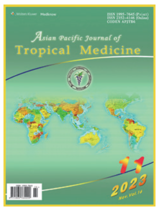

Review Article
Asian Pacific Journal of Tropical Medicine
apjtm.org

doi: 10.4103/1995-7645.390164
Impact Factor: 3.1

Applications of nanomaterials in mosquito vector control: A review

Sahadiya Mandodan, Aneha Kunnikuruvan, Bhagyashree Bora, Hemaladkshmi Padmanaban, Abhisubesh Vijayakumar, Kakhuangailiu Gangmei, Manikandan Sivaprakasam, Jibi Lukose, Mathivanan Ashokkumar, Vijayalakshmi Krishnamoorthy, Subbiah Poopathi✉

Unit of Microbiology and Immunology, ICMR-Vector Control Research Centre, Department of Health Research, Ministry of Health and Family Welfare, Puducherry 605006, India

ABSTRACT

The periodic outbreak of mosquito-borne diseases like dengue fever, zika fever, and yellow fever all over the world highlights the need for effective mosquito control methods targeting the biological system. Due to the lack of therapeutic measures, preventive treatments or vaccines against pathogens, insecticide resistance eventually lead the research focus towards novel technological applications in mosquito management. Nanomaterials with ovicidal, larvicidal, adulticidal, and repellent properties for controlling mosquito vectors are under research. A literature search was carried out for advancements in nanomaterials, insecticides, and mosquito control in PubMed/MEDLINE, Scopus, Google Scholar, ScienceDirect, and Web of Science. This paper aims to provide insights into various nanomaterials relevant to mosquito-borne diseases, *in vivo* and *in vitro* toxicity evaluation against mosquito species, mode of action, effect on non-target organisms, and ecological risks. Organic and inorganic materials that provide controlled release, target delivery, less dosage, prolonged efficacy, a reduction in the use of organic solvents and emulsifiers, and minimum pollution to the environment have already been explored. Indeed, further research on the ecological risk and economic feasibility of nanomaterials in mosquitocidal applications should be done prior to commercialization.

KEYWORDS: Nanomaterials; Nanoformulation; Nanopesticides; Mosquito control

1. Introduction

Humans have been fighting against mosquito vector-borne diseases (VBD) for centuries before the first discovery of mosquitoes as vectors of bancroftian filariasis in 1877 by Patrick Manson[1] in China, which eventually led to the birth of medical entomology and the subsequent development of mosquito control strategies[2]. Nowadays, mosquitoes (Diptera: Culicidae) are vectoring of pathogens and parasites causing dreadful diseases including dengue, chikungunya, malaria, West Nile fever, and yellow fever, which are causing the largest health burden and are major contributors to socio-economic disruption all over the world. VBDs account for 4.3 billion deaths each year[3]. Tropical and subtropical countries face the highest burden, especially for people with low socio-economic status. Despite various control measures adopted worldwide, there is an increase in overall malarial cases from 245 million cases in 2020 to 247 million cases in 2021. The African region is spotted with a higher burden, with around 95% of malaria cases and 96% of deaths reported in 2021, and a high prevalence

---

✉To whom correspondence may be addressed. E-mail: subbiahpoopathi@rediffmail.com

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-Non Commercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

©2023 *Asian Pacific Journal of Tropical Medicine* Produced by Wolters Kluwer-Medknow.

How to cite this article: Mandodan S, Kunnikuruvan A, Bora B, Padmanaban H, Vijayakumar A, Gangmei K, et al. Applications of nanomaterials in mosquito vector control: A review. Asian Pac J Trop Med 2023; 16(11): 479-489.

Article history: Received 13 May 2023 Revision 14 November 2023
Accepted 21 November 2023 Available online 30 November 2023

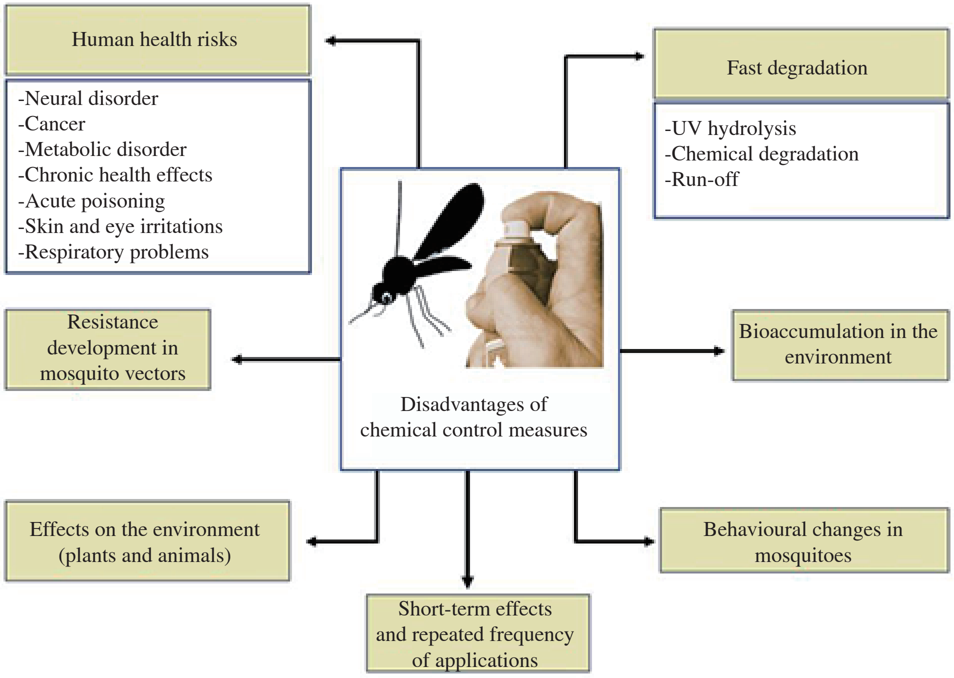

Figure 1. Disadvantages of chemical insecticides.

among children[4]. Over the past two decades, the global incidence of dengue virus has significantly increased, with deaths reaching 5.2 million in 2019[5]. The recent emergence or re-emergence of VBDs observed is attributed to climate change, urbanization, poor sanitation, globalization, and the overall socio-political contexts of the countries[6]. The COVID-19 pandemic has worsened the scenario further again due to the supply chain disruption of mosquito control programmes and the over-pressure on the health infrastructure[7].

