

Review

Autodissemination of Pyriproxyfen as Novel Strategy to Control Dengue Outbreaks: A Review

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Abstract: The new emergence and re-emergence of arbovirus infections vectored by *Aedes* mosquitoes have been spread across Southeast Asia, Central Africa, United States, tropical Oceania and become a major of public health concerns. These arbovirus diseases found to have a similar vector, symptoms of the diseases and environments. The situation has become complicated without any specific vaccine or treatment for the diseases. As far as we concern, vector control is the best defense with many challenges, a scattered breeding site and biological behavioral sometimes, more difficult to control. Herein, we present a review of studies on current techniques proposed to combat arbovirus infections vectored by *Aedes* mosquitoes. A crucial gap in a vector control program is the inability to eliminate and destroy the cryptic breeding site by using conventional control methods. The idea and proper concept of using mosquitoes to bring insecticide to their oviposition site had been getting more interest in people to explore. Autodissemination is a self-delivery technique by manipulating the behavior of mosquitoes, carrying the insecticide and disseminate to cryptic breeding sites. This technique has shown a promising result in some countries and can be considered as additional tools in a vector control program.

Keywords: *Aedes* spp.; dengue; vector control; autodissemination; pyriproxyfen

1. Introduction

To date, there have been reported more than 300 species of mosquitoes in the world with a small number of species are responsible for vector-borne diseases [1]. *Aedes aegypti* and *Aedes albopictus* are the most important vector for the transmission of dengue fever, Zika virus, and chikungunya. More than one-third of people populations affected and about one million annual deaths caused by mosquito infections [2]. Dengue transmission occurred when an infected patient gets bites by mosquitoes, and then it can carry the virus to another person.

Aedes aegypti is the most important disease vectors worldwide. It is the principal vector of dengue, chikungunya, yellow fever and zika viruses which extremely anthropophilic, frequent blood feeding behavior, long lifespan and closely associated with human, because of their ability to breed in people dwellings, preferring to feed on people even the presence of mammals [3]. The blood-feeding behavior becomes the primary concern because it is the major component of the dengue virus transmission. Most of the species have their own preferred distribution, thus, *Aedes aegypti* is a vital primary of dengue vector, both mosquitoes also available as an efficient vector for other human diseases such as zika virus and chikungunya virus. *Aedes albopictus* was found able to transmit over more than 20 arboviruses, increasing the risk of human against mosquito borne-disease [4] and was considered as secondary vector importance according to their zoophilic preferences [5] and significantly associated with the dengue cases with a low number of *Aedes aegypti*. Currently, in particular, areas, it becomes one of the most invasive mosquitoes in the global spread and several

vector competences performed has shown that *Aedes albopictus* much more superior in the survival rate compare to *Aedes aegypti* [6].

2. Dengue

Epidemics of dengue were reported in 1635 in the Caribbean and 1699 in Central America. Dengue fever (DF) is among the most common mosquito-borne infections in the world, yet it has long been categorized as a “neglected tropical disease” [3]. Chinese medical encyclopedia from the Jin Dynasty (265–420 AD) has recorded probably the first record of which associated with flying insects. The first recognized dengue epidemics occurred almost simultaneously in Asia, Africa, and North America in the 1780s. The first confirmed case report of the first dengue haemorrhagic fever in Southeast Asia has been recorded from Manila in 1953 and the second outbreaks in 1956. In Asia, the epidemic was spreading from Sri Lanka, India and China [7]. Two centuries later, dengue has become one the major public health and become endemic in more than 125 countries globally such as in Malaysia [8], China [9], Pakistan [10] and Sri Lanka [11]. Estimated about 120 million travelers to the subtropical and tropical regions with around two billion lived in developing countries [12]. About 40% of people are at risk of contracting with the dengue virus annually, and the mortality rate was 2.5% with more cases of classical dengue with severe symptoms [13]. The World Health Organization, (2016), estimated 390 million infectious in 128 countries, with approximately half million with dengue fever need hospitalization. In the year 2017, 83,849 cases were notified with 177 deaths with a reduction of the 17.3% cases compared to 101,357 cases reported in 2016. The decrement number of cases was contributed by integrated management among ministries, agencies, communities, and personnel. Dengue strategic plan for the Asia Pacific region was launched for a period of 2008 until 2015 with targeting to reduce the incidence rate of cases by at least 20% annually [14].

