



## REVIEW ARTICLE

### Integrated Strategies for the Control and Prevention of Dengue Vectors with Particular Reference to *Aedes aegypti*

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#### ABSTRACT

Dengue fever (DF) is one of the most threatening vector borne diseases, affecting both humans and animals, causing severe epidemics and has brought the world to take serious steps for its control and prevention. DF is a viral disease transmitted by *Aedes* mosquitoes. Unfortunately, due to unavailability of vaccine and lack of effective treatment, emphasis is given on its vector control. The only option left for its eradication is to restrict mosquito breeding. This can be achieved by chemical, biological and environment management methods. Use of botanicals is also an alternate and probably most effective approach for controlling DF vector. Community based eradication campaigns including educating people about its prevention and control measures and personal prophylaxis also play a vital role to prevent its occurrence. Likewise, use of nanotechnology and micro-emulsion, use of pheromones, insect sterilization techniques have also shown promising results in vector control. Utilization of only one method cannot control this dangerous disease but combination of all above interventions, discussed in the present paper, may prevent the DF vector and ultimately might help in the eradication programs of this disease.

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#### INTRODUCTION

Dengue fever (DF) is caused by one of the four serotypes (DEN-1, DEN- 2, DEN-3 and DEN-4) of genus *Flavivirus* and spread by mosquito vector mainly by *Aedes aegypti* and *Aedes albopictus* which belong to order *Diptera* and family *Culicidae*. DF mosquitoes typically bite during the day particularly in the early morning and late evening. DF first emerged in 1940 and then spread across tropics and subtropics (Kroeger and Nathan, 2006). The ecologic disruption in the Southeast Asia and Pacific theaters during and following World War II created ideal conditions for increased transmission of mosquito-borne diseases, and it was in this setting that a global pandemic of dengue began (Halstead, 1992). Reports have demonstrated that monkeys can also act as a source of transmitting DF virus to humans due to mutual sharing of same habitat. Mosquitoes that bite the monkey may acquire the virus and subsequently transfer virus to humans. So, monkeys can serve as major reservoir host

for the transmission of virus to humans (Holmes and Twiddy, 2003). Clinical cases have shown that early stages are similar to those of yellow fever. Fever and other symptoms seldom remain for more than seven days. The later stages of the illness often include a widespread rash (Farrar, 2008). Out of total dengue cases about less than 5% cases can be severe and a fraction of these cases can be fatal (Morens, 2009). About 50-100 million infections are reported annually and out of this more than 500,000 people suffered from dengue hemorrhagic fever (Halstead, 2007). An estimated 19,000 deaths are attributable to DF each year. Dengue hemorrhagic fever (DHF) and dengue shock syndrome are common names of severe DF that is distinguishable from classic DF because this is associated with spontaneous hemorrhage and an increase in vascular permeability which can lead to hypovolemic shock and death. Etiology of these conditions has been debated for decades but this problem remained unresolved and untreatable (Murgue, 2010). DHF is fastest growing viral disease. During 1970s and 1980s, DHF re-emerged

in most of the countries such as America and some others from which it had previously been eliminated (Gubler, 1987). After a few years of re-emergence, these countries experienced epidemics of DF, followed by hyper response and the emergence of DHF (Pinheiro and Corber, 1997).

Dengue virus transmission is due to multiple factors such as increase in population, local and international traveling and international trade of commodities (tires); changes in water resources being used, storage of waste water in open drums and lack of financial and effective resources necessary for control and preventive measures. In addition to the above mentioned factors, the rise in global temperature and humidity has also increased incidence of DF. Out of all these factors, the global warming is predominantly influencing the spread of DF vectors. As increased temperature favors development of adult mosquitoes and increase their number. During hotter summer, frequency of female mosquito biting increases and warmer winter empower mosquito's survival in previously cold areas. So, in some areas increased humidity, temperature and precipitation cause measurable increase in DF incidence (Hopp and Foley, 2003). Increased level of humidity favors long survival of eggs and female mosquito. During draught season, people used to store water in drums, container and tanks; this provides the more breeding sites to mosquitoes that results in spread of DF to cities (Gage *et al.*, 2008).