2. Current approaches in mosquito vector management

Mitigation of this menace is made possible through various vector control strategies, which have been initiated with the environmental management of mosquitoes. Prior to the development of chemical insecticides, people relied upon source reduction and improved screening of mosquitoes to control vectors. It was a breakthrough when Swiss chemist Paul Muller discovered dichlorodiphenyltrichloroethane (DDT) in 1939. DDT is a prime example of a widely used synthetic insecticide at the time. This ectoparasitic arthropod evolves quickly to adapt to the changing environment, and they have developed resistance to this endocrine disruptor as well as later developed synthetic chemical insecticides like pyrethroids, carbamates, organophosphates, and other organochlorines that also harm mankind and the environment[8]. In view of these detrimental consequences of chemical pesticides, the government placed strong regulations on their use, opening the door for more sustainable vector control methods, including biological measures employing natural enemies to control vectors and genetic control by adding any heritable element to the population at risk of mosquito-borne diseases, which lessened insect damage[9,10] (Figure 1).

The quick response of chemical control cannot be contested, especially when contrasted to other natural approaches, which can occasionally struggle to manage sudden outbreaks[11]. This has paved the way for integrated pest management, a new comprehensive approach employed in pest control that combines all available vector control strategies, including chemical, biological, genetic, cultural, and mechanical treatments, with a sustainable approach that considers the effects on the environment, animals, and human health. Integrated pest management continuously gathers information by evaluating all available methods for newer, more effective, and less harmful ones to the environment[11](Figure 2). The development of fresh, cutting-edge strategies for controlling insect pests have become imperative to overcome the emerging vector borne diseases transmitted by mosquitoes. In addition, arboviral infections like dengue, zika fever, and yellow fever that have periodic outbreaks spread by *Aedes* mosquitoes demand the development of new effective control methods in addition to currently available methods[12]. Considering the necessity for more biodegradable

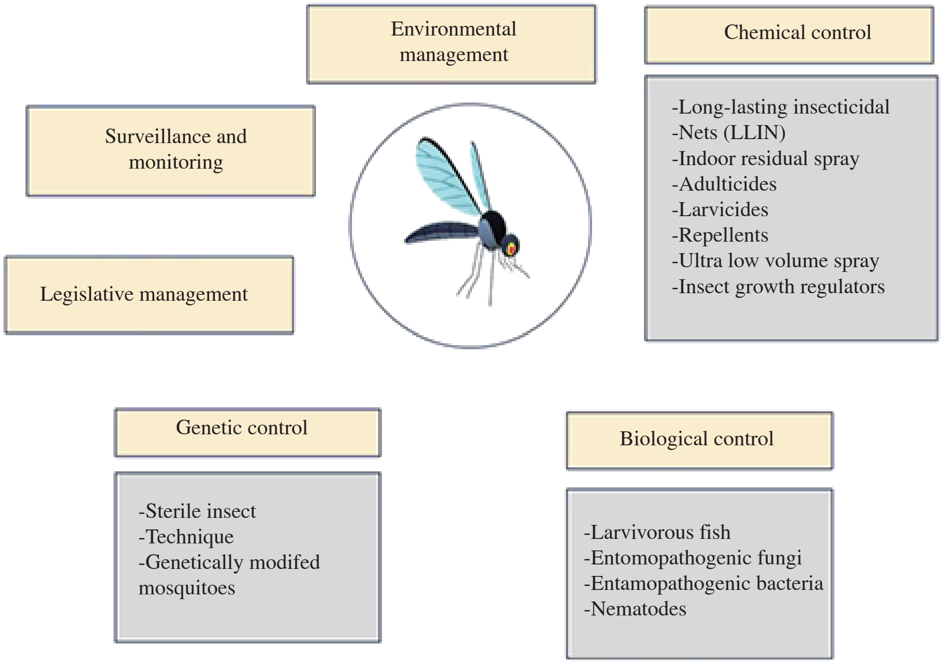

Figure 2. Various mosquito control strategies employed.

and target-specific mosquitocidal treatments, nanotechnology is considered as a promising field with the potential to transform clinical, industrial, and environmental applications, such as targeted drug delivery, cosmetics, biosensing, bioimaging, delivery of genes, antiparasitic agents, electronics, antimicrobial agents, catalysts for transplant monitoring, the food industry, and pest control[13]. It takes advantage of the material's properties at the nanometric scale through a top-down approach[14,15]. The notion of manipulating matter at the atomic scale as a modern interdisciplinary science was first articulated by Richard Feynman, the 1965 Nobel Prize winner in physics, in his speech titled "There's plenty of room at the bottom". Feynman is regarded as the founder of modern nanotechnology.

Various manufactured consumer goods containing nanostructured materials are available in the market. Electronics and medicine exploit nanostructured materials for intended purposes. Recent research and development practices are going on to employ the advantages of nanotechnology in the fields of agriculture and public health management. Nanotechnology is predicted to play a significant role in accelerating technical breakthroughs across several industrial sectors in the coming years. The focus of this paper is on the application and feasibility of nanotechnology in the control of mosquitoes and subsequent public health management due to the shortcomings of conventional control strategies. A comprehensive search was carried out for literature, including original articles and systematic reviews, on prominent public databases such as PubMed/MEDLINE, Scopus, Google Scholar, ScienceDirect, and Web of Science. Articles accessed through the Library & Information Centre (ICMR-Vector Control Research Centre). Throughout the search, we have used keywords such as "nanomaterials", "nanoinsecticides", "nanorepellents", "nanopesticides", "mosquito control", "larvicides", "mosquitocidal", and more, alone or in different combinations for an extensive exploration of advancement in this area.

3. What are nanomaterials?

Humanity is progressing from the macro to the micro to the nanoworld through a constant miniaturisation process and investigating tiny molecule's possibilities. We have been trained to view everything about our scale of comparison for control strategies. So, it is necessary to clarify what exactly are nanomaterials here. These are materials with a minimum of one external dimension measuring 100 nanometres (one-millionth of a millimetre) or less or with internal structures of 100 nanometres or less, irregular in shape, more robust, lighter, and with a high surface area-volume ratio which differs from corresponding bulk materials[14,15]. The smaller the material gets, the larger the proportion of atoms it has on its surface. Since nearly all the catalytic activity of a material is contained in the surface due to the presence of unsaturated atoms, the reactivity of the material increases and behaves differently in commensurate

