant mosquito vectors of different disease agents [3]. Mosquitoes are an effective disease vector for human and veterinary health [4]. Fortunately, found that less than 10% of mosquito species transmit human diseases, while only ~2.5% are confirmed vectors, another ~ 6.8% are potential vectors [5]. There are around 500 different species of anophelines, only about 100 of which have been implicated in malaria transmission, also, anophelines are vectors of many other human and animal pathogens [6, 7, 8]. Malaria infection caused by protozoan parasites of the genus *Plasmodium* [9]. Serious malaria agent, notably *P. falciparum* transmission by species within the *Anopheles gambiae* complex [10]. *Culex* mosquitoes are vectors for serious human diseases including about 38.5 million lymphatic filariasis and arboviruses such as: West Nile virus (WNV), Japanese encephalitis, St. Louis encephalitis [11, 12]. Whereas, *Aedes* spp. are responsible for affecting 3.9 billion people worldwide reported cases [13]. Each

year, dengue viruses transmitted by *Aedes* mosquitoes cause nearly 96 million symptomatic cases and 40,000 deaths. Meanwhile, there are over 3.9 billion people in 129 countries constantly facing the threat of dengue infection [14]. Mosquitoes transmit diseases; malaria alone killed an average of 700,000 people each year between 2000 and 2021. Moreover, it was estimated that mosquitoes transmit diseases to more than 700 million people each year, and they are responsible for one in 17 deaths [15].

The mosquito aquatic stage (egg, larva, and pupa) is considered the most effective time for control, because the insects are accessible in a small water body before spreading out as adults, moreover, mosquito immatures are most concentrated and immobile, making them the best stage to target for mosquito population control [16]. Vector survival at immature stages plays an important role in determining mosquito population abundance, which is an essential factor for predicting disease transmission [17]. Efforts to reverse the trend to a higher incidence of mosquito-borne outbreaks have mainly been based on the use of synthetic insecticides, particularly organophosphates and pyrethroids [15]. Their widespread misuse synthetic insecticides had been caused the development of mosquito's resistance. However, despite their widespread

use, these products have a significant negative impact on the environment. Besides, they encourage the emergence of secondary pests, and adversely affect beneficial and natural enemies present in the agroecosystem^[18].

Recently, natural biomosquitocides had been candidate in mosquito control programs: Phytochemicals have gained importance to overcome mosquito control problems as being considered natural, environmentally safe, biodegradability, low mammalian toxicity, inexpensive, biodegradable, target-specific alternatives have been considered to replace conventional mosquito control strategies and, more importantly, less prone to mosquito resistance^[19]. Plants and their derivative compounds are an appropriate alternative because of their effectiveness and lower toxicity to human health and the environment than conventional insecticides^[20]. The physiological role of juvenile hormone (JH) in insect development, metamorphosis and reproduction insect development is stimulated by a molting (ecdysone) hormone released from the prothoracic glands^[21]. Plants produce a broad range of bioactive chemical compounds, especially, juvenoid and ecdysteroid metabolites, disturb mosquito growth and other development parameters^[22, 23].

Another field deals with mosquito control over phytochemicals, the predators that can substantially alter prey populations by means of sub-lethal influences. It is well known that predation reduces vector populations through consumptive effects, but non-consumptive effects of predators can also greatly impact prey demographics. The prey-predator interactions in mosquito larval habitats are key ecological processes that influence mosquito population dynamics and community structure in aquatic ecosystems, the non-consumptive effects are often as large as, or larger than, the lethal effects of predators^[24, 25]. Anopheles and culex mosquitoes are found in the aquatic habitat, along with their effective predators, can be used in mosquitoes control program, most of these predators are polyphagous, which are having dynamic role in food chain and ecosystem, the aquatic predators in the orders Coleoptera, Hemiptera, Odonata and Diptera are known to attack and eat mosquito larvae^[26]. Mosquito survival and body size and other physiological parameters were reduced by nonconsumptive effects of predators^[27]. Nonlethal effects of predation on prey can include alterations in behavior or morphology in response to predation risk, which may impair prey growth and fitness^[28]. Elsewhere, chemical cues from caged mosquito predators (predator-released kairomones) act as non-consumptive (or non-lethal) threats that significantly alter mosquito development, often triggering a "fear" response that speeds up maturity at the cost of size. Also, these cues often release by caged fish or dragonfly larvae, provide a chemical indication of danger without direct predation, forcing the mosquito prey larvae to alter their life-history strategies to escape the threat^[29].

