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Effective Management of *Aedes aegypti* Linn. (Diptera: Culicidae) Population through Conventional to Genetic Control and Nanotechnology Approaches: A Short Review

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Abstract

There are many vector–borne illnesses known to be spread by the mosquito *Aedes aegypti* Linn. (Diptera: Culicidae), which kills millions of people each year worldwide. There is no vaccination available for *A. aegypti*–transmitted viral diseases so far. As a result, it is imperative to control the mosquitoes or vector population which may helpful to avoid the dispersal and causes of certain diseases. The most common and conventional mechanism to control mosquitoes population are physical, biological, and chemical control measures that have all been used to prevent *Aedes* species borne disease spreading. Among these the most effective method is chemical control method but it results into the environmental pollution and causes damage to non–target individuals as well. A manipulation through self–limiting using genetic engineering among mosquitoes is an effective substitute to one sex for the control of insect pests. Using the modern concept of gene manipulation, the lethal gene through an antidote (tetracycline) was repressed among male mosquitos *in vitro* and subsequently released in the natural environment to mate with normal female and give rise filial generation which will die during larval stage due to lack of tetracycline. The most profound and recent use of nanotechnology to generate more effective and less dangerous repellent and larvicidal compositions is another strategy under investigation. The development of novel nanotechnology–based formulations for containing natural and synthetic repellents is an important step toward more effective systems with fewer adverse side effects.

Keywords: Mosquito, *Aedes aegypti*, Biological control, Genetic control, Nanotechnology, Mosquito–borne diseases

1. Introduction

There are several vector–borne illnesses have emerged in recent decades as a result of climate change, population explosion, deforestation, urbanisation, and pesticide resistance. Many of them are spread by the mosquitoes *Aedes aegypti* (Diptera: Culicidae), which causes yellow fever, dengue fever, Zika, chikungunya, encephalitides, lymphatic filariasis and other diseases that afflict hundreds of millions of people each year [1–2]. Since 1940, the vaccine for yellow fever is available [3]. However, there is no vaccine available to protect against viral infections spread by *A. aegypti* so far. As a result, the only way to avoid these main illnesses is to limit the vector population, i.e. mosquitoes, through the use of chemical pesticides, biological control, etc. to target both adults and larvae [4–5]. But the use of pesticides may affect other lives adversely leading to imbalance in the ecosystem. Therefore, it is imperative to target those novel and effective chemicals that are larvacidal in nature and readily degradable, environment friendly, easy to get, safe and low–cost products with no adverse effect on the non–targeted populations [6]. The larvicidal compounds taken in consideration must be able to be utilised in both natural and man–made bodies of water, be non–toxic to non–targeted aquatic species, and be potentially connected to these water reservoirs [7]. The green synthesis of silver nanoparticles (Ag–NPs) utilising plant extracts as reducing, stabilising, and capping agents is an interesting alternative to the exclusively botanic larvicidal [8]. Due to the low toxicity, minimal environmental pollution, and no damage to non–targeted species, these larvicidal produced from plant extracts are a promising category of pesticides [9]. Plant–mediated silver nanoparticles (Ag–NPs) combine the microbicide properties of silver with the insecticidal activity of selected plants, resulting to increased efficiency at the nano scale (1–100nm) due to the high surface area to volume ratio (a/v) of nanoparticles. These characteristics allow Ag–NPs to achieve their insecticide effect at very low concentrations and found to be very effective against vector larvae [10–11]. Therefore, the present review was designed to address a complete knowledge about the control of *Aedes aegypti* (vector and source of different life threatening diseases in human) through different conventional approaches, modern genetic control method and most recent nanotechnological applications.

2. Methods to Control Vectors

2.1 Chemical control

DDT (dichlorodiphenyltrichloroethane) was the most widely used manmade organic pesticide in the twentieth century for active malaria control and lowering the life span of gravid female mosquitoes. Larvicides are pesticides that are put directly into water to reduce the quantity of larvae. Adulticides and synergists are used to suppress adult mosquito populations by concealing and spraying adult mosquitos. Adulticides and larvicides, as well as ovicidal qualities provided by several insect development regulators such as pyriproxyfen, diflubenzuron and methoprene are the most efficient substances utilised globally in mosquito control tactics as larvicides and adulticides [12]. The use of treated nets or diffusion stations formed from modified ovitraps is a novel method of dispersing pesticides (pyriproxyfen). In *Aedes aegypti* and *A.s albopictus* pupae, the technique resulted in significant fatality rates. Secondary metabolites (alkaloids, sterols, phenols, terpenes, slavanoids, carotenoids, and other substances) defend plants against microbiological parasites and arthropods including *Aedes aegypti*, *Culex quinquefasciatus*, *Anopheles gambiae*, and *Calocedrus decurrens* [10].