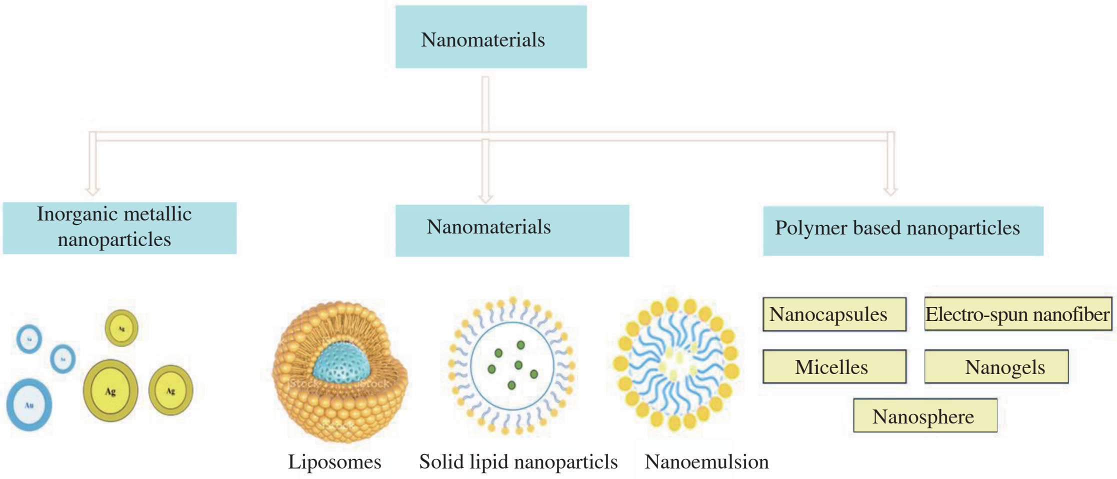

Figure 3. Major types of nanomaterials used in mosquito control.

with the bulk counterpart[15,16]. These properties make them a suitable candidate for use as a bioactive compound and controlled release carrier of active ingredients. They can be manufactured either top-down (from bulk materials to nanosized materials) or bottom-up methods (atoms aggregation or molecule assembly to nanosized particles)[14,15]. Materials used to make nanomaterials include emulsions, metal oxides, silicates, ceramics, materials with magnetic activity, semiconductor quantum dots, polymers, lipids, and dendrimers[14].

Nanomaterials are distinctive in their qualities and offer multiple insights for planned product development. There has been alarming discussion on nanostructured materials application in the pesticide industry. Nanopesticides are developed either by processing active ingredients into nanosized pesticide formulations or by encapsulating them inside a carrier molecule, through nanotechnological processes based on our intended properties, such as biodegradability, controlled release, specificity, protection of active ingredients from degradation, bioavailability, *etc*.

4. Nanomaterials in mosquito control

Nanopesticides provide a much environment-friendly approach to pest control as they require fewer quantities of pesticides, eliminate volatile organic solvents, and have higher efficacy while relegating conventional pesticides to a secondary role[17]. It was reported that nanomodified permethrin has enhanced larvicidal activity, shelf life, and target specificity against *Aedes* (*Ae.*) *aegypti* with minimal effect to non-target organisms in contrast with bulk form of water-insoluble permethrin currently available in the market[17,18]. These tiny and flimsy particles can penetrate the negatively charged outer biological membrane of mosquito larvae, thereby reducing the amount of active ingredients required and having no detrimental effects on humans, animals, and the environment (one health)[19,20]. The aforementioned advantages of nanomaterials can be incorporated into the new formulations of adulticides, pupicides, larvicides, ovicides, and repellents for effective mosquito control and thereby improving their efficacy. Normal insecticide formulations include at least one active ingredient along with some inert substances such as additives and adjuvants and those formulations are made as wettable powders, emulsifiable concentrates, granules, dust, and gels. Any formulations containing components at nanometric scales are referred to as a nanoformulation which is expected to release active ingredients or facilitate mosquito toxicity in a previously designed manner for better efficacy[20,21].

These nanoscale particles change the physicochemical features of formulations, providing appealing advantages and increased effectiveness. Varieties of organic and inorganic nanomaterials are currently under research in various laboratories for better mosquitocidal activity. It can be produced *via* physical, chemical and biological methods. Upon processing, the former two methods produce harmful by-products and are not economically viable. As a result, the focus has now been directed towards the green synthesis of nanomaterials[22].

Different forms of nanomaterials comprising organic and inorganic materials with appropriate functions, such as inorganic metallic nanoparticles, organic polymer-based formulations, nanoemulsions, nanosuspension, nanofibre, lipid-based formulations *etc*. have been reported. Controlled release formulations allow the precise and synchronized release of active substances at their target sites[23].

Their large surface area and specific reactivity to environmental variables facilitate them to be an ideal delivery vehicle. Different nanostructures and nanoencapsulations applied in mosquito control are discussed based on their physicochemical nature (Figure 3).