Mosquito control with sublethal effects of microbial agents: bacteria (like *Bacillus velezensis*, *Wolbachia* and *Bacillus thuringiensis* var. *israelensis*), fungi (such as *Beauveria bassiana*, *Metarhizium anisopliae*) and viruses

(choloryridoviruses) that don't immediately kill them. Instead, they cause developmental delays, reduce reproductive success and shorten lifespans, which leading to lower mosquito populations over time, through significant physiological and reproductive damage to mosquitoes, then ultimately suppressing future population growth and disease transmission^[30, 31].

In nature, gravid mosquitoes use chemosensory (olfactory, gustatory, or both) cues to select oviposition sites suitable for their offspring, these cues emit from plant infusions, microbes, mosquito immature stages, and predators. Attractants and stimulants are cues that could show the availability of food (plant infusions and microbes) and suitable conditions (the presence of conspecifics), but repellents and deterrents show the risk of predation, infection with pathogens, or strong competition^[32].

2. Sublethal effect of bioinsecticides

The sublethal effects includes physiological, behavioural and rather than immatures mortality. The physiological parameters are mostly representing by reducing gonads and accessory reproductive organs, erosion of gut and integument epidermis, peritrophic envelope, gastric cecae, salivary glands, Malpighian tubules, fat bodies. Besides, low fecundity and fertility had strongly been related with small body size as result of the sublethal effect of the bioinsecticides. Moreover, malformations of body parts, segmental appendages and sensory chaetotaxy are reducing fitness and unbalancing escape against predators and parasite.

2.1 Sublethal effect of bacteria

In mosquitoes exposed to sublethal level, these impacts can be easily detected in terms of diminished population of mosquito larvae, adult emergence, adult survival, and their fertility^[33]. Exposure to LC70 *Bti* doses for 48 h as third-instar larvae reduced longevity of adult *An. coluzzii* mosquitoes, and is associated with larger adult size, female had 12% longer wings than the control group^[34]. However, exposure to sublethal concentrations of *Bti* (SerotypeH-14) on second instar *Aedes aegypti* larvae were increased duration of larval development and reduced adult body size^[35]. *Bacillus thuringiensis israelensis* and *Bacillus sphaericus* biopesticides tend to remain longer in the environment, particularly in dirty water, and hence may be a viable choice for long-term mosquito control, they have the least adverse effect on living things like humans, domestic animals, and wildlife. *Brevibacillus laterosporus* 615 crystals purified from *B. laterosporus* are as toxic to *Aedes aegypti* and *Anophele stephensi* as *Bti* LAT006 (isolate 615) are most toxic strain^[36]. After treatment larvae *Aedes albopictus* with *Bti* at LC50 for emerged parental adults; lower blood- engorgement rate and lesser fecundity, while for the resulted -free living- offspring larvae, they took a longer time to develop from egg to adult with significant low fecundity^[37]. Results were obtained by Flores *et al.* (2004)^[38] concluded that survival reduction then fellow that reduced number of gonotrophic cycles in *Ae. Aegypti* females exposed to VectoBac aqueous suspension (*Bacillus thuringiensis* var.

israelensis H-14, 600 ITU/mg), therefore at the concentration 0.41 ppm of VectoBac significantly shortened the duration of the developmental cycle of the exposed mosquitoes. Also, A significant effect was found on the fecundity of adults; age-specific fecundity was markedly lower for the LC50 and LC70 treatments compared to the control.

Wolbachia is safe for humans and the environment, *Wolbachia* is a naturally intracellular endosymbiont bacteria and carried by the majority of insect species in around 76% may be infected of insects [39]. *Wolbachia* cause a reproductive manipulation known as cytoplasmic incompatibility, cytoplasmic incompatibility occurs when *Wolbachia*-carrying males mate with *Wolbachia*-free females and the result of these pairings is that the eggs produced do not hatch. Whether for *Wolbachia*-carrying females, cytoplasmic incompatibility boosts the natural immune response of the mosquitoes against viral infection and then diseases transmission [40]. Zhang *et al.* (2020) [41] showed that *Wolbachia*-carry *Culex pipiens pallens* does not easily get infected to become a host vector for mosquito-borne diseases, therefore, it is uncappable to easily transmit those disease-agents to people. However, to diminish the population of *Cx. quinquefasciatus* from Myanmar during 1960s, *Wolbachia* endosymbiotic bacteria induce cytoplasmic incompatibility in mosquitoes causing sterility across their populations [42].