3. Control of mosquitoes

Dengue (DENV), Zika virus (ZIKV) and Chikungunya (CHIKV) are mainly transmitted by *Aedes* mosquitoes, especially *Ae. aegypti* and *Ae. albopictus*. At this moment, there is no curative treatment or vaccines are available. Therefore, control of dengue vector is crucial to reduce the transmission of dengue fever. The combination of multidisciplinary approach with local authorities, mobilization of the community and integration of vector control must be together to ensure the successful of the strategy. However, there are a lot of challenges with a lack of strategy to respond against dengue outbreaks, unmanaged and rapid urbanization, poor sanitation system and bad disposal management in the communities [15].

One of the most effective alternatives is to control the level of vector populations. However, most of the vector control strategies nowadays are solely depended on chemical-based, thus without fully monitoring, it will increase the insecticide resistance phenomena. This situation was identified by the WHO and other agencies with demand for more sustainable and reliable strategies [16]. The occurrence of insecticide resistance may be different among the geographically distribution, with a high number of used by household and agriculture. It is essentially important to find a novel strategy of surveillance and prevention for dengue management [17]. The development of resistance may become faster and severely than our expectation. It is also essential to control *Aedes* mosquito populations by eliminating of container habit that enhances oviposition and facilitates the development of the *Ae. aegypti* larva.

There are several ways to control vector population, which is through source reduction, biological control, genetic manipulation and chemical control. However, the best vector control strategy is to combine source reduction methods, law enforcement and controlling the use of insecticide usage, which are crucial for the successful of the program [18]. The responsible agencies should prepare several strategies on mosquito management such as performing location assessment, insecticide treatment, educating the public, establishing the policy and regulation, conducting mosquito surveillance and utilizing new technologies [19,20]. World Health Organization (WHO) has announced a concept of Integrated Vector Management to optimize the use of resources in the management of vector programs. The IVM aims to prevent the transmission of vector-borne diseases

such as dengue, chikungunya, malaria and zika virus [21]. However, without a proper direction, the efficacy of the integrated vector control management would not be able to fully be utilized.

4. Insect Growth Regulators as an alternative?

Insect Growth Regulators are the third generation of insecticide with a different type compare to another insecticide depending on their mechanism through the influence of insect development, disrupting the activities of endocrine system and metamorphosis [22]. The first generation was characterized by the chemical which arises from a decade or centuries. The chemical includes oils and arsenic. The second generation of insecticides was carbamates, organophosphates, and organochlorides. This insecticide was found during the synthesis programs with the discovery of DDT. Other's definition is also referring to the process to the bioactive compound by directed synthesis or involving the physiology and ecology to produce an environmentally friendly chemical [23]

IGRs have a selective mechanism in their mode of action with a major impact to inhibit the development of insect into adults. The mechanism of IGR delays the transformation and inhibits the cuticle formation in an immature stage of insects [24] An IGR will be induced during the early stage of the insects and kill the insect before the insects become adults and unable to reproduce any progeny. The IGR is a form of "birth control" and can be described as control of insects through the release of hormones/ IGR into the populations. There is not a necessity for the IGR to be high toxicity to the target sites but may lead to a change and abnormalities against the insect survival. Two compounds are playing the roles in regulating the development of insects, (i) ecdysone (called as molting hormone MH), (ii) juvenile hormone (JH) which directly interfered with the growth and development of the target insects. These compounds interfere with insect metamorphosis, embryogenesis or reproduction.

Pyriproxyfen is a powerful JH agonist which affects the physiology of metamorphosis, embryogenesis, and reproductivity in insects with a unique mode of action. In general, pyriproxyfen is used in larvicidal activities to control mosquitoes in the form of Sumilarv. It is useful in inhibiting the emergence of adult *Aedes* ranged from 0.000048 ppm [25] to 0.33 ppm [26]. Thus, *Aedes albopictus* was found to inhibit the emergence at LC₅₀ and LC₉₀ with 0.0012 and 0.021 ppm [27]. These studies showed the superior activities of pyriproxyfen against *Aedes* species in laboratory settings.