The increased occurrence of DF and its high mortality rate has brought the world to take serious steps for its prevention and control. Previously, old civilized communities of different countries adapted various traditional protocols to control mosquito population. Use of burned plant materials proved to be effective to drive away mosquitoes. About 39% of Malawians burn wood dung or leaves (Ziba *et al.*, 1994), 3% of rural Zimbabweans used burned plants and 15% used coils (Lukwa *et al.*, 1999), 100% of Kenyans people burned plants to repel mosquitoes (Seyoum *et al.*, 2002) and 55% people of Guinea Bissau used burned plants or hung them in their homes to get rid of mosquitoes (Palsson and Jaenson, 1999). From prehistoric times, Indian people have been using *Azadirachta indica*, commonly known as neem, against household and storage pests. Furthermore, they traditionally burned neem leaves in the evening to repel mosquitoes. It is reported that neem plant is effective against more than 500 species of insects. Recently, *A. indica* has attracted global attentions because of its potential as a natural source of environment friendly pesticides (Isman *et al.*, 2011; Mehlhorn, 2011).

In this regard, vector control proved most successful and excellent method to decrease incidence of mosquito borne diseases. Due to the emergence of resistance against various insecticides and potential environmental issues associated with some synthetic insecticides such as DDT has indicated that additional approaches to control the proliferation of mosquito population would be an urgent priority research (Grodner, 1997).

So far, no vaccine has been developed for prophylaxis of DF because the presence of more than one viral strains make it difficult. These factors contribute towards slow progress in controlling all serotypes simultaneously (Hombach, 2007). Recently, attenuated vaccines and second-generation recombinant vaccines are

under development (Webster *et al.*, 2009). To evaluate the efficacy of a chimeric tetravalent vaccine, large scale trials are going on since February 2009 in Washington (NIHA, 2010). If these trials are successful, then a vaccine might be licensed within next five years. Despite all these efforts, there is no chance of vaccine availability in near future. Furthermore, because of the non availability of effective and specific treatment against DF, the supportive therapy is the only remedy to replace the heavy blood loss. In supportive therapy, the intravenous fluids are administered to counter the hemo-concentrations and platelet transfusions in case of severe thrombocytopenia (Wills and Holstead, 2008).

Because of the high cost of developing new drugs and vaccines, development of drug resistance, and concerns over drug residues associated with the continuous use of chemicals, there is a renewed interest in the use of botanicals for the safe, effective and cheap control of pests of agriculture and public health importance (Yildirim *et al.*, 2012). Scientists all over the world are now actively engaged in research into the use of plants and plant-derived products to fight against dengue vector. Botanical products are effective, have no harmful effects on environment and non-targeted organisms, easily biodegradable, inexpensive and readily available in many areas of the world (Su and Mulla, 1999). Plants and plant derived products are rich in natural phytochemicals (Fan *et al.*, 2011), which make them effective against different microbes and pests. Some of these chemicals have also been used successfully for controlling dengue vector because of their larvicidal, ovicidal and skin repellent effects (Shalan *et al.*, 2005).

Because of above mentioned constraints in the methods used for the control and treatment of DF, control of *Aedes* mosquitoes is the only viable option (WHO, 2009). Therefore, in this paper integrated strategies for the prevention and control of DF have been discussed in the following sections.

**Effective and focused surveillance:** Effective and focused surveillance is fundamental in setting the objectives and evaluating a vector borne disease control program. Unfortunately, these programs are not aimed on vector eradication. Singapore's experience with dengue demonstrated that current vector control efforts are not sustainable. For sustainable succession program, Singapore needs to adopt a vector control program which is based on carefully collected epidemiological and entomological data and there is need to strengthen disease surveillance programs (Ooi *et al.*, 2006).

Surveillance programs should determine the vector density as it is easier and inexpensive method in controlling *A. aegypti* (Tun-Lin *et al.*, 1995). So, an effective surveillance focusing on vector eradication, which provides fundamental information about vector density and its breeding habitat, will be helpful in *A. aegypti* control.

**Environmental management and community based eradication campaigns:** Environmental management should be aimed to reduce vector breeding sites, especially in close vicinity with humans and therefore minimize human-vector contact. These changes can be

made for attaining long lasting effects which include modifying building designs such as roof gutters, covering containers and other potential breeding sites to prevent *Aedes* breeding (NG, 2008).