2.2 Sublethal effect of fungi

Sublethal effects of entomopathogenic fungi (EPF) on mosquitoes, such as *Beauveria bassiana*, *Metarhizium anisopliae*, and *Leptolegnia chapmanii* reduce survival, impaired reproduction, feeding inhibition, and altered behavior in mosquitoes that survive initial infection. The fungi *Metarhizium anisopliae* and *Beauveria bassiana* are highly virulent control tools for insect pests and have been under evaluation for the control of globally important mosquito vectors such as *Aedes aegypti* [43].

Leptolegnia chapmanii had demonstrated marked pathogenicity toward the larvae of a number of mosquito species with little or no effect on non-target insects [44]. *Ae. aegypti* females that survived infection with *L. chapmanii* laid fewer eggs, had a smaller number of gonotrophic cycles, had shorter wings, and were less fertile than controls, significant reduction in the number of adults in the mid- and long-term infection. Infected *Ae. aegypti* larvae with *L. chapmanii* zoospore, reduces the reproductive capacity of larvae that survive the infection [45]. George *et al.* (2011) [46] observed another facet of sublethal effects, a reduction in host-seeking behavior *An. stephensi* when exposed to fungal spores of both *B. bassiana* and *Metarhizium acridum*. Another study showed 63% and 43% reduction in blood feeding of *Ae. aegypti* and *An. stephensi*, fertility decreased in both species, with a reduction of 83% for *Ae. aegypti* and 74% for *An. stephensi* on the seventh day following fungal administration. Moreover, histological effect was revealed poor and abnormal follicle development in both mosquito species, reduction in the attraction rate towards the odor was observed three days post-fungal administration [47].

2.3 Sublethal effect of viruses

replication of *Invertebrate iridescent virus 6* strain in *Aedes aegypti* larvae was extended development times, reduced pupal and adult weights, and lowered fecundity [48]. In mosquitoes (Diptera: Culicidae), *invertebrate iridescent virus 6* (IIV-6) usually causes covert (inapparent) infection that reduces fitness. The treated larvae with deactivated IIV-6 virus, females laid significantly fewer eggs, produced between 20 and 35% fewer progeny and had reduced longevity compared to other treatments, wing length was shortest as result of sublethal effects of IIV-6 in *Ae. aegypti* may be mainly due to virus replication [30]. Mosquito chloxyridoviruses are among the most important pathogens of mosquitoes worldwide, sublethal viral infections—primarily caused by mosquito densovirus and some baculoviruses—are increasingly used in biological mosquito management of *Aedes albopictus* and *Aedes aegypti* mosquitoes [49].

Signs of infection in *Culex pipiens* larvae exposed to invertebrate iridescent virus were observed between the second and the fourth days post-exposure in 99% of the cases. Several tissues were found to be infected and the common sites of replication, but were mostly the fat body, epidermis and epithelial derivatives, such as the imaginal discs and the tracheal epithelium. Moreover, infection in the salivary glands, gastric ceca and posterior gut [50]. Cytopathic effect was observed in cultured *Culiseta annulata* and *Culiseta morsitans* mosquito cells 7 days after inoculation with diluted mosquito iridescent virus suspension [51].

