

Nano-revolution in Vector-Borne disease management: Exploring control strategies and mechanisms

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Abstract

Vector-borne diseases (VBDs) are complex socio-ecological systems that have an impact on many facets of our planet and go well beyond human health. Even though previous study has focused on the direct consequences of vector-borne illnesses on human health and death, it is evident that these diseases are part of a complex web of interactions. The environment, ecology, diseases, and societal reactions are closely associated with vector-borne diseases, resulting in feedback loops that facilitate the spread of disease. As a result, they have permanently altered the course of human history. The application of nanoparticles produced by various processes as novel insecticides has attracted a lot of interest. Silver nanoparticles plays a crucial role along with gold, zinc oxide and other nanoparticles in the control of (VBDs). Many research have examined the toxic effect against a variety of pests and insect vectors, with a focus on mosquitoes. Using nanoparticles as cutting-edge insecticides is a promising line of inquiry in the battle against VBDs. This review encompasses around the various nanoparticles (NP's) and their mode of action and various control strategies against vectors.

Keywords: Vector borne diseases (VBDs), Nanoparticles (NP's), Silver nanoparticles, mode of action, control strategies

Introduction

A rise in human mobility, globalization, and climate change has resulted in the ecological spread of highly invasive species. These invading species, which include arthropods, can produce fatal diseases that spread like epidemics or pandemics. The most significant in that respect are mosquitoes (Diptera: Culicidae), which serve as carriers of numerous dangerous parasites and infections. The most dangerous of these are the genera *Anopheles*, *Aedes*, and *Culex*, which are the carriers of the most significant infections and are responsible for diseases like Dengue, malaria, yellow fever, filariasis, Japanese encephalitis, and Zika [1]. In the past and present, vector-borne diseases (VBDs) like malaria, dengue, Zika, Chikungunya, and Japanese encephalitis have had a significant global impact on public health. Although many illnesses cannot spread directly from person to person, they can spread when circumstances allow germs, hosts, and the environment to interact. The threat posed by insect-borne diseases to human health has grown in recent years due to changes in social and environmental conditions, including global climate change and international trade, which have led to the reproduction and spread of these diseases. In 2020, there were an anticipated 241 million malaria cases and 627,000 malaria deaths globally, according to WHO's most recent World Malaria Report. This translates to roughly 69,000 extra deaths and 14 million more illnesses in 2020 compared to 2019. In addition, dengue was endemic in Pakistan during September 2019 to November 2021, with 102,404 cases recorded, including 278 deaths (case fatality ratio, or CFR): 0.27%). Thus, we must address the key VBDs that are emerging and reemerging as well as the difficulties in controlling them. In this review, three main categories of nanoparticles (NPs) were discussed. (Fig 1). Type 2 NPs are nonmetal-based (like Si and Ca), Type 3 NPs are some complex polymers (like chitosan and plant extract), and

Type 1 NPs are metal-based (like Ag, Cu, and Ti), which are the most commonly employed to repel insects. Due to its significant effect on insect antioxidant and detoxifying enzymes, which results in ROS-mediated apoptosis, DNA damage, and autophagy, Ag has the highest proportion among Type 1 reagents. For Type 1, this is how most metals function. But Type 2's primary insecticidal principle is different; for instance, desiccation, abrasion of the body wall, and obstruction of the spiracles are the reasons for SiO₂ NPs' toxicity. Furthermore, the various functions of nanoparticles used as pesticides can be used to classify them. Metal-based NPs are most frequently used in Type 1, which primarily consists of NPs for direct use as insecticides. When it comes to Type 2, NPs operate as carriers for the active substances that suppress insects [2].