In addition to the larvicidal impact, PPF has been reported to reduce the longevity, fertility, and fecundity in exposed mosquitoes. This is a novel strategy as the mosquitoes exposed to the PPF are laying unviable of eggs. Earlier studies on *Aedes aegypti* using sublethal dose demonstrated the effects on fecundity and fertility [28]. Due to the low persistence in environment, specific activity against insect stages and non-toxic on mammal, it is considered as an alternative to the conventional insecticide. Furthermore, PPF has been evaluated as a safe insecticide for application in drinking water with minimal impacts on non-target aquatic insects and the environment.

5. Pull and Push Concept: Autodissemination potential against *Aedes* spp. mosquitoes

Autodissemination is a novel technology to control mosquito populations by exploiting the ability of female mosquitoes to find a suitable breeding site, and on the skip-oviposition, the mosquito will lay their eggs in different containers between the single gonotrophic. The contaminated mosquito is carrying a small particle of insecticide and transfer to other via mating, oviposition in the hidden and cryptic breeding sites (**Figure 1**) that human may not be able to assess during the inspection [29]. Autodissemination can be considered as pull and push technologies with the attraction and dispersal concept which beneficiary and cost-effective to the vector control program [30]. For autodissemination technique to be a successful, specific prerequisite are needed to be followed. 1) The ability of autodissemination station to attract mosquitoes, 2) Autodissemination station can be able to transfer the chemical to the mosquitoes and 3) Insecticide distribution from the exposed mosquitoes to the breeding sites [31,32]. As for the additional, requirement is the chemical in used can be working at a low concentration, sustainable in the environment for a long time [29,31].

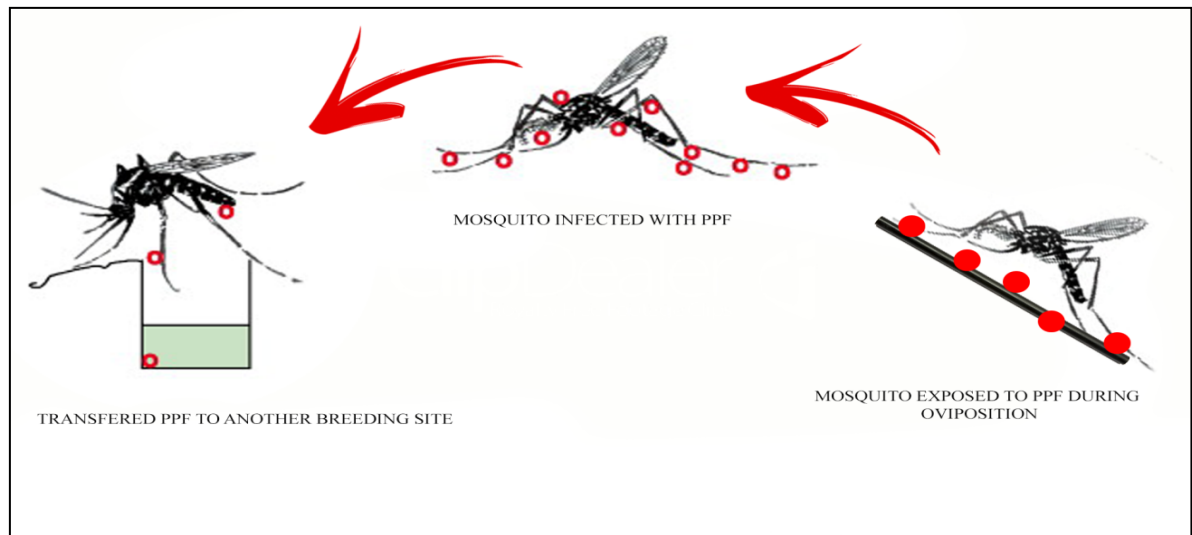


Figure 1. The mechanism of autodissemination of pyriproxyfen by female mosquitoes from exposure containers to other breeding sites.

6. History of Autodissemination Methods

The concept of autodissemination device has been tested by others weed and pests [33,34]. The automatic device using fungi BCAs working as a lure, once the insect attracted and entered the device. It became contaminated and left the device and transferred the BCA into populations. The used of BCAs dissemination against honey-bee was significantly more efficient than conventional sprayer to spread the inoculums against a pest-infested flower [35]. To enhance the impact of BCAs, “push-pull” strategy had been used by stimulating the insects out from the population (“push”) with feeding the deterrents and extracted (“pull”) into the trap. The deterrent, lures must be more favorable and attractive than the crop to encourage the insect to enter the traps. In several studies, autodissemination are shown a promising result within the pest population, using an attractant device as the initial source of infection [36,37].