2.4 Sublethal effect of plant extracts

After treatment *A. aegypti* fourth instar larvae, with ethanol extract of *Ocimum sanctum* leaves, there was increase in the larval duration and immature deformities as larva-pupa intermediate and pupa-adult intermediate, therefore, suggesting presence of juvenile hormone mimic or juvenile analogue activity in the ethanol extract of *Ocimum sanctum* leaves [52]. Treatments with the sublethal dose of extracts: *Andrographis paniculata*, *Polyalthia longifolia* and *Bougainvillea spectabilis*, the gonotrophic cycle of *Cx. Quinquefasciatus* had been affected. Moreover, reproduction reduced more than 90% control of in the tested group of treated males with untreated females (T♂ x UT♀), with high sterility index. Moreover, treatment with column fraction extended of total developmental period significantly when compared with control. Various fatal deformities be exhibited; including molt inhibition and morphological abnormalities especially during molting and myelinization processes. Deformities that developed in the treatment of *A. paniculata* (MeOH: EA 4:1) may be attributed to the dechitinizing effect of the extract with the formation of larval- pupal intermediates and Pupal- adult intermediates. Moreover, dissection of the gonads after treatment with column fractions shows that the testicular development was drastically affected, and ovaries showed variation in length and size and number of ovarioles [53]. The sublethal concentration of the phenolic extracts from *Z. jujuba* leaf significantly prolonged the larval duration and reduced the adult lifespan of treated fourth instar larvae of *Ae. aegypti*, and

reduced the general fitness of the offsprings. Fertility and fecundity decrease would adversely affect the reproductive capability and survivorship of the successive generations of the treated mosquitoes [54]. Muthukrishnan and pushapalatha (2001) [55] showed that emergence failure 50% of *Cx quinquefasciatus*, *Ae aegypti* and *An. stephensi* larvae treated with (LC50) leaf extracts of *Callophyllum inophyllum*, *Solanum surattense*, and *Samadera indica*, moreover, significant fecundity decreased of all that emerged adults with sterility index between 82 and 93%, application *Ae. aegypti* larvae with extracts, essential oil, and gel from *Lavender angustifolia*, caused many malformations. Moreover, an alive larvae treated with low concentrations showed shrink abdominal segments, neck elongation, siphon swell and malform, disappearance of head appendages, and impede growth with intermediate stages, with pupation failure [56]. The synthesized AgNPs extracts of four plants i.e. *Azadirachta indica*, *Zingiber officinale*, *Syzygium aromaticum* and *Datura stramonium* had been tested. In LC50 treatment, the female longevity at was found to be the maximum by 34 days and that of the male by *Z. officinale* 14 days and 15 days for control, whereas for *A. indica*, 11 days for female and 5 days for male larvae fail to develop into a pupa, an intermediate stage [57]. The late third instar larvae of *Ae. albopictus* and *Ae. Aegypti* were exposed to LC50, and larvae that survived were further free cultured. Overall, *Ipomea cairica* crude extracts affected the whole life history of both *Aedes* species two generations. Significantly lower fecundity and fertility in *Ae. Albopictus* into 50.2 and 17.18 percentages. Besides, 56 and 17 percents for *Ae. Aegypti* respectively, and subsequently reduce the next generation population. Consequently, adults of the offspring's *Ae. albopictus* and *Ae. aegypti* decreased their fecundity by 34.68% and 16.61% compared to the respective controls [58]. The EI50 value of *C. botrys* whole-plant n-hexane extract was 312.3 ppm, and at 125 ppm, The adult emergence inhibition 76.8% in comparison with more than 90% emergence for control [59]. phytochemical screening showed that there were 5 secondary metabolites (alkaloids, terpenoids, steroids, tannins, saponins) in bitter melon (*Momordica charantia* L.), and two metabolites (Flavonoids, Tanin) in Basil (*Ocimum basilicum* L.) had been conducted on eggs of *A. aegypti* mosquitoes - vector of dengue fever virus - by testing the parameters; hatchability of eggs-larvae, development of larvae-pupae, and pupae-adult. However, hatchability rate of eggs-larva decreases, and the development of larvae-pupae declines, but there is no downturn in the development of pupae-adult (100%) with effective concentration at 800 ppm. [60]. Three plant extracts *Thevetia neriiifolia*, *Plumeria acuiifolia* and *Lantana camara* Examined for adult's emergence inhibition. According to values of IC50 (85.5 ppm, 108.7 ppm and 317.4 ppm), the plant extract *T. neriiifolia* proved to be more effective against *A. aegypti* larvae, followed by *P. acuiifolia* and *L. camara* by about 1.3 and 3.7 folds, respectively [61]. Sublethal effects of carvacrol-rich oregano essential oil and pure carvacrol on *Cx. pipiens* biotype *molestus*, the autogenous member of the *Cx. pipiens* species complex, after the exposure of 3rd–4th instar larvae to LC50 concentrations. The short-term (24 h) larvicidal treatment with

the sublethal concentrations of both tested materials exhibited; Significant delayed mortality for surviving larvae and pupae, morphological abnormalities that were observed at the larval and pupal stages along with failed adult emergence [62]. Topical application of two diterpene secondary metabolites with JH antagonist activity from two plants: *Lindera erythrocarpa* and *Solidago serotina*, caused reduction in the expression of Met target genes and retardation of follicle development in mosquito ovaries. Hence, the newly discovered Plant Juvenile Hormone Antagonists (PJHAs) may lead to development of a new class of safe and effective pesticides [63].