5. Inorganic metallic nanoparticles

Metallic nanoparticles having unique interactions with biomembranes were previously generated *via* physical and chemical approaches, but these technologies were later shown to be neither feasible nor environmentally benign. This chemical technique for the synthesis of metallic nanoparticle is based on the concept of metal ion reduction and utilises synthetic reducing and stabilising agents, which are frequently shown to be toxic. As a result, research and development efforts are increasingly focusing on the biosynthesis of nanoparticles utilising plant extracts, bacteria, or fungi to reduce metal ions and stabilise their structures[24–26]. Silver nanoparticles (AgNP) synthesized from aqueous extract of leaves of *Azadirachta indica* (Neem plant) against the larvae of *Ae. aegypti* and *Culex* (*Cx.*) *quinquefasciatus* and identified as a potential tool with both *Ae. aegypti* (LC_{50}=0.006 mg/L, LC_{90}=0.04 mg/L) and *Cx. quinquefasciatus* (LC_{50}=0.047 and LC_{90}=23 mg/L). While developing bacterial-based nanoparticles, the DNA and metabolites produced by bacteria act as reducing and stabilizing agents for the synthesis[27]. A similar line of observation was reported in another study where AgNPs biosynthesized using *Barleria cristata* leaf extract revealed higher toxicity in comparison with aqueous leaf extracts of the same for *Anopheles* (*An.*) *subpictus*, *Ae. albopictus*, and *Cx. tritaeniorhynchus* larvae with LC_{50} values of 12.46 mg/L, 13.49 mg/L, and 15.01 mg/L, respectively[28]. In the case of bacterial-based nanoparticles, DNA and metabolites act as reducing and stabilizing agents[29]. *Bacillus thuringiensis* was used to synthesise AgNPs against *Ae. aegypti*, which has shown significant larvicidal action on the 3rd instar larvae with LC_{50}=0.10 mg/L and LC_{90}=0.39 mg/L at all doses tested (0.03, 0.06, 0.09, 0.12, and 0.15 mg/L)[30]. Another 2 bacterial isolates, *Pantoea stewartii* (H2) and *Priestia aryabhattai* (H3) were used to synthesise AgNP against mosquito larvae. Pantoea stewartii-based AgNP has shown high toxicity against *Cx. quinquefasciatus* (LC_{50}=14.829 μg/mL), followed by *An. stephensi* (LC_{50}=20.977 μg/mL) and *Ae. aegypti* (LC_{50}=30.584 μg/mL). Whereas *Priestia aryabhattai*-based AgNP has demonstrated larvicidal activity in the order of *An. stephensi* (LC_{50}=14.015 μg/mL), followed by *Ae. aegypti* (LC_{50}=20.668 μg/mL) and *Cx. quinquefasciatus* (LC_{50}=10.736 μg/mL). There was no visible effect on non-target organisms after 48 hours of exposure to the same. Subsequent histopathological studies also revealed the effect of silver nanoparticles as the midgut and epithelial membrane as damaged[31]. AgNPs produced by *Bacillus cereus* VCRC 641 were evaluated for larvicidal efficacy for *Ae. aegypti*, *Cx. quinquefasciatus*, and *An. stephensi* and the toxicity increased 117-fold more potential than the actual bacterial cell lysate[32]. Beside silver, other metal sources included are gold, cadmium, titanium, iron, palladium, and zinc[33,34]. Gold nanoparticles were synthesised by using *Aspergillus niger* against all available larval instars of *Cx. quinquefasciatus*, *An. stephensi*, as well as *Ae. aegypti* were found more effective with 100% mortality in a 48-hour exposure[35]. Cobalt oxide nanoparticles (CO_3O_4-NPs) and magnesium oxide nanoparticles (MgO-NPs) were synthesized using *Hibiscus rosa* sinensis as the reducing and stabilizing agent and evaluated for larvicidal activity against *Ae. aegypti* and leishmanicidal activity against *Leishmania tropica*. CO_3O_4-NPs have shown relatively more significant larvicidal activity than MgO-NPs. These variations in mortality between CO_3O_4-NPs (67.2%±1.7% at 200 ppm) and MgO-NPs (49.2%±8.1% at 400 ppm) are due to the variation in surface properties. Larvicidal potential of nanoparticles in future dengue control and anti-leishmanial activity in therapeutic strategies for leishmaniasis were reported[36]. Larvicidal and leishmanicidal activity of nanoparticles was demonstrated in another study for zinc oxide nanoparticles (ZnO-NPs) synthesized from aqueous fruit extracts of *Myristica fragrans*. The nanoparticles have shown larvicidal activity against *Ae. aegypti* (77.3%±1.8%) and in addition to that, they have remarkable leishmanicidal activity against both the promastigote (71.50%±0.70%) and amastigote (61.41%±0.71%) forms of the *Leishmania* parasite[37]. Most researches in nanoparticles were focused on the utilization of AgNP among other metallic nanoparticles to control the larval stages of mosquitoes. Even though it has shown an opportunistic effect in laboratory settings, its effectiveness, interaction with aquatic organisms and overall safety in the field have to be studied further.

6. Lipid–based nanoparticles

Lipid nanoparticles are classified into different subtypes. A majority of them are spherical, with a minimum of one aqueous compartment surrounded by one or more lipid bilayers. They are unique in that they are based on a simple structure, self-assembly, biocompatibility, and high bioavailability[38]. This property of prolonged existence is mainly exploited in the development of better mosquito repellents.

6.1. Liposomes

Liposomes are made up of unilamellar or multilamellar phospholipid bilayers that can trap hydrophilic compounds of interest in the central aqueous portion and hydrophobic and lipophilic molecules in the outer membrane. It has the remarkable characteristics of taking in active substances from its surroundings, and thereby expanding and prolonging its function in a system. These properties are exploited in the encapsulation process of drugs[39,40]. In previous study done by Sanei-Dehkordi *et al.*[41], eugenol, clove essential oil, cinnamaldehyde, and cinnamon essential oil were used to improve natural larvicide efficacy against *An. stephensi* by nanoliposome preparation. Increased efficacy was found at LC_{50} levels of 6-12-fold for eugenol and cinnamaldehyde and 2-6-fold for the other two essential oils. Cells will uptake liposomes at the target site through adjuvants, antibodies, antigens, or other specific ligands[41]. This property is exploited for the encapsulation of chloroquine for target drug delivery in malaria treatment and thereby increases the availability of the drug, reduces the drug dose, and has fewer side effects[42].

6.2. Solid lipid nanoparticles (SLP)

Solid lipid nanoparticles are a colloidal dispersion with a solid biodegradable matrix used as an alternative to liposome carriers[43]. A green potent nanorepellent of SLPs containing 1% essential oil of *Zataria multiflora* was developed against *An. stephensi* with three times longer protection than the unformulated one[44]. A novel formulation of nanostructured lipid carrier, a kind of solid lipid nanoparticle, was prepared by blending with fennel (*Foeniculum vulgare*) and green tea oils (*Camellia sinensis*) and investigated for its larvicidal and adulticidal properties against *Cx. pipiens* mosquitoes in the laboratory as well as in the field. It has shown promising in vitro field larvicidal and adulticidal effects for both nanoconverted fennel (LC_{50}=251.71 ppm and 0.25% for larvae and adults, respectively) and green tea oil (LC_{50}=278.63 ppm and 0.40%) in comparison with crude fennel (LC_{50}=643.81 ppm and 2.80%) and crude green tea oil (LC_{50}=746.52 ppm and 4.21%). Subsequent field study of these nanomaterials has revealed their efficacy with minimal effects on non-target organisms and found no environmental damage[45].

6.3. Nanoemulsions (NE)

Nanosized emulsions with dispersion phase nanodroplets can be formed as oil in a water system, water in the oil phase, or as previously made NE dispersing again in any of these phases (W/O/W or O/W/O) can act as a nanocarrier for the controlled release of therapeutic agents[38,39]. Hydrophilic active ingredients can be encapsulated in a W/O or W/OW emulsion, whereas lipophilic substances can be encapsulated in an O/W emulsion. The smaller size of a NE increases its surface area, bioavailability, and solubility, reducing the need for emulsifiers and surfactants in aquatic applications. Castor oil (*Ricinus communis*) containing NE has been formulated and screened for 24 hours against larvae of *An. culicifacies*, and compared to its bulk emulsion. It is found that there is high efficacy associated with NE (LC_{50}=3.4 ppm) in comparison with ordinary emulsion (52.31 ppm), and NE is considered a safe and effective alternative for mosquito control[46]. In another study, stable *Eucalyptus* (*Eucalyptus globulus*) oil-based NE was formulated, characterized, and screened for larvicidal activity against early third-instar larvae of *Cx. quinquefasciatus* mosquitoes for 24 hours at various concentrations and compared with its bulk counterpart. With 250 ppm NE, 98% of deaths occurred within 4 hours of treatment, and has shown better effectiveness than bulk emulsion[47]. O/W NE prepared from the essential oil of basil (*Ocimum basilicum*) through ultrasonication revealed time- and dose-dependent larvicidal activity for *Ae. aegypti*[48]. A neem oil-based O/W stable NE of varying droplet size has been used for checking larvicidal activity against *Cx. quinquefasciatus* and identified a pattern of decrease in LC_{50} with a decrease in droplet size, hence being suggested as a potential larvicidal agent[49].