The autodissemination has widely been used against diamondback moth, *P. xylostella* using *Z. radican* and Rhinoceros beetle, *Oryctes rhinoceros* using *Metarhizium anisopliae*. The manipulation of DBM behavior using semiochemical such as pheromones has been used to attract and developed epizootic population before the critical level achieved [33]. Other studies in Klang and Selangor, Malaysia found the mortalities of *Oryctes rhinoceros* was 75% to 90% infected by *M. anisopliae* with the percentage trapped adult leaving the traps was ranging 85% to 95% [36].

For mosquito population control, autodissemination using pyriproxyfen has not reached enough number of operational field level and nowadays received much attention since the year 2009 following the previous successes [38]. The first trial was shown in a laboratory [39], and then the concept was further by other [40] (**Table 1**). The assumptions of abilities in mosquitoes in carrying insecticide to their preferred breeding sites compared to a human operator are more superior. The used of a small particle in pyriproxyfen with contaminating dusted mosquitoes can affect and transferred the effect control to the whole areas is the key to success to the technique [41].

A novel was developed based on the behavior of mosquitoes “skip oviposition” using female mosquito to transfer small particle of insecticide to the cryptic breeding sites. Thus, interrupting the development of the larvae and subsequently killed and reduced the population in the particular areas. In 2009, a significant trial for an autodissemination concept with pyriproxyfen was conducted in

Table 1 Overview of autodissemination trials conducted under semi-field and open field trials.

Study site	Settings	Target species	AI	Duration (days/months)	Result	References
Bangkok, Thailand	SF	<i>Ae. aegypti</i>	PPF	16d	<ul style="list-style-type: none">- The first demonstrated of autodissemination concept against Aedes mosquito which are from the resting place to the breeding sites.- Inhibition in adult emergence was shown proving the abilities of autodissemination of PPF. However, not 100% mortalities were recorded from each cup.- The male mosquitoes may also play an important role as a transportation of the PPF.	[39]
Iquitos, Peru	OF	<i>Ae. aegypti</i>	PPF	6m	<ul style="list-style-type: none">- This is the first study reported in open field settings with 49 – 84% mortalities larva in sentinel sites.- The use of 3 -5 % breeding site treated with PPF caused > 95% contamination in sentinel sites.- Overall number of mosquito reduction (EI) was 42 – 98% during the trials.	[41]
Rome, Italy	OF	<i>Ae. albopictus</i>	PPF	Mixed (min: 7d; max: 20d)	<ul style="list-style-type: none">- Two different setting of trials and showed a different range of mortalities against pupae ranging 20.8 to 71.2% compared to control.- However, higher concentration of pyriproxyfen (5%) showed a better dissemination with higher mortalities in sentinel sites.	[31]

Rayong Province, Thailand	OF	<i>Ae. aegypti</i>	PPF	6w	<ul style="list-style-type: none">- A significant different was recorded against eggs laid ($p < 0.05$) and larva mortalities ($p < 0.01$). However, there is no evidence of pyriproxyfen transferred between a treated device to water-holding containers.	[42]
Nagasaki, Japan	SF	<i>Ae. albopictus</i>	PPF	Up to 44d	<ul style="list-style-type: none">- All monitored parameter (number of eggs laid, pupae and egg hatch) showed a significant reduced in PPF treatment compared to the control. Moreover, in larva bioassays was significantly increased in larva mortality.- The PPF treated bed net could be transferred on mosquitoes and subsequently suppress the mosquito density.	[43]
Southern Tanzania	SF	<i>An. arabiensis</i>	PPF	17m	<ul style="list-style-type: none">- The first study conducted against malaria vector in African (<i>An. arabiensis</i>).- The mean number of adult emergence rates were significantly higher in treatment compared to the control.- A higher number of autodissemination clay pots point (8 autodissemination device) have showed a better reduction in pupae collection and adult emergence rather than using one clay pots, respectively.	[44]
NJ, USA	OF	<i>Ae. albopictus</i>	PPF	Yearly	<ul style="list-style-type: none">- A direct treatment using point source treatment showed a high number of larval mortalities in 2010 compared 2011.- The mosquitoes were found able to disseminate PPF up to 200 meters.	[45]