By adopting certain environment management practices such as removing, covering and treating larval sites show better results as compared to outdoor application of insecticide which has poor penetration at the potential breeding sites of mosquito vector. By taking long term steps of physical changes in environment, that are termed as environmental modifications, the incidence of DF can be reduced (Walker, 2002). These modifications should be done at larger scale under the great amount of financial aid and manpower. Modification at local level is of no significance and may be ineffective at alternative sites of vector breeding near human habitats (Mutero *et al.*, 2004). Well targeted local modification of environment can be successful in some cases. The sustained environmental interventions are effective, inexpensive and environment friendly as compared to chemical methods (Utzing *et al.*, 2001).

Use of ovitraps in different areas such as in Singapore is also proved to be effective for control of *A. aegypti* larvae. Larvicidal ovitraps consist of a black, water-filled cylindrical container with a flotation device made up of a wire mesh and 2 wooden paddles. Eggs laid by mosquitoes on the wooden paddle hatch, larvae develop in the water under the wire mesh and ultimately resultant adult mosquito's also trapped (Lok *et al.*, 1977).

Community based eradication campaigns are made with the objective of educating the public about the strategies for the elimination of breeding sites to reduce mosquito production. In this method, the public or community people are divided into different groups because all the people of community are not well educated and their level of understanding is not same. In some countries like Cuba, community involvement has been very useful for the effective eradication of *A. aegypti* mosquitoes from the environment (Vanlerberghe *et al.*,

2010). However, to get maximum vector control, community involvement should be used in combination of other methods to limit vector density (Pérez-Guerra *et al.*, 2009; Shriram *et al.*, 2009), such as the combination of community based campaigns and chemical control have shown significant results in controlling *A. aegypti* in Cuba state (Baly *et al.*, 2007).

Community participation is key to success either it is biological, chemical, or environment based strategy (Yap, 1984). Community based eradication campaigns are most economical interventions for government as compared to other campaigns. Furthermore, it is almost impossible to achieve sustainable success in controlling dengue vector, without integration of community to other control methods (Gubler, 1997) because such campaigns result in mobilizing and channeling the household behaviors, thus, eliminating vector breeding sites (Parks *et al.*, 2005). However, the success of community based campaigns depends on the knowledge, the behavior of the community members and practices involved (Whiteford, 1997; Nam *et al.*, 2005).

**Chemical control:** Chemicals have played a major role for the effective control of dengue vector for several years. In 1940s, use of insecticide resulted towards the less emphasis on biological and environmental methods of controlling vectors. Dichlorodiphenyltrichloroethane (DDT) was the first chemical used to control *A. aegypti* but development of DDT resistance was a key factor which contributed towards the re-emergence of *A. aegypti* (Curtis and Lines, 2000). Studies have also shown the development of cross resistance in *A. aegypti* to other chemicals such as organophosphates and carbamates (Rawlins, 1998; Olivares-Pérez *et al.*, 2011). Recently, development of multiple resistances in *A. aegypti* has also been reported in different countries such as Latin America (Rodríguez *et al.*, 2007) and French West Indies (Marcombe *et al.*, 2009). Resistance of *A. aegypti* to various chemicals has been described in detail in table 1.

**Table 1:** Reports on insecticides resistance against *Aedes aegypti* during last decade

Class of Insecticide	Insecticide	Country	References	
Organochlorine	DDT	Latin America	Rodríguez <i>et al.</i> (2007)	
		Japan	Kawada <i>et al.</i> (2009)	
		India	Tikar <i>et al.</i> (2009)	
		Latin America	Polson <i>et al.</i> (2011)	
Organophosphates	Temephos	Colombia	Ocampo <i>et al.</i> (2011)	
		Brazil	Macoris <i>et al.</i> (2003)	
		Thailand	Ponlawat <i>et al.</i> (2005)	
		Argentina	Macoris <i>et al.</i> (2007)	
		Brazil	Rodríguez <i>et al.</i> (2007)	
		Argentina	Linás <i>et al.</i> (2010)	
	Malathion	Brazil	Lima <i>et al.</i> (2011)	
		Brazil	Fontoura <i>et al.</i> (2012)	
		India	Tikar <i>et al.</i> (2009)	
		Trinidad and Tobago	Polson <i>et al.</i> (2011)	
		Malaysia	Rong <i>et al.</i> (2012)	
		India	Tikar <i>et al.</i> (2009)	
Pyrethroids	Chlorpyrifos	Pakistan	Khan <i>et al.</i> (2011)	
		India	Tikar <i>et al.</i> (2009)	
	Fenthion	Permethrin	Indonesia	Ahmad <i>et al.</i> (2007)
		Mexico	Garcia <i>et al.</i> (2009)	
		Malaysia	Rong <i>et al.</i> (2012)	
		Brazil	Lima <i>et al.</i> (2011)	
		French Guiana	Dusfour <i>et al.</i> (2011)	
		Africa	Constant <i>et al.</i> (2012)	
Carbamates	Amidocarb and propoxur	Thailand	Phanpoowong <i>et al.</i> (2012)	
		Malaysia	Rong <i>et al.</i> (2012)	