7. Polymer-based nanoparticles

Depending on the structure and required qualities, both synthetic and natural polymers are utilised. Active substances can be enclosed in the core, trapped inside the matrix, chemically bound to the polymer, or attached to the surface of the nanoparticles[50]. The most common ones are nanocapsules, which have an oily core in which the drug is normally dissolved and is also surrounded by a polymeric shell that regulates the pace at which the drug is released. Nanospheres are made up of a continuous polymeric mesh that can hold the drug inside or adsorb it on the surface[51]. Other than nanospheres and nanocapsules, the most popular polymer-based nanoinsecticides forms are micelles, nanogels, and electro-spun nanofiber[52]. Polymer-based nanoparticles have been applied in different formulations of pesticides for the protection of active ingredients[53,54]. Polymeric materials of natural as well as synthetic origin are applied based on their biodegradability, environmental compatibility, and economic feasibility[55].

The second most plentiful polymer is chitosan, derived from chitin, which has proved a promising delivery agent for insecticides and is widely used in the development of nanoinsecticides[56].

Table 1. Polymer based nanoparticles developed in laboratories.

No.	Polymer used	Active ingredient	Encapsulation efficiency (%)	Biological application	References
1	Gelatin	*Piper aduncum* EO	84.5±0.4	Larvicides	[63]
2	Gelatin	*Piper hispidinervum* EO	82.2±0.4	Larvicides	[63]
3	Poly (ethylene glycol)	*Geranium maculatum* EO	77.0±7.0	Larvicides	[64]
4	Poly (ethylene glycol)	*Citrus bergamia* EO	68.0±5.0	Larvicides	[64]
5	Chitosan	*Geranium maculatum* EO	38.0±4.0	Larvicides	[64]
6	Chitosan	*Citrus bergamia* EO	22.0±3.0	Larvicides	[64]
7	Chitosan	*Siparuna guianensis* EO	84.8±4.0	Larvicides	[65]
8	Poly (e-caprolactone)	*Citronella* oil	83.0	Repellents	[66]
9	Pectin	*Cedrus deodara* EO	60.0	Larvicides	[67]
10	Poly (e-caprolactone)	IR3535	60.0	Repellents	[68]
11	Poly (e-caprolactone)	Geraniol	99.0	Repellents	[68]

[*]EO: Essential oil.

A Ca-alginate-chitosan-based controlled release formulation of imidacloprid has been prepared, and a release study has been conducted against *Ae. aegypti* larvae, which showed that 6.11 mg/L is sufficient to kill the larvae[57]. Chitosan nanoparticles were synthesised using chitosan naturally derived from shrimp shells and tested on third-instar larvae of *Ae. aegypti* and showed potential toxicity when compared to commercially available ones[58]. Alginate polysaccharides derived from brown microalgae are another suitable polymer with the property to form a gel that is used to prepare nanocapsules[59]. Studies have been done to overcome the low stability of alginate and exploit its unique gel-forming property by mixing it with other polymers like chitosan, cellulose, or polyethylene glycol (PEG)[60]. A nanofibrous system incorporating citronella oil was developed *via* electrospinning with polyvinylpyrrolidone and cellulose used as biodegradable polymers, which resulted in the long-term release of citronella oil for up to 4 weeks and increased repellent activity against *Ae. albopictus*[61]. Scientists synthesized and characterized nano-DEPA using an organic repellent, diethylphenylacetamide (DEPA), through polymerization with PEG through the phase inversion method. The effectiveness of bulk DEPA and nano-DEPA was evaluated by conducting larvicidal bioassays and histopathological studies. The results revealed that nano-DEPA exhibited superior efficacy even at lower concentrations compared to bulk-DEPA and suggested its potential application in fabric impregnation for mosquito control[62]. Different kinds of polymers and active ingredients were exploited for various biological applications in mosquito control programmes (Table 1).

8. Limitations and challenges

Nanotechnology has achieved success in the pharmaceutical industry in recent years. Control of mosquitoes with the help of nanomaterials still poses a challenge due to the lack of basic understanding of the interaction between insects and nanosized materials. The ecotoxicity of nanomaterials is still under research. The composites used may contaminate the environment by incorporating into the food chain, and pose a health risk to mammals through inhalation or any dermal contact due to their small size. Most of the nanomaterials under research are based on inorganic metallic nanoparticles. This, in turn, can cause health risks when it persists for a longer time in the environment and the consequent toxicological studies are restricted in laboratories and time-consuming. Most of the nano-based formulations under research are mainly solid formulations, which form a major obstacle to targeting mosquitoes, as manufacturers prefer liquid-based formulations for mosquitocidal applications. Moreover, a complete quality assessment programme for nanoparticles is a challenge for researchers and manufacturers due to their small size and unpredictability in the environment. A comprehensive study on the mode of action, pharmacokinetics, production, formulation, cost-effectiveness, environmental impact assessment, and effect on non-target organisms is necessary before commercialization.

9. Future perspectives

Nanomaterials can be employed in mosquito-borne disease management through vector management with nanoinsecticides[64] and nanorepllents[66], early diagnosis through nanobiosensor[69], and treatment through nanomedicines[70]. Up to now, based on laboratory evaluation and very limited field tests[45], nanomaterials have promised a lead in the fight against mosquito-borne diseases that can compete with conventional pesticides in terms of both cost and performance. Before commercialization, production methods have to be optimised to ensure quality, dosage, effectiveness and consistency. It should be followed by stringent safety evaluation, and clinical research in collaboration with researchers, regulatory authorities, environmentalists, legislative authorities, and manufacturers. Future researches in developing nanoinsecticide formulations can be incorporated with additional *in vivo* toxicological studies in animal models to understand the effect on mammals. The inclusion of *in silico* approach upon developing nanomaterials can reduce the time required for traditional ecotoxicological studies and resource scarcity for the experiment. These computational and machine-learning techniques will be helpful to predict the nanoparticle interaction with the target species and with the environment. Even though experimental validation is crucial, this *in silico* approach would be helpful to understand the behaviour of the nanomaterials in the environment including transport, accumulation, and transformation in the environment. It is recommended to consider mosquito habitat and behaviour for developing specific formulation strategies. Liquid formulations or hydrophilic substance-based composites are preferred for aquatic habitat treatments. Biodegradable or eco-friendly materials like biopolymers are preferred for formulation development due to their renewable nature and natural breakdown. Nanostructures, with nanometer scale dimensions, require careful consideration of potential human, plant, and animal exposure.