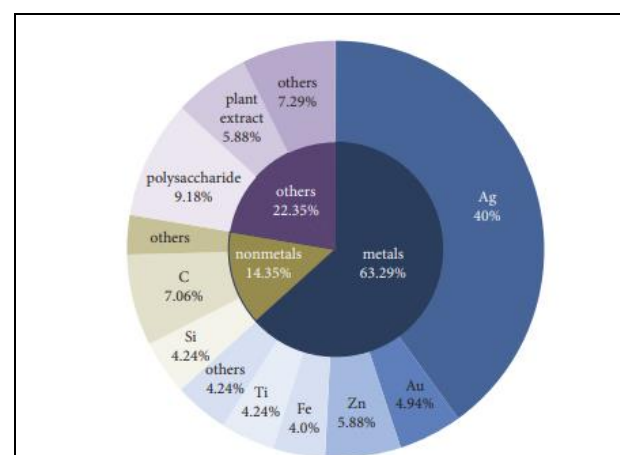


Fig 1: Classification of NP's. Based on various attributes, NPs used as insect repellent can be broadly categorized into three groups. Of them, nonmetal-based NPs like Si- and C-based make up just 14.35%, while metal-based NPs make up the largest percentage at 63.29% [2].

When vector-borne illness epidemics occur in poor nations, controlling mosquito populations is a major problem. Commonly used substances for controlling mosquitoes in both their immature (egg, larva, and pupa) and mature stages are synthetic (chemical) pesticides. Side effects on non-target populations (particularly people), adverse effects on the environment (contaminating soil, water, and air), and the emergence of resistance have all significantly increased in recent years. Moreover, applying synthetic repellents on exposed skin to ward against mosquito bites is a popular strategy to lessen mosquito-borne illness transmission and annoyance. Concerns exist, nevertheless, regarding their safety and toxicity. Because of these restrictions, scientists have had to create novel substances to repel mosquitoes and stop mosquito bites [3].

Techniques for vector control

1. Chemical regulation

The most popular synthetic pesticide of the 20th century for controlling malaria and shortening the life of gravid female mosquitoes was DDT (dichlorodiphenyltrichloroethane). Pesticides known as larvicides are poured directly into water to minimize the number of larvae. By hiding and spraying adult mosquitoes, adulticides and synergists are used to reduce adult mosquito populations. Larvicides and adulticides are the most effective compounds used worldwide in mosquito control strategies, along with the ovicidal properties offered by numerous insect development regulators like pyriproxyfen, diflubenzuron, and Methoprene [4].

2. Bioregulation

Bio-pesticides have gained a lot of attention recently as an efficient mosquito control technique because of their

involvement in enhancing vertebrate safety and reducing environmental impact. Fish, fungi, viruses, bacteria, and protozoa have all been discovered as potential biopesticides for controlling mosquitoes [4].

3. Mechanical control (trapping): Odor is frequently employed in mass trapping to draw mosquitoes. *Aedes* traps, such as ovitraps or sticky/gravid traps, are used to catch gravid females. Bio-agent sentinel traps are used to catch females who are looking for a place to lay their eggs. The eggs of *Aedes* mosquitoes are laid in tiny containers. With only a little chance of turning into a major supply of adult mosquitoes, ovitraps can be used perpetually when combined with a larvicide or autocidal. Egg-laying strips coated with pesticide may also be used. It is possible to use organic infusions (hay, grass, and oak) to enhance the appeal of ovitraps [4].

The function of nanotechnology in vector detection and control

The formulations based on nanotechnology release active ingredients into the environment in a controlled or delayed manner, minimizing human exposure and prolonging the duration of impact (for instance, through skin penetration). Encapsulation provides further protection for the chemical component against various environmental factors such as temperature, oxidation, light, and humidity. A wide range of matrices, both natural and synthetic, including proteins, polymers, polysaccharides, lipids, and others, can be used to create nanocarriers. The most sought characteristics of these matrices are their low cost, biodegradability, and biocompatibility [4].