Furthermore, use of synthetic chemicals has also been limited because of their carcinogenicity, teratogenicity, residual toxicity, ability to create hormonal imbalance, spermatotoxicity, long degradation period and food residues (Khater, 2011). The toxicity of Temephos on non-targeted natural organism has been shown in many ecological systems, especially in aquatic ecology, which is the breeding habitat of many insect predators of *A. aegypti* larvae. In this study, the toxic effects of Temephos against *A. aegypti* larvae, under simulated daily water consumptions were observed (Uthai *et al.*, 2011).

Another disadvantage of using chemicals is that they kill natural enemies or beneficial predators that are helpful in vector control (Bommarco *et al.*, 2011). However, botanical insecticides are safe and desirable alternatives to chemical insecticides (Khater, 2012).

The application method of insecticides is also important. They can either be applied as non-residual application (effective over a short time-scale) or as a residual (persistent) application (effective over a period of weeks or months). The later application may kill even immature stages of development. Space spraying of insecticides is less effective as compared to treating water containers with insecticides which show better and long living effect (Lofgren *et al.*, 1970). The use of chemicals has reduced the number of dengue cases and deaths by 53% (Suaya *et al.*, 2007), but, the harmful effects of insecticide sprays on environment and natural ecosystem can never be ignored.

So, there is need to minimize the development of resistance and to study the mechanism of resistance development and to develop alternative or rotational use of insecticides to prolong their efficacy.

**Use of insect growth regulators:** Use of insect growth regulators (IGR) for controlling mosquito's population is also an effective method. IGR are chemical compounds that alter growth and development in insects. They interfere with the normal development resulting in insect's death before they reach their adult stage. Different new larvicidal IGR such as diflubenzuron, pyriproxyfen, methoprene and endotoxins obtained from *Bacillus sphaericus* and *Bacillus thuringiensis israelensis* are effective against *A. aegypti* (Grodner, 1997).

Kamal and Khater (2010) evaluated the biological effects of IGR, pyriproxyfen and diflubenzuron against larvae of the mosquito *A. aegypti*. Results revealed that larval treatment with these IGR caused the significant reduction in the reproductive potential of mosquito adults that emerged from these treatments. Pyriproxyfen caused a 33.2% decrease in egg production as compared to 25.5% for diflubenzuron. The reduction in egg hatchability was 40.6 and 36.2% for pyriproxyfen and diflubenzuron respectively.

IGR are divided into two general categories based on mode of action (a) Chitin synthesis inhibitors (b) substances which interfering with the action of insect hormones. Chitin synthesis inhibitors, triazine/pyrimidine derivatives, buprofezin and conventional benzoylureas, reduce the ability of insects to produce new exoskeletons at molting stage and block the synthesis of chitin. They also cause high egg mortality. Belinato *et al.* (2013) evaluated the effect of triflumuron, a chitin synthesis

inhibitor, against *A. aegypti*, *A. albopictus* and *Culex quinquefasciatus* under laboratory conditions and concluded that triflumuron was effective in emergence inhibition of *Cx. quinquefasciatus* and *A. albopictus*. Triflumuron was also effective against *A. aegypti*. Exposure of *A. aegypti* populations to the triflumuron (EI<sub>99</sub>) resulted in complete inhibition of adult emergence.

Growth and development of insects are regulated by hormones: prothoracicotropic hormones or brain hormone, ecdysteroids and juvenile hormones (Retnakaran *et al.*, 1995). The juvenile hormone analogues initiate the activity of naturally occurring juvenile hormone analogues and prevent metamorphosis to the adult stage. Application of juvenile hormone analogues to early instar larvae would result in the development of supernumerary instars, whereas treatment at the later stage would result in abnormal pupation and development of intermediates and larval-pupal mosaics (Khater, 2003).