10. Conclusions

Mosquito-borne diseases such as malaria, filaria, dengue fever, zika fever, and yellow fever pose a great challenge through their repeated outbreaks. No effective specific medications, antiviral drugs, or vaccines are available in clinics to counter these disease burdens yet. Mosquitoes develop repeated resistance against many insecticides in use, and nanotechnology is paving the way for new research and development aimed at increasing the efficacy of mosquito control programmes through the application of properties like the controlled release, target delivery, active ingredient protection, *etc*. Different nanomaterials with intended properties, such as metallic nanoparticles, nanoliposomes, nanoemulsions, nanogels, nanocapsules, nanospheres, and solid lipid nanoparticles, have been developed; all formulations are effective in the delivery of active ingredients. For larger-scale application and commercial preparation of nano-based pesticides, new rules have to be established, and any other environmental hazards and the overall feasibility of them in controlling the target species without affecting the non-target organisms should be investigated further.

Conflict of interest statement

The authors declare that they have no conflict of interest.

Acknowledgements

The first author acknowledges the PhD guide (S. Poopathi). The authors also acknowledge our institution ICMR-Vector Control Research Centre for its support in the research and development in the area of control of VBD and hope for further support in future.

Funding

The authors declare that the first author received UGC NFOBC fellowship during the preparation of the manuscript from the Ministry of Social Justice and Family Welfare, India.

Authors' contributions

All authors conceptualized and designed the research, with SM, AK, MS, and AV conducting literature searches and data analysis. SP developed the research framework, and SM wrote the manuscript. KG, JL, BB, HP, and MA undertook data interpretation and manuscript revisions. VK and MA finalized the edited manuscript. SP supervised the project.

References

[1] Troyo A, Gonzalez-Sequeira MP, Aguirre-Salazar M, Cambronero-Ortiz I, Chaves-Gonzalez LE, Mejias-Alpizar MJ, et al. Acknowledging extraordinary women in the history of medical entomology. *Parasit Vectors* 2022; **15**(1): 114.

[2] Service MW. A short history of early medical entomology. *J Med Entomol* 1978; **14**(6): 603-626.

[3] World Health Organization 2017. *Fact sheet: Vector–borne diseases.* [Online]. Available from: http://www.who.int/mediacentre/factsheets/fs387/en/. [Accessed on 13 May 2023].

[4] World Health Organization. *World malaria report 2022.* [Online]. Available from: https://www.who.int/teams/global-malaria-programme/reports/world-malaria-report-2022. [Accessed on 13 May 2023].

[5] World Health Organization. *Dengue and severe dengue. 2022.* [Online]. Available from: https://www.who.int/news-room/fact-sheets. [Accessed

on 13 May 2023].

[6] Ryan SJ, Lippi CA, Bardosh KL, Frydenlund EF, Gaff HD, Naveed H, et al. Direct and indirect social drivers and impacts of vector-borne diseases. In: *Population biology of vector–borne diseases*. Strand: Oxford University Press; 2021, p. 247-266.

[7] Weiss DJ, Bertozzi-Villa A, Rumisha SF, Amratia P, Arambepola R, Battle KE, et al. Indirect effects of the COVID-19 pandemic on malaria intervention coverage, morbidity, and mortality in Africa: A geospatial modelling analysis. *Lancet Infect Dis* 2021; **21**(1): 59-69.

[8] Sengul Demirak MS, Canpolat E. Plant-based bioinsecticides for mosquito control: Impact on insecticide resistance and disease transmission. *Insects* 2022; **13**(2): 162.

[9] Chandra G, Bhattacharjee I, Chatterjee SN, Ghosh A. Mosquito control by *Larvivorous* fish. *Indian J Med Res* 2008; **127**(1): 13.

[10] Wang GH, Gamez S, Raban RR, Marshall JM, Alphey L, Li M, et al. Combating mosquito-borne diseases using genetic control technologies. *Nat Commun* 2021; **12**(1): 4388.

[11] Deguine JP, Aubertot JN, Flor RJ, Lescourret F, Wyckhuys KA, Ratnadass A. Integrated pest management: Good intentions, hard realities: A review. *Agron Sustain Dev* 2021; **41**(3): 38.

[12] Campos EVR, de Oliveira JL, Abrantes DC, Rogério CB, Bueno C, Miranda VR, et al. Recent developments in nanotechnology for detection and control of *Aedes aegypti*-borne diseases. *Front Bioeng Biotechnol* 2020; **8**: 102.

[13] Benelli G, Lukehart CM. Applications of green-synthesized nanoparticles in pharmacology, parasitology and entomology. *J Clust Sci* 2017; **28**(1): 1-2.

[14] Bhattacharyya A, Bhaumik A, Rani PU, Mandal S, Epidi TT. Nano-particles-A recent approach to insect pest control. *Afr J Biotechnol* 2010; **9**(24): 3489-3493.

[15] Niemeyer CM. Nanoparticles, proteins, and nucleic acids: Biotechnology meets materials science. *Angew Chem Int Ed* 2001; **40**(22): 4128-4158.

[16] Goodsell DS. *Bionanotechnology: Lessons from nature*. Wiley, Hoboken; 2004.

[17] Ghormade V, Deshpande MV, Paknikar KM. Perspectives for nano-biotechnology enabled protection and nutrition of plants. *Biotechnol Adv* 2011; **29**(6): 792-803.

[18] Kumar RSS, Shiny PJ, Anjali CH, Jerobin J, Goshen KM, Magdassi S, et al. Distinctive effects of nano-sized permethrin in the environment. *Environ Sci Pollut Res* 2013; **20**(4): 2593-2602.

[19] Sap-Iam N, Homklinchan C, Larpudomlert R, Warisnoicharoen W, Sereemaspun A, Dubas ST. UV irradiation-induced silver nanoparticles as mosquito larvicides. *Appl Sci* 2010; **10**(23): 3132-3136.

[20] Benelli G, Maggi F, Pavela R, Murugan K, Govindarajan M, Vaseeharan B, et al. Mosquito control with green nanopesticides: Towards the One Health approach? A review of non-target effects. *Environ Sci Pollut Res* 2018; **25**(11): 10184-10206.

[21] Al-Samarrai AM. Nanoparticles as alternative to pesticides in management plant diseases-a review. *Int J Sci Res Publ* 2012; **2**(4): 1-4.

[22] Ahmed T, Hyder MZ, Liaqat I, Scholz M. Climatic conditions: Conventional and nanotechnology-based methods for the control of mosquito vectors causing human health issues. *Int J Environ Res Public Health* 2019; **16**(17): 3165.