2.2 Biological control

Due to their role in increasing vertebrate safety and lowering environmental impact, bio–pesticides have received a lot of attention in recent years as an effective mosquito control method. Bacteria, fungus, viruses, protozoa, and fish have all been identified as possible bio–pesticides for mosquito control. Both binary toxins (Bin) including BinA (42 kDa) and BinB (51 kDa) are insecticidal proteins identified in *Bacillus sphaericus* (Bs) bacterium that are particularly dangerous to mosquitoes. BinA Recombinant bacteria carrying these toxins separately showed that BinA is extremely harmful at high doses in the absence of BinB, but BinB alone is not toxic. After eating btx (factor in a highly toxic strain of *B. sphaericus)*; the BinA and BinB is solubilise in the midgut of mosquito larvae, where proteases transform them into 39 kDa and 43 kDa proteins, respectively. After processing, btx–active proteins connect to receptors on the brush border membrane of the midgut, where they are ingested, causing cell lysis and, eventually, midgut lysis and inflammation, which leads to the insect's death [13]. The Cyt (cytolysins) and Cry (crystal delta–endotoxins), two insecticidal protein families discovered in Bti (*Bacillus thuringiensis* subspecies *israelensis*) bacteria, have also been shown to be effective in mosquito control [14]. The Cry proteins attach to particular receptors on the insect's midgut epithelium, while Cyt proteins do not. After Bti crystals are consumed, proteases break them down into little particles. By disturbing the osmotic equilibrium of epithelial cells and causing holes in the membrane, the activated fragments cause cell death [15].

2.3 Mechanical control (trapping)

In mass trapping, odour is commonly used to attract mosquitos. Gravid females are captured using *Aedes* traps such as sticky/gravid traps or ovitraps. Females on the search for an area to deposit their eggs are captured using bio–agent–sentinel traps. *Aedes* mosquitoes lay their eggs in small containers. The uses of a larvicide or an autocidal allow the ovitraps to be used indefinitely with just a slight risk of becoming a main source of adult mosquitoes. The insecticide–treated egg–laying strips may also being employed [16]. Organic infusions (hay, grass, and oak) might be utilised to make ovitraps more attractive. Researchers developed a massive autocidal gravid trap that produces water vapours and other volatile attractants at a faster rate in order to maximise mosquito capture [17]. When paired with certain appealing incentives, push–pull strategies are an excellent mosquito control strategy. By using insecticide–treated goods or indoor residual spraying, it makes use of pesticides' spatial repellent and contact discomfort. Other types of traps used to manage several mosquitos' species include host seeking traps, light traps, bed net traps, sentinel traps, entry and exit traps, capture–kill traps, and chemical–based traps. Centers for Disease Control and Prevention (CDC) has informed that light traps (CO_2 from dry ice) catch 400–500% more mosquitos in a same way [18–19].

2.4 Environmental control

One method of source reduction is to prevent *Aedes* spp. (mosquitos) from utilising possible breeding places. The removal of temporary water tanks and the closure of permanent water reservoirs are the cornerstones of this plan. Mosquitoes are attracted to small and medium–sized fake water containers and tyres placed in or near homes, and this is often the first line of defence against them. Source reduction impacts the spread of local mosquitoes by diminishing existing oviposition locations [20–21]. In Brazil, a source reduction drive against *A. aegypti* was initiated, with nylon netting used to cover up the most productive breeding sites, such as water tanks and metal barrels, leading to a long decrease in female mosquito populations, proving the effectiveness of targeting on preferred breeding sites. Unfortunately, this technique fails to locate cryptic productive sites like natural ponds and leaf litter, which are typically hidden or inaccessible [22].

2.5 Genetic control

A self–limiting gene has been introduced into mosquito populations using genetic engineering as an alternative to sterilising males for insect population control [23]. The British biotech company Oxitec coined the term RIDL i.e. "*Release of Insects Carrying a Dominant Lethal Gene*" (www.oxitec.com). If the lethal gene is repressed with an antidote (tetracycline), mosquitos can be grown to adult in breeding sites before being released into the wild as males, who then mate with wild females and produce progeny that die at the larval stage if tetracycline is not present. In field trials in the Cayman Islands in 2009–2010, a self–limiting strain of *A. aegypti* OX513A was demonstrated to decrease a natural population of *A. aegypti* [24]. In Malaysia OX513A males were found to have similar lifespans and spreading abilities, whereas the most recent release of OX513A males in Brazil resulted in a significant decline of the target wild population [25–26]. Trials in Brazil were also used to develop LA513A, a strain of *A. aegypti* engineered to carry a non–sex–specific, dominant, repressible, late–acting lethal genetic system that causes death at the pupal stage rather than the larval stage, avoiding density–dependent effects on larval development in wild populations [27]. In the absence of tetracycline, larvae with one or more copies of the LA513A insertion grow properly, although the great majority (95–97%) die during pupal stage [27].