**Biological control:** Biological control includes the utilization of natural resources, natural enemies and biological toxins to reduce dengue vectors (Lloyd, 2003). Biological control strategy is better than using chemicals because it has no bad effect and disturbance on ecosystem. This approach includes target killing of vector by using larvivorous fish, copepods and bacterial agents. Two bacteria *Bacillus thuringiensis* (Bti) and *Bacillus sphaericus* have proved effective for the control of dengue vector. Due to its high specificity, Bti has been found to be more effective against mosquitoes which breed in relatively unpolluted water such as *A. aegypti* species (Lacey and Undeen, 1986). Bti has been used as multipurpose agent for prevention of epidemics of DF.

Polanczyk *et al.* (2003) reported that entomopathogenic bacterium *Bacillus thuringiensis israelensis* can safely be used in water for controlling of *A. aegypti*. The use and potential of *Bacillus thuringiensis israelensis* against the mosquito vector is described. Emphasis is given on the importance of using this bacterium which could contribute significantly in solving the mosquito problem without affecting the environment, humans and other invertebrate organisms in critical regions.

In an epidemic situation, the use of ultra-low volume spraying of permethrin and microbial agent Bti has shown both larvicidal and adulticidal effects against *A. aegypti* (Tidwell *et al.*, 1994). Furthermore, world health organization has recommended that the use of Bti is safer for drinking-water treatment. Microbial larvicides used in drinking water and sensitive areas are not harmful to vertebrates as they do not persist or accumulate in environment and body tissues (WHO, 1999). Likewise, using larvivorous fish to overcome vector population has no harmful effect on drinking water and poses no threat to biodiversity of natural ecosystem. A successful trial has been made in Cambodia to check the effectiveness of introducing larvivorous guppy fish (*Poecilia reticulata*) into water storage containers. The trial was successful because household water containers, in which trial was done, showed a 79% reduction in *Aedes* index as compared to control houses (Seng, 2008).

A small crustacean such as *mesocyclops* if introduced in household water containers and tanks eats the newly hatched larvae of *A. Aegypti*. The use of copepod has been successfully used in Vietnam for the reduction of *A. aegypti* (walker, 2002). In Vietnam, the use of copepod *Mesocyclops* as a biological agent showed effective results in controlling dengue vector (Kay and Vu, 2005). This method has also been used successfully with community participation in Thailand where introduction of *Mesocyclops thermocyclopoides* in household containers controlled *A. aegypti* by eating its larvae (Kittayapong *et al.*, 2006).

In case of *A. aegypti*, the immature stages of the mosquito in household water containers provide a suitable target for the introduction of biological agents. But these agents should not be harmful, should be cheaper, their production should be easier on large scale and be culturally and socially acceptable to the target population. Important significance of biological control is that larvivorous fish, insects and copepods can be obtained from local resources and are inexpensive and can be maintained in households by short training (Kay *et al.*, 2002). Basic cause of failure in achieving success in biological control of vector emergence is failure in maintenance of larvivorous population during the period of controlling intervention.

**Use of photosensitizers:** There is need to develop new and ecologically safe technologies to control mosquito populations. In this regards, use of photosensitizers is also an alternative and safer strategy. Photosensitizers are activated by artificial light sources or by illumination with sunlight. The subsequent exposure of such insects to UV/visible light leads in inducing lethal photochemical reactions and death. The most popular and effective photosensitizers are porphyrins (e.g. hematoporphyrin) and xanthenes (e.g. phloxin B) which are known to have greatest photo-insecticidal activity. These compounds are non-toxic, non-mutagenic and have low impact on the environment (Ragaei and Khater, 2004; Lukšienė *et al.*, 2007; Awad *et al.*, 2008).

Lucantoni *et al.* (2011) reported that Photo-Mediated C14 meso-mono (N-tetradecylpyridyl) porphine molecule can be used as an excellent photolarvicidal agent against *A. aegypti*. This study suggests that photo-sensitizing agents can be used as an excellent alternative tool for the development of new larvicides against *A. aegypti*.

**Genetic modification of vector species:** Genetic modification of vector species is another option for their effective and long term control. Some researchers have practiced the genetic selection of vector strains that are unable to transmit disease (Collins *et al.*, 1986; Wu and Tesh, 1990). Advancement in molecular genetics has made it possible to build such genetic constructs that block and reduce the transmission of disease and pathogens (De Lara Capurro *et al.*, 2000; Ito *et al.*, 2002). Some technological challenges and gaps have remained in the completion of attaining these genetic modifications in a single vector population (Alphey *et al.*, 2002). An approach based on mosquitoes carrying a conditional dominant lethal gene is being developed to control the

transmission of dengue viruses by vector population suppression (Valdez *et al.*, 2011).