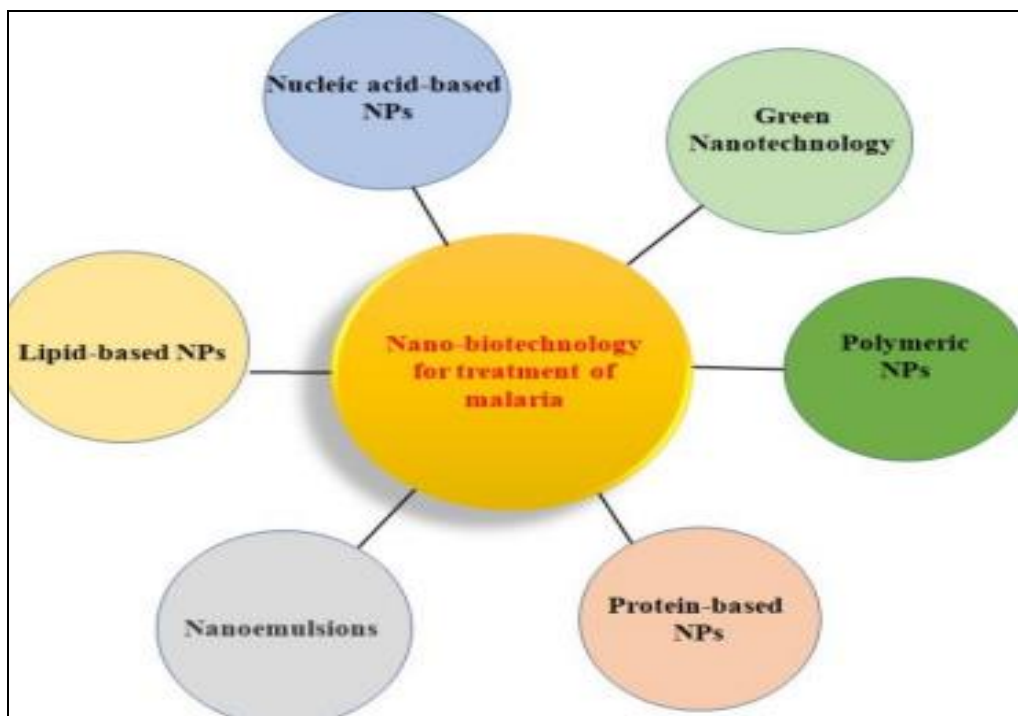


Fig 2: Different nanocarrier systems for treating malaria vectors [4].

Metallic nanoparticles

There are two methods for producing metallic nanoparticles: top-down and bottom-up. Top-down techniques involve use

physical or chemical ways to reduce a starting material from a macroscale to a nanoscale. Conversely, in bottom-up approaches, the nanoparticles are created atom by atom

starting at the atomic level. The environmentally friendly, non-toxic, and clean synthesis of metallic nanoparticles by green synthesis could be a dependable method for producing nanoparticles. This tactic is regarded as the insecticidal activity's next-generation instrument. The application of nanoparticles as innovative insecticides has garnered attention, and there have been a number of recent research looking into the use of nanoparticles against insects [5].

Organic nanoparticles

Organic nanoparticles are systems for material encapsulation that have applications in food, medicine, and cosmetics. Similar to metallic nanoparticles, several forms of organic nanoparticles can be produced via top-down and bottom-up methods. These include nanoemulsions (NE), nanocapsules, liposomes, dendrimers, micelles, and niosomes. The primary nanostructures utilized in organic nanoparticles are nanoemulsions [5].

Mode of action of nanoparticles on *Aedes Aegypti* Larvae

Since plants contain a diverse variety of active compounds, it is possible to investigate different modes of action on the insect larval stage. The denature of essential proteins, increased permeability of the cuticular membrane leading to the loss of liquid and intracellular components, inhibition of enzymes, and destruction of the cell membrane are the most commonly proposed mechanisms. It is also possible that interactions between oil components result in synergism or antagonistic effects, which prevent the larvae from progressing to the next stage of pupal development and formation. Additionally, the size of the nanoscale particles and a slower, longer release of active chemicals from the nanostructure particle have been linked to the larvicidal activity. Additionally, exposure to nanoparticles can have a variety of effects in insects, including genotoxicity, changes in metabolic pathways, affects on the midgut, and exterior damage to the cuticula (Fig 3) [5].