					<ul style="list-style-type: none">- However, the area-wide treatment unable to reduce mosquito populations and the rainfall may playing an important role in reducing the effectiveness of PPF in the field.	
Amazonas, Brazil	OF	<i>Ae. aegypti</i> <i>Ae. albopictus</i>	PPF	20m	<ul style="list-style-type: none">- The coverage of pyriproxyfen contamination was > 85% with sentinel ovitrap distance up to 397m.- Larval bioassay showed 75.1% (after treatment) compared to 4.2% (before treatment) in all ovitrap against all species collected.- High density number of Aedes sp. could facilitated the effectiveness of autodissemination approach in this area.	[46]
Kentucky, USA	OF	<i>Ae. aegypti</i> <i>Ae. albopictus</i>	PPF	20w	<ul style="list-style-type: none">- A significant contamination result was collected in larval mortality ranging 40% to 70% up to 150m from the release station points.- Larval bioassay also showed a significant reduction in mosquito survival compared with control. Mosquito are able to transfer insecticide to other breeding sites.	[29]
NJ, USA	SF/ OF	<i>Ae. albopictus</i>	PPF	2013-2014 (8-12w post-deployment)	<ul style="list-style-type: none">- SF: most of the mosquito showed a strong preference against cryptic breeding sites.- OF: Increasing in pupal mortality and PPF contamination was observed in 2014 compared to 2013.- However, the overall number of larvae mortality was ranging from11% to 22%.	[47]
Florida, USA	OF	<i>Ae. aegypti</i> <i>Ae. albopictus</i>	PPF	2w	<ul style="list-style-type: none">- A significant of larvae mortality (45%) was observed in treatment cup (Site 1),	[48]

					<p>however, no significant different was detected in Site 2.</p> <ul style="list-style-type: none">- The abundance of ovisites, climatic conditions and population dynamic may affect the efficacy of ADS.	
Amazonas, Brazil	OF	<i>Ae. aegypti</i> <i>Ae. albopictus</i> <i>Culex</i> spp <i>Limatus</i> spp.	PPF	24m	<ul style="list-style-type: none">- During PPF intervention, there was a reduction in juvenile collection (80%-90%) and <i>Aedes</i> mortality increased ranged 2% to 80% and 7% to 90%, respectively.- Overall, for all species, the mean number of juvenile mortalities was increased (1.9% to 79.7%), adult emergence (1177 to 56) and house infestation (85% to 33%).	[49]
Florida, USA	OF	<i>Ae. albopictus</i>	PPF NyGuard	6w	<ul style="list-style-type: none">- Direct treatment of PPF (treated tyre pile) showed a significant juvenile mortality, however, there is no evidence of autodissemination activities in other ovitrap was observed. The PPF was effectively kill the larvae up to 4 weeks.	[50]
CA, USA	OF	<i>Culex quinquefasciatus</i>	PPF S-methoprene	8w	<ul style="list-style-type: none">- a high number of emergence inhibition (100%) was recorded against <i>Culex quinquefasciatus</i> for the first 3 weeks. However, the efficacy of the insecticide was reduced to 69% (PPF) and 68% (methoprene) at 4 weeks.- The result also been obstructed by the high mortality in control sites.	[51]
Florida,USA	SF	<i>Ae. aegypti</i> / <i>Ae. albopictus</i>	PPF	-	<ul style="list-style-type: none">- A significant inhibition of emergence was observed i) direct trap (100%), ii) in ovitrap (81% - 94%).	[52]