Transgenic organisms are genetically altered by artificial introduction of DNA from another organism and the artificial gene sequence is referred to as a transgene. Plants with such transgenes are called genetically modified crops that can be used for the control of mosquito population (Charles, 2001). There are many reports that demonstrate the negative impact of genetically modified crops on natural enemies which remains a controversial topic (Lövei *et al.*, 2009).

Another recent advancement in controlling dengue vector is the discovery of endosymbiotic bacterium *Wolbachia*, naturally present in insect populations, which can inhibit replication of the dengue virus in *A. aegypti* mosquitoes. So, there is need to introduce these strains of *Wolbachia* into wild populations of *A. aegypti*, potentially replacing field populations in a way that could reduce or even eliminate dengue transmission (Jeffery *et al.*, 2009).

**Use of pheromones:** Pheromones are defined as class of semi chemicals which are released by insects and other animals to communicate with other individuals of the same species. These are behavioral or signaling chemicals which play an essential role in arthropod life cycle. They provide the means whereby host and oviposition sites are located and recognized (Mordue Luntz, 2003). There are five principal uses for sex pheromones: population monitoring, mass trapping of insects, movement studies, detection of exotic pests and mating disruption. Due to some difficulties with high populations of insects, these programs should not be used alone in vector control program but it should be used as tactic within a suite of integrated insect management options (Welter *et al.*, 2005).

Cabrera and Jaffe (2007) has experimentally proved that both males and females produce an aggregation pheromones which attracts opposite sex towards the swarm and it modulates the lekking behavior among *Aedes* mosquitoes which can help to use it as an alternative strategy for its control. Pheromone programs can be helpful in detection of population density of *A. aegypti* mosquitoes at a particular region or area.

**Use of sterile insect technique:** Reproductive competition through sterile insect technique (SIT) could be an additional powerful tool to control populations of mosquitoes. Successive releases of sterile males are helpful in reducing the number of offspring in the following generations and may help in controlling the population density of mosquito species in urban areas where it threatens the health of human populations (Dumont and Chiroleu, 2010). In different experiments favorable results were obtained in terms of vector control using SIT. Induction of sterility through irradiation causes random dominant lethal mutations in the germinal cells resulting in the death of the developing embryos after fertilization (Helinski *et al.*, 2009). Oliva *et al.* (2012) reported that SIT offers a promising strategy for mosquito-borne diseases prevention and control. They studied the effect of irradiation on sexual maturation and mating success of males and concluded that sterile males could be sufficiently competitive to mate with wild

females and SIT can act as an important component for suppressing a wild population of *A. albopictus*. SIT can also be helpful in controlling *A. aegypti* population like that of *A. albopictus*.

**Use of nanotechnology and microemulsion:** In recent times, the advanced approach of nanotechnology and microemulsion could be the effective method for mosquito's control. Very fine droplets of size 1-100 nm in diameter are used for pest and insect control. Owolade *et al.* (2008) reported that nanoparticles could be used for the development of new insecticide. In this context, Salunkhe *et al.* (2011) studied the larvicidal activities of mycosynthesized silver nanoparticles against *A. aegypti* and *Anopheles stephensi*. Likewise, some other fungus mediated gold and silver nanoparticles have also been studied against *A. aegypti* larvae (Soni and Prakash, 2012). Silver nanoparticles showed high larvicidal activity as compared to gold nanoparticles which suggested that use of fungus (*Chrysosporium tropicum*) mediated silver and gold nanoparticles is a fast, environment friendly, and excellent approach for mosquito control. This could be a new alternative approach for control of *A. aegypti*.

Nanoemulsion is a transparent mixture of oil, surfactant and water with a very low viscosity, usually the product of its high water content. Wang *et al.* (2007) conducted first attempt for the development of preparation of water soluble oil emulsion for insect control.  $\beta$ -cypermethrin incorporated nanomulsion and oil loaded microcapsule have also been reported for controlling insects (Moretti *et al.*, 2002). Later on, Nuchuchua *et al.*

(2009) evaluated the repellent effect of nanoemulsion composed of citronella oil, hairy basil oil, and vetiver oil against *A. aegypti*. They reported that the use of 5% (w/w) hairy basil oil, 5% (w/w) vetiver oil (5%), and 10% (w/w) citronella oil could improve physical stability and prolong mosquito protection time for 4.7 hours due to the combination of these three essential oils as well as small droplet size of nanoemulsion.