[23] De A, Bose R, Kumar A, Mozumdar S. In: *Management of insect pests using nanotechnology: As modern approaches*. Targeted delivery of pesticides using biodegradable polymeric nanoparticles. New Delhi: Springer; 2014.

[24] Benelli G. Mode of action of nanoparticles against insects. *Environ Sci Pollut Res* 2018; **25**(13): 12329-12341.

[25] Kumar S, Lather V, Pandita D. Green synthesis of therapeutic nanoparticles: An expanding horizon. *Nanomedicine* 2010; **10**(15): 2451-2471.

[26] Rajan R, Chandran K, Harper SL, Yun SI, Kalaichelvan PT. Plant extract synthesized silver nanoparticles: An ongoing source of novel biocompatible materials. *Ind Crops Prod* 2015; **70**: 356-373.

[27] Poopathi S, De Britto LJ, Praba VL, Mani C, Praveen M. Synthesis of silver nanoparticles from *Azadirachta indica*-a most effective method for mosquito control. *Environ Sci Pollut Res* 2015; **22**(4): 2956-2963.

[28] Govindarajan M, Benelli G. Facile biosynthesis of silver nanoparticles using *Barleria cristata*: Mosquitocidal potential and biotoxicity on three non-target aquatic organisms. *Parasitol Res* 2016; **115**(3): 925-935.

[29] Dhand C, Dwivedi N, Loh XJ, Ying AN, Verma NK, Beuerman RW, et al. Methods and strategies for the synthesis of diverse nanoparticles and their applications: A comprehensive overview. *Rsc Adv* 2015; **5**(127): 105003-105037.

[30] Najitha BA, Balasubramanian C, Moorthi PV. Biosynthesis of silver nanoparticles using *Bacillus thuringiensis* against dengue vector, *Aedes aegypti* (Diptera: Culicidae). *Parasitol Res* 2014; **113**(1): 311-316.

[31] Wilson JJ, Harimuralikrishnaa T, Sivakumar T, Mahendran S, Ponmanickam P, Thangaraj R, et al. Biogenic synthesis of silver nanoparticles using *Pantoea stewartii* and *Priestia aryabhattai* and their antimicrobial, larvicidal, histopathological, and biotoxicity potential. *Bioengineering* 2023; **10**(2): 248.

[32] Manikandan S, Jibi L, Abhisubesh V, Hemaladkshmi P, Aneha K, Sahadiya M, et al. Biosynthesis of silver nanoparticles mediated by entomopathogenic bacteria: *Bacillus cereus* VCRC 641 against *Aedes aegypti*, *Anopheles stephensi* and *Culex quinquefasciatus*. *World J Adv Res Rev* 2022; **16**(1): 311-319.

[33] Narayanan KB, Sakthivel N. Coriander leaf mediated biosynthesis of gold nanoparticles. *Mater Lett* 2008; **62**(30): 4588-4590.

[34] Suganya P, Vaseeharan B, Vijayakumar S, Balan B, Govindarajan M, Naiyf SA, et al. Biopolymer zein-coated gold nanoparticles: Synthesis,

antibacterial potential, toxicity and histopathological effects against the zika virus vector *Aedes aegypti*. *J Photochem Photobiol B: Biol* 2017; **173**: 404-411.

[35]Soni N, Prakash S. Synthesis of gold nanoparticles by the fungus *Aspergillus niger* and its efficacy against mosquito larvae. *Parasitol Res* 2012; **2**(1): 1-7.

[36]Khan MA, Ali F, Faisal S, Rizwan M, Hussain Z, Zaman N, et al. Exploring the therapeutic potential of *Hibiscus rosa* sinensis synthesized cobalt oxide (CO_3O_4-NPs) and magnesium oxide nanoparticles (MgO-NPs). *Saudi J Biol Sci* 2021; **28**(9): 5157-5167.

[37]Faisal S, Jan H, Shah SA, Shah S, Khan A, Akbar MT, et al. Green synthesis of zinc oxide (ZnO) nanoparticles using aqueous fruit extracts of *Myristica fragrans*: Their characterizations and biological and environmental applications. *ACS Omega* 2021; **6**(14): 9709-9722.

[38]Mitchell MJ, Billingsley MM, Haley RM, Wechsler ME, Peppas NA, Langer R. Engineering precision nanoparticles for drug delivery. *Nat Rev Drug Discov* 2021; **20**(2): 101-124.

[39]Koning GA, Storm G. Targeted drug delivery systems for the intracellular delivery of macromolecular drugs. *Drug Discov Today* 2003; **11**(8): 482-483.

[40]Sercombe L, Veerati T, Moheimani F, Wu SY, Sood AK, Hua S. Advances and challenges of liposome assisted drug delivery. *Front Pharmacol* 2015; **6**: 286.

[41]Sanei-Dehkordi A, Heiran R, Roozitalab G, Elahi N, Osanloo M. Larvicidal effects of nanoliposomes containing clove and cinnamon essential oils, eugenol, and cinnamaldehyde against the main malaria vector, *Anopheles stephensi* liston. *Psyche: J Entomol* 2022; doi: https://doi.org/10.1155/2022/9991238.

[42]Owais M, Varshney GC, Choudhury A, Chandra S, Gupta CM. Chloroquine encapsulated in malaria-infected erythrocyte-specific antibody-bearing liposomes effectively controls chloroquine-resistant *Plasmodium berghei* infections in mice. *Antimicrob Agents Chemother* 1995; **39**(1): 180-184.

[43]Shidhaye SS, Vaidya R, Sutar S, Patwardhan A, Kadam VJ. Solid lipid nanoparticles and nanostructured lipid carriers-innovative generations of solid lipid carriers. *Curr Drug Deliv* 2008; **5**(4): 324-331.

[44]Kelidari HR, Moemenbellah-Fard MD, Morteza-Semnani K, Amoozegar F, Shahriari-Namadi M, Saeedi M, et al. Solid-lipid nanoparticles (SLNs) containing *Zataria multiflora* essential oil with no-cytotoxicity and potent repellent activity against *Anopheles stephensi*. *J Parasit Dis* 2021; **45**(1): 101-108.

[45]Radwan IT, Baz MM, Khater H, Selim AM. Nanostructured lipid carriers (NLC) for biologically active green tea and fennel natural oils delivery: Larvicidal and adulticidal activities against *Culex pipiens*. *Molecules* 2022; **27**(6): 1939.

[46]Sogan N, Kapoor N, Kala S, Patanjali PK, Nagpal BN, Vikram K, et al. Larvicidal activity of castor oil nanoemulsion against malaria vector *Anopheles culicifacies*. *Int J Mosq Res* 2018; **5**(3): 1-6.