					<ul style="list-style-type: none">- The exposure against in2Care for 48H significantly reduced the longevity of adult mosquitoes.	
NJ, USA	OF	<i>Ae. albopictus</i>	PPF	7m	<ul style="list-style-type: none">- A significant difference was reported in pupa mortality 12.4% compared to control (0.5%)- The number of mean egg/ovicup and mean larvae in ovitrap were also reduced and significantly different compared to control sites.	[30]
USA	OF	<i>Ae. albopictus</i>	PPF	12w	<ul style="list-style-type: none">- Most of the finding show a promising result with dispersal mechanism can reach 200m.- One of the robust demonstrations and control methods of autodissemination approached in the field, even the percentage of contamination ranging 30%-80% and pupal mortality < 50%	[26]
LA, USA	SF	<i>An. quadrimaculatus</i>	PPF Triflumuron novaluron		<ul style="list-style-type: none">- Novaluron was able to be transferred with a greater efficacy compared to triflumuron and PPF.- Need field trials to confirm the abilities of novaluron as one of the suitable tools in <i>Anopheles</i> controls.	[53]
Southern Tanzania	SF	<i>An. arabiensis</i>	PPF	27m	<ul style="list-style-type: none">- A significant reduction in <i>An. arabiensis</i> population compared to the control chamber.- This is the first study demonstrated the abilities of malaria vector to disseminate PPF and subsequently reduced the populations.	[54]

					<ul style="list-style-type: none">- BGST was found as one of the effective tools to adapt as an autodissemination stations.- Autodissemination approach was consistently shown an impact against mosquito abundances.- The effectiveness of autodissemination strategy were also depended by the distance, local density of adult mosquito and time of the implementations.	[55]
Madeira, Portugal	OF	<i>Ae. aegypti</i>	PPF	12m		
Serdang, Malaysia	OF	<i>Ae. aegypti/</i> <i>Ae. albopictus</i>	PPF	4m	<ul style="list-style-type: none">- There was a significant reduction in egg collection after 3 months of intervention by using autodissemination stations ($p < 0.05$).- All eggs directly collected from autodissemination station shown a significant emergence inhibition compared to the conventional ovitrap.	[56]
NJ, USA	OF	<i>Ae. albopictus</i>	PPF	36m	<ul style="list-style-type: none">- The larva and pupal mortalities was ranging 12-19% in the treatment areas.- Even though, the number of eggs was significantly reduced in 2014, there is no significant different was observed in 2015 and 2016.- The impact of autodissemination against mosquito population was lower compared to the previous trials.- A few numbers of problems and limitation was observed due to the reduction in autodissemination effectiveness such as logistical and technical problems (blockage and exit size of ADS) and limited access to individual properties	[57]

4 Abbreviations: SF, semi-field; OF, open field; PPF, Pyriproxyfen; EI, emergence inhibitions; d, days; w, weeks; m, months; ADS, autodissemination station;
5 BGST, Biogents Sentinel traps;

Iquitos, Peru. The placement of the autodissemination was 5% from the available resting areas achieved 42-98% reduction in adult emergence with a maximum number of mortalities was 98% (38). The commercial of pyriproxyfen as an emulsifiable concentration showed, can be transferred as far as 200 m from the treated areas. However, other factors also contributed to the effectiveness of PPF distribution such as rainfall, coverage areas and geographical variations [45].

Recently, the effectiveness of autodissemination methods using pyriproxyfen has been studied in Trenton, New Jersey, which is reported with high *Aedes albopictus* populations [30]. The result has shown a reduction number in some dengue cases, fewer numbers of eggs and residual effects of pyriproxyfen were found within the treatment areas. Autodissemination has also been studied by the different condition in small-scale field trials against *Aedes albopictus* and *Aedes aegypti* [31,52]. However, in 2014, the first study against *Anopheles arabiensis* has been conducted in Tanzania, Africa, observed 82% of inhibition in adult mosquitoes by using the autodissemination of PPF and similarly with other findings against *Culex quinquefasciatus* and *Anopheles gambiae* [58]. This strategy is shown promising result and can be considered as an alternative for the future malaria vector control [44]. In contrast, the large-scale autodissemination approach needs further investigation.

8. Recent Advance in Autodissemination on Mosquitoes

“Boost SIT” with the combination of two methods is a releasing sterile insect mosquito with a pyriproxyfen. Despite the failure of mating, the percentage of pyriproxyfen contamination between the populations is high. During the mating, male mosquitoes will contaminate female at the same time can contaminate the breeding sites too. Currently, ongoing research has been conducted to explore the effects of PPF against mosquito competitiveness, the amount of PPF needed from males to females and then, from females to breeding sites and the design of smart machine to release the mosquitoes in a large scale [59].