**Use of botanicals:** Scientists have proved that the phytochemicals obtained from different plants have ovicidal, larvicidal, adulticidal and repellent effects against *A. aegypti*. The use of botanicals in control of dengue is very effective and useful method and considerable work has been done in this field (for detail see Table 2).

The use of insect repellent compounds dates back to ancient times as plant oils, smokes and tars were used to repel or kill insects. The use of repellents by travelers may reduce the incidence of disease from local to temperate areas. DEET (N,N-diethyl-m-toluamide) is a broad spectrum and most efficient mosquito repellent being used on skin, but unfortunately, this may cause environmental and human health risks (Pitasawat *et al.*, 2003). However, plant-based repellents are efficient and better than synthetic repellents. Nerio *et al.* (2010) reviewed some useful ideas for improvement of repellency of essential oils. A large number of essential oils producing plants have been extensively studied such as *Cymbopogon* spp, *Eucalyptus* spp, *Ocimum* spp, the Osage orange (*Maclura pomifera*) and catnip (*Nepeta*

**Table 2:** Plants reported for their insecticidal, growth inhibition and repellent activity against *Aedes aegypti* (1990-2013)

Plants Scientific Names	Plants English Names	Type of Activity	References
<i>Tagetes minuta</i>	Southern Cone Marigold	Larvicidal	Green <i>et al.</i> (1991)
<i>Tagetes erecta</i>	Mexican Marigold	Larvicidal	Perich <i>et al.</i> (1994)
<i>Lantana camara</i>	Spanish Flag	Repellent	Dua <i>et al.</i> (1996)
<i>Mentha piperita</i>	Peppermint	Larvicidal and Repellent	Ansari <i>et al.</i> (1999)
<i>Azadirachta indica</i>	Neem	Anti-pupational and Repellent	Nagpal <i>et al.</i> (2001)
		Larvicidal and Repellent	Kumar <i>et al.</i> (2011)
<i>Ocimum sanctum</i>	Holy Basil	Larvicidal	Pathak <i>et al.</i> (2000)
<i>Ferronia elephantum</i>	Bela	Repellent	Venkatachalam (2001)
<i>Solanum nigrum</i>	Black Nightshade	Larvicidal	Singh <i>et al.</i> (2001)
<i>Poncirus trifoliata</i>	Trifoliolate Orange	Larvicidal and ovicidal	Cheng <i>et al.</i> (2004)
<i>Malus domestica</i>	Apple	Antiviral and Antioxidant	Boyer and Liu (2004)
<i>Fagonia indica</i>	Fagonia	Larvicidal	Chaubal <i>et al.</i> (2005)
<i>Arachis hypogaea</i>	Groundnut	Larvicidal	Chaubal <i>et al.</i> (2005)
<i>Sterculia guttata</i>	Spotted Sterculia	Larvicidal	Katade <i>et al.</i> (2006)
<i>Balanites aegyptiaca</i>	Soap Berry	Larvicidal	Wiesman <i>et al.</i> (2006)
<i>Spilanthes acmella</i>	Toothache plant	Larvicidal	Pandey <i>et al.</i> (2007)
<i>Spilanthes paniculata</i>	Toothache plant	Larvicidal	Pandey <i>et al.</i> (2007)
<i>Solanum xanthocarpum</i>	Sun Berry	Larvicidal	Mohan <i>et al.</i> (2007)
<i>Syzygium cumini</i>	Jambul	Larvicidal	Kumar <i>et al.</i> (2007)
<i>Piper cubeba</i>	Tailed Pepper	Larvicidal	Murthy and Rani (2009)
<i>Syzygium cumini</i>	Jambul	Larvicidal	Murthy and Rani (2009)
<i>Cassia fistula</i>	Golden Shower tree	Larvicidal and Ovicidal	Govindarajan (2009)
<i>Citrus lemon</i>	Lemon	Antiviral and Immunoregulatory	Akhila <i>et al.</i> (2009)
<i>Carica papaya</i>	Papaw	Antiviral and Immunoregulatory	Lee <i>et al.</i> (2010)
<i>Eclipta alba</i>	False Daisy	Larvicidal and Ovicidal	Govindarajan and Karupannan (2011)
<i>Eucalyptus sp.</i>	Black Gum	Repellent	Mandal (2012)
<i>Piper nigrum</i>	Black Pepper	Larvicidal	Grzybowski <i>et al.</i> (2012)
<i>Annona muricata</i>	Brazilian Pawpaw	Larvicidal	Grzybowski <i>et al.</i> (2012)
<i>Calotropis procera</i>	Sodom Apple	Larvicidal	Bansal <i>et al.</i> (2012)
<i>Tephrosia purpurea</i>	Fish Poison	Larvicidal	Bansal <i>et al.</i> (2012)
<i>Prosopis juliflora</i>	Honey Mesquite	Larvicidal	Bansal <i>et al.</i> (2012)
<i>Curcuma longa</i>	Turmeric	Larvicidal and anti-pupational	Kalaivani and Nathan (2012)
<i>Zingiber officinale</i>	Ginger	Larvicidal and anti-pupational	Kalaivani and Nathan (2012)
<i>Caulerpa racemosa</i>	Sea Grapes	Larvicidal	Ali <i>et al.</i> (2013)