The ultrastructural effect of f Clove Oil (*Syzygium aromaticum*) with Lc50 was studied on the cuticle, muscles, and midgut of third-instar larvae of *Cx. pipiens*. The results showed histopathological changes; Disruption and separation of the epicuticle and endocuticle layers, Degeneration, vacuolization, and necrosis of the muscle fibers and erosion of midgut cells with loss microvilli and peritrophic membrane [16]. The ultrastructure histopathological effect of a lower dose from *Ocimum kilimandscharicum* extract on midgut epithelium of the *Cx. pipiens* larvae. The histopathological study showed that larvae treated with *C. kilimandscharicum* extract had cytopathological alterations of the midgut epithelium with cellular destruction, and vacuolization of epithelial cells. Also, revealed disrupted microvilli in the midgut along with cell organelles disintegration [64].

Application of *An. gambiae* larvae with sublethal concentration of emulsified *O. kilimandscharicum* oil formulation, most of the treated larvae were revealed growth disruption; As larval–pupal intermediary which were subjected to of the formulation, insufficient cuticle myelination, crumbled mouthparts and wings within the pupal exuvial, crumbled mouthparts and wings within the pupal exuviae, and the emerged adults were incapable of breaking from the pupal caste and perished on the surface of the water [65]. Extracts of *Artemisia herb alba*, *Lavandula multifida*, *Peganum harmala* and *Ruta chalepensis* against the 3rd instar larvae of *Cx. pipiens* was performed under laboratory evaluation, results were revealed significant decrease in growth index in treated individuals (2.00 - 8.90) when compared to control (11.25). Moreover, the sublethal concentrations of the acetone extracts reduced fecundity in the progeny of *C. pipiens* mosquitoes ranged 61% (*R. chalepensis*) - 73% (*A. herb alba*), whereas, hexane extracts induced sterility ranged 55 % (*A. herb alba*) - 64% (*R. choleresis*) [66].

Sublethal exposure of the promising vector-control bioinsecticide spinetoram to *Ae. aegypti* larvae alter adult performance and susceptibility to dengue virus infection. It was found that the surviving adult mosquitoes were significantly smaller and exhibited weaker blood-feeding capacity than control females. To reach the adult stage after different concentrations of spinetoram treatment, these mosquitoes generally had a longer development time with an average of 14.5 d as compared to 8 d in the control group. Treatment with spinetoram at 50 µg/L significantly affected the survival of *Ae. aegypti* during the developmental phase. The survival rates of the F1 generations were significantly lower as compared to the control group. Therefore, that spinetoram could cause transgenerational sublethal effects on the F1 mosquitoes [67].

2.5 Sublethal effect of predation

The presence of predators can shape the population dynamics of prey; the mosquito larva habit and their life trait are significantly affected in presence of predator or predator cues. In aquatic ecosystems, sublethal effects are governed by olfactory cues, including predator kairomones and chemical alarm cues from the prey^[68].

Kairomones incurs a cost to the predator of prey avoidance, these compounds may be necessary for the predator for other reasons or they may be necessary by-products of metabolic pathways, n-alkanes and other long-chain hydrocarbons like H and T are important components of insect cuticle and cuticular hydrocarbon composition is species specific^[69]. Cuticular hydrocarbons can have various roles including preventing desiccation, providing physical protection and reducing permeability. They can also be important semiochemicals, acting as recognition cues in social insects and sex pheromones in non-social insects^[70], and as signals for task allocation among social insects^[71]. In aquatic habitat, exposure to predators is known to affect a variety of traits including behavior, size, development, and survival^[72]. Non-consumptive effects of predators are the result of the prey initiating anti-predator behavioral and/or physiological trait changes that can aid in predator avoidance^[73]. Exposure to cues from a living predator affected both body size and latency to blood feed in females, moreover, sublethal predator treatments lack larval density, cohort generation time, effects of treatment combinations on larval development time and fecundity were ultimately manifested as effects on life-table traits estimated from adult survival and reproduction^[74].