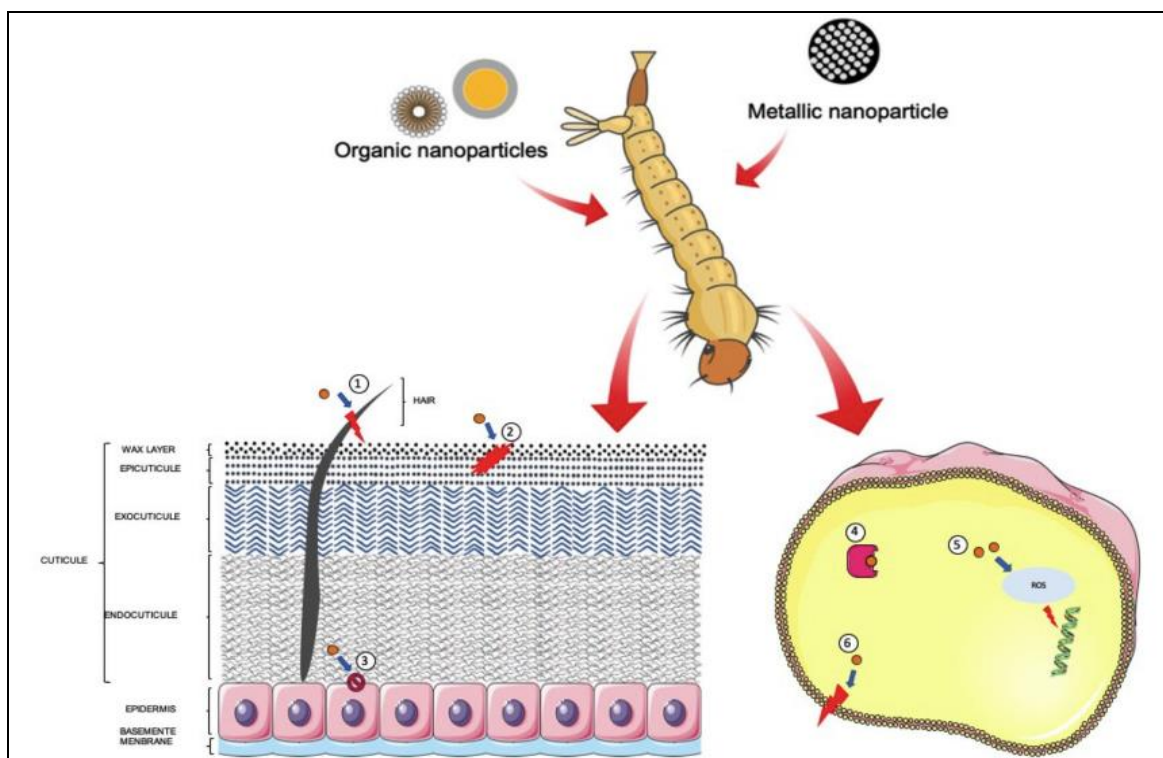


Fig 3: An illustration of how nanoparticles affect *A. aegypti* larvae. 1. Hair damage. 2. Damage to the cuticles. 3. The epidermis is disturbed. 4. Inhibition by enzymes. 5. Production of ROS, or reactive oxygen species. 6. The cell membrane being disrupted [5].

An overview of the various plant-derived nanoparticle types

This Special issue discusses and publishes the synthesis, characterization, and uses of several plant-derived nanoparticles kinds. One of the simplest to make types of silver nanoparticles are plant-based ones (AgNPs). A reducing biological agent and a silver metal ion solution are needed for the environmentally friendly synthesis of silver nanoparticles. Reducing and stabilizing Ag ions with a combination of biomolecules, such as polysaccharides, vitamins, amino acids, proteins, phenolics, saponins, alkaloids, and/or terpenes, is the simplest and least expensive way to produce AgNPs. It is possible to use almost any plant to prepare AgNPs. Due to their simple synthesis, easy surface functionalization, and special qualities—such as their high potential for application in medicine, low toxicity, and extremely biocompatible

nature—gold nanoparticles, or AuNPs, have drawn a lot of attention. When gold nanoparticles are produced, different chemical moieties in biogenic complexes function as reducing agents, which lowers gold metal ions and causes nanoparticle formation. Due to its many potential uses in biomedicine, cosmetics, electronics, and optics, zinc oxide nanoparticles, or ZnONPs, have drawn a lot of attention in recent years. Numerous studies on the production and application of ZnONPs by microbes, plants, and other species have been published to far. Their easy, safe, and inexpensive synthesis has sparked attention in numerous investigations. A wide range of plant parts, including as flowers, roots, seeds, and leaves, can be used to make ZnONPs. Copper (Cu) is a relatively inexpensive metal that is more economical than Au and Ag. CuNPs are produced by reducing aqueous Cu ions using various plant extracts [6].