[47]Sugumar S, Clarke SK, Nirmala MJ, Tyagi BK, Mukherjee A, Chandrasekaran N. Nanoemulsion of eucalyptus oil and its larvicidal activity against *Culex quinquefasciatus*. *Bull Entomol Res* 2014; **104**(3): 393-402.

[48]Ghosh V, Mukherjee A, Chandrasekaran N. Formulation and characterization of plant essential oil based nanoemulsion: Evaluation of its larvicidal activity against *Aedes aegypti*. *Asian J Chem* 2013; **25**(Supplementary issue): S321.

[49]Anjali CH, Sharma Y, Mukherjee A, Chandrasekaran N. Neem oil (*Azadirachta indica*) nanoemulsion-a potent larvicidal agent against *Culex quinquefasciatus*. *Pest Manag Sci* 2012; **68**(2): 158-163.

[50]Pisoschi AM, Pop A, Cimpeanu C, Turcu V, Predoi G, Iordache F. Nanoencapsulation techniques for compounds and products with antioxidant and antimicrobial activity-A critical view. *Eur J Med Chem* 2018; **157**: 1326-1345.

[51]Zielińska A, Carreiró F, Oliveira AM, Neves A, Pires B, Venkatesh DN, Souto EB. Polymeric nanoparticles: Production, characterization, toxicology and ecotoxicology. *Molecules* 2020; **25**(16): 3731.

[52]Kah M, Hofmann T. Nanopesticide research: Current trends and future priorities. *Environ Int* 2014; **63**: 224-235.

[53]Nuruzzaman MD, Rahman MM, Liu Y, Naidu R. Nanoencapsulation, nano-guard for pesticides: A new window for safe application. *J Agric Food Chem* 2016; **64**(7): 1447-1483.

[54]Sun C, Zeng Z, Cui H, Verheggen F. Polymer-based nanoinsecticides: Current developments, environmental risks and future challenges-a review. *Biotechnologie, Agronomie, Société et Environnement* 2020; **24**: 61-69.

[55]Perlatti B, de Souza Bergo PL, das Graças Fernandes da Silva MF, Fernandes JB, Forim MR. Polymeric nanoparticle-based insecticides: A controlled release purpose for agrochemicals. In: *Insecticides–Development of safer and more effective technologies; 2013.* [Online]. Available from: http://dx.doi.org/10.5772/53355. [Accessed on 13 May 2023].

[56]Kashyap PL, Xiang X, Heiden P. Chitosan nanoparticle-based delivery systems for sustainable agriculture. *Int J Biol Macromol* 2015; **77**: 36-51.

[57]Lim GP, Ahmad MS. Development of Ca-alginate-chitosan microcapsules for encapsulation and controlled release of imidacloprid to control dengue outbreaks. *J Ind Eng Chem* 2017; **56**: 382-393.

[58]Anand M, Sathyapriya P, Maruthupandy M, Beevi AH. Synthesis of chitosan nanoparticles by TPP and their potential mosquito larvicidal application. *Front Med* 2018; **2**(2): 72-78.

[59]Jerobinm J, Sureshkumar RS, Anjali CH, Mukherjee A, Chandrasekaran N. Biodegradable polymer-based encapsulation of neem oil nanoemulsion for controlled release of Aza-A. *Carbohydr Polym* 2012;

90(4): 1750-1756.

[60]Kumar S, Chauhan N, Gopal M, Kumar R, Dilbaghi N. Development and evaluation of alginate-chitosan nanocapsules for controlled release of acetamiprid. *Int J Biol Macromol* 2015; **81**: 631-637.

[61]Iliou K, Kikionis S, Petrakis PV, Ioannou E, Roussis V. Citronella oil-loaded electrospun micro/nanofibrous matrices as sustained repellency systems for the Asian tiger mosquito *Aedes albopictus*. *Pest Manag Sci* 2019; **75**(8): 2142-2147.

[62]Balaji APB, Ashu A, Manigandan S, Sastry TP, Mukherjee A, Chandrasekaran N. Polymeric nanoencapsulation of insect repellent: Evaluation of its bioefficacy on *Culex quinquefasciatus* mosquito population and effective impregnation onto cotton fabrics for insect repellent clothing. *J King Saud Univ Sci* 2017; **29**(4): 517-527.

[63]Silva LS, Mar JM, Azevedo SG, Rabelo MS, Bezerra JA, Campelo PH, et al. Encapsulation of *Piper aduncum* and *Piper hispidinervum* essential oils in gelatine nanoparticles: A possible sustainable control tool of *Aedes aegypti*, *Tetranychus urticae* and *Cerataphis lataniae*. *J Sci Food Agr* 2019; **99**(2): 685-695.

[64]Werdin Gonzalez JO, Jesser EN, Yeguerman CA, Ferrero AA, Fernández Band B. Polymer nanoparticles containing essential oils: New options for mosquito control. *Environ Sci Pollut Res* 2017; **24**: 17006-17015.

[65]Ferreira PT, Haddi K, Corrêa RFT, Zapata VL, Piau TB, Souza LF, et al. Prolonged mosquitocidal activity of *Siparuna guianensis* essential oil encapsulated in chitosan nanoparticles. *PLoS Negl Trop Dis* 2019; **13**(8): e0007624.

[66]Pardini F, Iregui Á, Faccia P, Amalvy J, González A, Irusta L. Development and characterization of electrosprayed microcaspules of poly ε-caprolactone with citronella oil for mosquito-repellent application. *Int J Polym Anal Charact* 2021; **26**(6): 497-516.

[67]Kala S, Sogan N, Naik SN, Agarwal A, Kumar J. Impregnation of pectin-cedarwood essential oil nanocapsules onto mini cotton bag improves larvicidal performances. *Sci Rep* 2020; **10**(1): 14107.

[68]Abrantes DC, Rogerio CB, Campos EV, Germano-Costa T, Vigato AA, Machado IP, et al. Repellent active ingredients encapsulated in polymeric nanoparticles: Potential alternative formulations to control arboviruses. *J Nanobiotechnol* 2022; **20**(1): 1-6.

[69]Manta P, Kumar D, Kapoor DN. A novel gold nanosensor and ‘Blockade-of-Binding’ based immunochromatographic rapid antigen test kit for zika virus. *Mater Lett* 2022; **309**: 131322.

[70]Usman M, Farrukh MA. Formulation of polymeric iron nano-chloroquine phosphate anti-malarial drug *via* polyol method. *Mater Today Proc* 2018; **5**(7): 15595-15602.

Publisher’s note

The Publisher of the *Journal* remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.