The effects of habitat complexity and predation by the ambush predators *Toxorhynchites rutilus* and *Corethrella appendiculata* on their mosquito prey *Aedes albopictus* and *Ochlerotatus triseriatus* in container analogs of tree holes, whose presence shortened development time. However, when predators were present, survivorship of both prey species was skewed in favor of males, therefore, predation risk differs between prey sexes^[75]. Accumulating evidence indicates that species interactions can indirectly alter interactions with other community members, including natural food web consisting of the human malaria parasite *P. falciparum*, the mosquito vector *Anopheles coluzzii* and a backswimmer *A. jaczewskii*. For example, presence of predators can induce behavioral defenses in the prey, resulting in a change in prey susceptibility to parasites, when exposed to predators during larval development can have strong carry-over effects on adult phenotypes. Then, using an epidemiological model, larval predator exposure should overall significantly decrease malaria transmission. Therefore, environmental stressors effect on disease ecology and epidemiology^[76]. Cator *et al.* (2020)^[77] concluded that exposure to predation cues was significantly decreased mosquito body size in both sexes, lowered mosquito lifespan. Vector lifespan contributes disproportionately to disease transmission because older vectors are more likely to have been exposed to pathogens, more likely to already be infectious after having survived the extrinsic incubation period, and more likely to survive long enough to bite subsequent

hosts. It is well-established that smaller mosquito body size is associated with shorter mosquito lifespan and may limit the transmission of mosquito-borne diseases^[78]. Exposure to predation cues significantly lowered mosquito survival, and this non-consumptive effect has also been observed in dragonfly larvae prey (*Leucorrhinia intacta*)^[79]. In pioneer Russell (*et al.*, 2022)^[27] study, in addition to consumptive effects of mosquito predators, mosquito survival decreases among the *Aedes*, *Anopheles*, and *Culex* genera due to nonconsumptive effects, predators are likely decreasing the number of mosquitoes per host by reducing mosquito survive, and by reducing mosquito fecundity through effects on body size. Moreover, predators are decreasing the proportion of mosquitoes that are infectious by shortening the vector lifespan with effects on body size and longevity. Incorporating both of consumptive and nonconsumptive predator effects is vital for accurate mathematical models of mosquito-borne diseases, for example, the entomological inoculation rate (EIR), it calculates the exact number of infectious bites an individual receives from a mosquito over a specific period, such as per person per year^[80].

To assess the phenotypic and behavioral effects of mosquito exposure to predators; the predators, *A. jaczewskii* and *Pantala flavescens*, significantly prolonged the development time of *An. coluzzii*, reduced adult size and gravid females used various cues from predators as attractants to select oviposition sites^[81]. Behavior exposed to conspecifics that have been killed by notonectid predators^[82]. Also, when facing the risk of predation, *Aedes aegypti* larvae spent more time near the container's edges and exhibited discrete feeding behaviors or avoidance of the risk of predation^[83]. In *Cx. restuans*, both freezing (hanging at the water's surface or drifting in the water column) and fleeing (moving for nearly a full minute without resting) behaviors were observed as responses to conspecific alarm cues^[84]. Also, *Cx. restuans* larvae have also learned to recognize a salamander predator's odor as a threat, after experiencing the predator's odor paired with conspecific alarm cues^[85], and *Ae. triseriatus* larvae were exposed to chemical cues of *Toxorhynchites rutilus* predation until adult emergence, females exhibited significantly shorter development times under high nutrient availability^[86]. However, in comparison to how other changes in size can have important consequences for population dynamics and disease transmission. In *Ae. albopictus*, larger adults have greater reproductive success. While, smaller males have been shown to produce less sperm^[87]. Larger female body size consistently correlates with higher fecundity, when measured as the number of mature follicles in the ovaries^[88]. and in larger females, more spermathecae have been observed to contain sperm^[89]. The non-consumptive effects of *Lz. fuscana* on *An. stephensi* were mostly represented, as the age at pupation decreased and wing length increased more than the control in the presence of predator cues, and caged *An. stephensi* laid significantly lower eggs in the presence of predator cues and *Lz. Fuscana*^[90]. Also, fertility of *Culex pervigilans* and the resulting mosquito population was influenced in the presence of *A. wakefieldi* predator or their cues^[91]. Similarly, larval exposure to chemical