*cataria*). Many plants oils and their constituents have been commercialized as insect repellents in last ten years, such as soybean, lemon grass, cinnamon and citronella oil from *Azadirachta indica* when formulated as 2% in coconut oil, showed excellent repelling effects by providing complete protection for 12 hours from mosquitoes (Sharma, 1993).

A number of essential oils of plant origin have larvicidal effect along with reducing the development of insects, suppressing adult's emergence and also cause abnormalities during the development of insects (Shalaby and Khater, 2005; Khater and Shalaby, 2008; Khater and Khater, 2009; Khater *et al.*, 2011).

**Mode of action of plants and essential oils:** Aromatic plants contain many compounds that can act as ovicides, larvicides, adulticides and also produce repellent effects against insects. They have capacity to change insect feeding behavior, growth rate, molting and effect behavior during mating and oviposition. Essential oils obtained from plants are lipophilic in nature and interfere with basic metabolic, biochemical, physiological and behavioral functions of insects. The rapid action against some insects is indicative of a neurotoxic mode of action, and there is evidence for interference with the neuromodulator octopamine or GABA-gated chloride channels (Enan, 2005).

Several essential oil compounds have been demonstrated to act on octopaminergic system of insects. Octopamine is circulating neurohormone - neuromodulator (Hollingsworth *et al.*, 1984) and its disruption results in complete breakdown of nervous system in insects. Plant volatile oils have long been known to affect the behavioral responses of pests, with the monoterpeneoid components proved to be most effective to be used as insecticides or antifeedants (Palevitch and Craker, 1994).

Different botanicals have different mode of action in controlling insect population and have been found to be effective against *A. aegypti*. For example *Azadirachta indica* (neem) contains azadirachtin (C<sub>35</sub>H<sub>44</sub>O<sub>16</sub>), a nortriterpenoid molecule which is the most active constituent of neem, have various effects against insects. The effects of azadirachtin on insects include feeding and oviposition deterrence, growth inhibition, and fecundity and fitness reductions (Schmutterer, 1990). This substance interferes with synthesis of the insect molting hormone and has significant effect on insect behavior. It also leads to sterility in female insects due to its adverse effects on ovarian development, fecundity and fertility (Isman and Akhtar, 2007). *Azadirachta indica* has been found to have anti-pupational and repellent effects against *A. aegypti* (Nagpal *et al.*, 2001). Likewise, different plants contain different active constituents that have different mode of action against *A. aegypti*.

**Conclusion:** Dengue Fever has now become a major global threat. To protect human life and prevent further epidemics of dengue, we need to translate our understanding and thinking to use our socio-ecological and biological systems in an effective way. Due to unavailability of vaccine in near future, we should depend on the interventions that are currently available. Use of different botanicals as mentioned in this paper has been proved to be effective and safer for the control of DF. So,

we need to develop phytochemicals having long lasting effects against dengue vector and less harmful effects on environment as compared to synthetic chemicals. We need to adopt advanced techniques for vector control such as application of nanotechnology and microemulsion; use of photosensitizers and insect sterility technique can give excellent and sustainable effects.

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