To enhance the persistence of insecticide and attraction, dual treatment system has been used for the autodissemination stations, an EC formulation, and granule formulation showed, that the mosquito can carry the insecticide up to 200 m along the residential areas detected by residue analysis [26]. Other studies using a combination of *Beauveria bassiana* (entomopathogenic fungi) and PPF also gave 100% larval mortality in a laboratory; however, the study did not include any field trials [52, 60]. Another approach by using a combination of oil and pyriproxyfen to enhance the attachment of the particle on the female and increase the transfer of pyriproxyfen to the oviposition sites [61].

9. An Innovation of Autodissemination Device

9.1. Auto-Dissemination Augmented by Males (ADAM)

Auto Dissemination Augmented by Males (ADAM) was developed by using the combination of autodissemination and autocidal concept, by enhancing the abilities of male *Aedes* mosquitoes (29). The technique used mosquitoes as a transporter to transfer PPF dust females via mating attempts, and subsequently, it will transfer the PPF to cryptic breeding sites during the oviposition. They found a significant cross-contaminate between males and females who are suitable to release the ADAM in the areas with a low density of *Aedes* populations. Although the density of adult mosquito was declined after four weeks of treatment, further study on the mosquito behavior, study area with a different ecological context, as well as the size of the field trials is needed to validate the efficacy of ADAM in the vector control program [62].

9.2. In2Care Mosquito Trap

The In2Care mosquito trap has been approved by the United States Environmental Protection Agency (EPA) for the professional used against *Aedes* mosquitoes. It was the first commercial trap controlling both larvae and adult mosquitoes using pyriproxyfen, that can be disseminated by effected female mosquitoes and *Beauveria bassiana*, a fungus with slow-killing abilities on an adult. During the oviposition, female mosquitoes will make a tarsal in touch with a contaminated gauze with PPF and *B. bassiana*, indirectly, both agents will stick to their bodies and able to auto disseminate

PPF to the other breeding sites within their flight range [52]. The In2Care mosquito traps manipulate the behavior of female mosquitoes by “skip oviposition” and finding cryptic breeding sites and the same time. *B. bassiana* spore will grow hyphae, feed upon the bodies, reproduce and kill the mosquitoes within 18 h [63].

9.3. *AedesTech Mosquito Home (AHM)*

AHM work by using a “Pull” and “Push” control strategy combining the Lure-Kill technology with the objectives to reduce *Aedes* population and Interrupting dengue transmission. It has potential to target larval breeding sites that cannot be reached by traditional larvicidal applications (cryptic breeding sites). The concept “Pull” is using a formulation with an attractant ingredient lure against female mosquitoes to breed inside AHM. “Push” referred to the contaminated mosquitoes and dispersed after ovipositing their eggs, in this method, female’s mosquitoes are used as a carrier for the transfer of delivery to other containers and thus, disseminating insecticide to the larval habitats. The formula solutions and AHM device have been designed with a sustainable feature. Gravity is used to control the level of formation in the casing. During the evaporation, water is released in the casing, filling it back to the pre-set level and the evaporation rate will always be kept at the optimum level which is sufficient for the development of *Aedes* from egg to pupae [56].

10. Status and ongoing studies in Malaysia

A study on autodissemination using pyriproxyfen is not well established in Malaysia. Most of the test studies conducted were to evaluate the effectiveness of pyriproxyfen against *Aedes* sp. Mosquitoes. In 2014, a total of 350 autodissemination devices were deployed in three blocks consisting of 27 stories with ten unit house per floors. Four units of autodissemination were placed in each level at distance of 5m from apartment units. After the exposure periods, there is no survival larva in the trap, and significant reduction to a dengue cases number was observed from 53 cases (2013) to 13 cases (2014). To date, based on previous studies conducted in apartment residential, ongoing studies on five-story shop houses, Shah Alam, evaluate the impact between mosquito populations and the efficacy of autodissemination and to develop new mathematical modeling using a different situation of placement, meteorological data and identify the weakness and strength of the device

11. Conclusion

Vector control program for arbovirus transmitted by mosquitoes will bring many obstacles, however, with a new advantage and technologies, it may be a possibility in the foreseeable future. Considering one of the techniques and the abilities of autodissemination as a self-delivery technique by manipulating the behavior of mosquitoes, carrying the insecticide and disseminate to cryptic breeding sites, has shown a promising result in some countries and can be considered as additional tools in a vector control program.

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