Table 1: Various nanoparticle forms and how they affect different species of mosquitoes [2].

Nanoparticles	Source	Target's species	Lethal indices (LC ₅₀)
Ag	<i>Bacillus marisflavi</i> [53]	<i>Ae. aegypti</i>	13.96 ppm
Ag		<i>Cx. quinquefasciatus</i>	24.54 ppm
Ag		<i>An. stephensi</i>	29.14 ppm
Ag	<i>Ipomoea batatas</i> [54]	<i>Ae. aegypti</i>	17.578 µg/mL
Ag		<i>Cx. quinquefasciatus</i>	10.069 µg/mL
Ag		<i>An. stephensi</i>	12.568 µg/mL
Ag	<i>Cassia roxburghii</i> [55]	<i>Ae. aegypti</i>	26.35 µg/mL
Ag		<i>Cx. quinquefasciatus</i>	28.67 µg/mL
Ag		<i>An. stephensi</i>	31.27 µg/mL
Au	<i>Parmelia sulcata</i> [56]	<i>Ae. aegypti</i>	70.16 ppm
ZnO	<i>Cucurbita</i> [57]	<i>Cx. tritaeniorhynchus</i>	39.007 ppm
ZnO	Chemical method [58]	<i>Cx. quinquefasciatus</i>	291.0 mg/L
ZnO	<i>Pseudomonas aeruginosa</i> [59]	<i>Culex pipiens</i>	75 ppm
ZnO	<i>Cucurbita</i> [59]	<i>Cx. tritaeniorhynchus</i>	44.68 ppm
MgO	<i>Penicillium chrysogenum</i> [60]	<i>An. stephensi</i>	12.5–15.5 ppm
MgO	Chemical method [58]	<i>Cx. quinquefasciatus</i>	83.4 mg/L
CuO	Chemical method [58]	<i>Cx. quinquefasciatus</i>	100.8 mg/L
CuO	<i>Tridax procumbens</i> [61]	<i>Ae. aegypti</i>	4.209 mg/L
SiO ₂	Chemical method [58]	<i>Cx. quinquefasciatus</i>	27.81 mg/L
Se	<i>Nilgiranthus ciliatus</i> [62]	<i>Ae. aegypti</i>	0.92 mg/L

Future perspectives

The current analysis shows that there is a large vacuum in the literature on nanoparticle toxicity against veterinary, medicinal, and agricultural arthropods. Research organizations worldwide are showing a great deal of interest in the possibility of environmentally friendly nanoparticle production technologies, which could lead to new approaches for the management of arthropod pests and vectors. However, our understanding in this field of study is still limited, even with the diligent efforts of some researchers to elucidate the mechanisms by which silica, alumina, silver, gold, titania, and graphene nanoparticles produce toxicity in arthropods. Additionally, more research is required to understand the mechanisms underlying the toxicity of copper, iron, and chitosan nanoparticles, three significant nanomaterial classes employed in parasitological and entomological studies.

Conclusion

The research on vector-borne diseases (VBDs) has advanced considerably throughout time, moving beyond the limited emphasis on how these illnesses directly affect human health. We now understand the complex interactions that exist between vector-borne diseases (VBDs), the environment, disease loads, vector ecology, and societal responses. This intricacy has illuminated the significant historical impact of VBDs on human cultures. Using nanoparticles as cutting-edge insecticides is a promising line of inquiry in the battle against VBDs. Even though their efficacy against arthropod pests and vectors has been extensively studied, little is known about the underlying mechanisms. A few notable exceptions are nanoparticles that have shown promise in pest control, such as graphene oxide, silver, alumina, and silica. Specifically, metal nanoparticles have demonstrated the capacity to interact with essential components of proteins and nucleic acids, causing disruptions to cellular functions and ultimately resulting in cell death. One intriguing component of silver nanoparticles method of action is their ability to regulate important insect genes, causing developmental defects and reproductive failures in the targeted pests. Looking ahead, it

is evident that using nanoparticles as pesticides has a lot of potential for controlling vector-borne illnesses and eliminating agricultural pests.

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