2.6 Role of nanotechnology in detection and control the vector

The nanotechnology based formulations release active substances into the environment in a regulated or delayed manner, extending the period of effect and minimising human exposure (for example, by permeation through the skin). The chemical component is additionally protected by encapsulation against damage due by temperature, oxidation, light, and humidity, among other things [28]. For the development of nanocarriers, a variety of matrices (both synthetic and natural) can be employed, including proteins, polymers, polysaccharides, lipids, and others. The most desired properties of such matrices are biodegradability and biocompatibility, as well as low cost [29]. Gomes *et al*. successfully enclosed DEET (N,N′–diethyl–m–toluamide) in polymeric nanospheres, resulting in particles with an average diameter of 114±37 nm, a low polydispersion index, and time–dependent stability [30]. The repellence potential of nano–encapsulated DEET lasted more than 9 hours that is far longer than that of free DEET. The scientists noted the discovery that the release mechanism was temperature sensitive as a key benefit since the release rate could be controlled by changing the temperature [30]. Silva *et al*. encapsulated essential oils of *Piper aduncum* L. and *P. hispidinervum* C. in gelatin nanoparticles and investigated their efficiency against *A. aegypti* Linn. According to the findings, the EOs exhibited a high encapsulation efficacy (about 80%), an average size of 100–200 nm, and a zeta potential of around 40 mV. Both encapsulated EOs reached deadly dosages within 24 hours of exposure, resulting in the pests' ultimate death [31].

Forgearin *et al*. designed, characterised and tested permethrin–loaded lipid nanocapsules as clothing repellents. The formulations had a monomodal size distribution and a permethrin concentration of 4.6±0.1 mg/mL, with a mean particle diameter of 201±4 nm. Even after washing and with the influence of temperature, the polyester fabrics containing the nanoparticles had higher permethrin concentrations than those carrying only the free component. According to the findings, the revolutionary nanoparticle repellent spray might be used to impregnate clothing and protect humans from insects [32].

Werdin González *et al*. designed and investigated polymeric nanoparticles for encapsulating essential oils like geranium (*Geranium* sp.) and bergamot (*Citrus bergamia*) which is made up of PEG (Polyethylene glycol) and chitosan (PEG–chitosan NPs) [33]. The immediate and long–term larvicidal effects of the chemical in mosquitoes were investigated as well. According to physicochemical characterization, the PEG nanoparticles containing the essential oils had a mean size of 255 nm and encapsulation efficiencies of 68–77%, whereas the chitosan nanoparticles had a mean size of 535 nm and encapsulation efficiencies of 22–38%. The formulations based on chitosan demonstrated the best larvicidal activity (acute and residual). These findings suggest that polymeric nanoparticles containing essential oils might be employed as larvicidal therapies that are both environmentally friendly and effective [34]. The spherical, monodispersed essential oils in gelatin nanoparticles with 100 nm in size range showed better than 80% encapsulation efficiency to kill *A. aegypti* within 24 hours of exposure, with fatality rates beyond 80% [31]. The nanoparticle based methodologies have been highlighted in Fig.1.

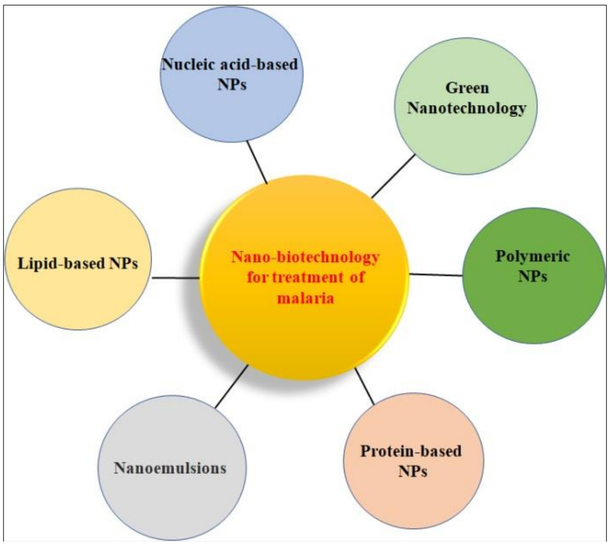

Fig 1: Effects of various nanocarrier system for the treatment of malaria vector.

3. **Conclusions**

During the control of mosquitoes, the DDT, a man-made organic insecticide was utilised, that shortens mosquito lifespan. The larvicides are sprayed directly into water to control the population of vector by killing larvae or by reducing life span of adults. Bio–pesticides are very effective by causing puncture in cell membrane leads to death of mosquitoes, as well as they are environment friendly and nontoxic to non–targeted species. Trapping is also done to catch the female vector population and their eggs to control the adult population. The CDC light traps are most effective among different traps as that catches 400–500% more vector population in the same way. The easiest way to control *Aedes* population is removing of temporary water tanks that become the breeding place for mosquitos. Sterilising of male done by genetic manipulation in insect population is a new and effective mechanism of mosquitos' control. Most recently, the nanotechnology is found to be the best way in detection and control of vector with undesirable side effects. Nanoparticles are used with some plant extract or some other material for the development of novel pesticides. Pesticides associated with AgNPs are reported which are very effective to control the vector population. These are environmental friendly but very toxic to only targeted species and is nontoxic to non–targeted species. This shows potentials of nanoparticles for use as part of integrated approach towards the fight against mosquito vectors.

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