cues from the predatory fish *Hypseleotris galii* reduces adult size of *Ae. notoscriptus*, the main vector of canine heartworm, *Dirofilaria immitis* in Australia [92]. However, smaller *Ae. Albopictus* females are more likely to become infected with dengue and to disseminate the virus than larger females [93]. Furthermore, small females have been shown to be more likely than large females to take multiple bloodmeals within a single gonotrophic cycle [94], and the lifetime cumulative number of bloodmeals is also higher among smaller females [95].

2.6 Oviposition deterrence

There are several potent botanical extracts and essential oils that exhibit strong oviposition-deterrent activity against mosquito vectors, like *Aedes*, *Anopheles*, and *Culex* by releasing volatile compounds, which are masking olfactory cues that mosquitoes use to identify breeding sites and inducing neurological or behavioral avoidance [96]. The hexane extract of *Limonia acidissima* (Linn.) showed 100% oviposition deterrent activity at 62.5 ppm concentration against *Cx. quinquefasciatus* and *Ae. aegypti* adult females [97]. Coria *et al.*, (2008) [98] reported 100% oviposition deterrent was obtained with *Melia azedarach* L. leaf extract at 1 g/L concentration against *Ae. aegypti*. Oviposition deterrent depends on mosquito species, so that, *Mentha spicata* (L.), essential oil at the concentration 60 µg/cm² exhibited 60%, 46%, and 79% oviposition deterrence against *Ae. aegypti*, *An. gambiae*, and *Cx. quinquefasciatus*, respectively [99].

Oviposition avoidance in response to predators was strongest in response to fish and insects, but there are limited exceptions that some mosquitoes are attracted to cyclopoid crustaceans [100]. Western mosquitofish (*Gambusia affinis*) and Central newts (*Notophthalmus viridescens louisianensis*) release kairomones that deter certain species of *Culex* mosquitoes [101]. Moreover, the bacterium *Pantoea pleuroti*, isolated from the skin of the fish, repels oviposition of *Culex laticinctus* Edwards and *Culiseta longiareolata* Macquart mosquitoes similarly to the way in which live fish repel them [102]. The oviposition behaviour of *A. aegypti* in recipients containing larvivorous fish *Betta splendens*, revealed that, gravid female deposits with *B. splendens* less than control and the oviposition activity index (OAI) was -0.627 [103]. In addition, *Culex* vectors demonstrated predator avoidance behavior during oviposition [27]. In temporary pools, larvae of the mosquito *Culiseta longiareolata* Macquart are highly vulnerable to the common predatory backswimmer, *Notonecta maculata* Fabricius, this predator releases two hydrocarbons, n-heneicosane and n-tricosane, which repel ovipositing females of *C. longiareolata* [104]. *A. jaczewskii* Predator-released hydrocarbons repel oviposition by a mosquito *An. Coluzzi* [76].

3. Conclusion

Mosquitoes have variable direct serious roles for human beings; transmission of many fatal disease agents, annoyance by blood-feeding habit and even as they one of the phoretic insects for smaller arthropods as "hitchhikers". After urbanization, there are increasing in anthropophilic mosquito species as a result of feeding acclimation with urban

environment and reducing in their natural forest habitats. On ecological consideration; Mosquitoes in food chain are mainly primary consumers and they are main source for aquatic and wildlife secondary consumers, recycling solid organic matter by saprophytic filtrate-feeding habit and pollinators, therefore not out be repel mosquito's role in biotic ecosystem.

In view of mosquito control managements, the recent controlling programs are leaving mosquito control with synthetic or growth regulator insecticides, to avoid environmental deteriorations nor offspring resistance. Therefore, botanical and microbial natural insecticides, and predators are using with lethal doses and direct consumption mosquito aquatic stages. Furthermore, through the last two decades, to minimize the mosquito populations under control by reducing generations fitness, and to conserve trophic habitat equilibrium at the same time, laboratory studies and semifield experiments are emphasizing on sublethal activity of the ecofriendly bioinsecticides, and non-consumptive role of mosquito predators. Today, the collective sublethal effects of bioinsecticides are more active in mosquito control than their direct mortality.

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