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***Thesis :***

***The use of nanoparticles as control tool  
for vector borne diseases: a  
comprehensive literature review***

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# ***Acknowledgements***

## ***At the conclusion of this submission***

*First of all praise to Allah the Almighty the Most Merciful who has given us the courage and strength to carry out this modest work that is the fruit of our last five years of study and for all its benefits.*

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*We would also like to thank all the teachers of the Departmentof Natural and Life Sciences*

*Finally, we would like to thank all those who helped us*



# *Dedication*



*To my dear parents: may God accept them in his vast paradise;*

*To my dear brothers and sisters: Zina, Riadh, Kamel, Salah, especially Mourad for his help in this work, Hanene, Zakariya for their constant encouragement and moral support,*

*To my little family, wife nadia, son and daughter: Mohamed and hadjer*

*To all the children of my brothers and sisters,*

*To my entire family for their support throughout my academic career,*

*To My Friend and pair of this work khaled bouafia,*

*To all my friends and colleague at work,*

*We hope this work will deliver on your alleged promises and infallible support leaks,*

*Thanks for always being there for me.*



## *Dedication*

*To my dear parents: may God accept them in his vast  
paradise;*

*To my entire family for their support throughout my academic  
career,*

*To My Friend and pair of this work Rafik Dhemchi,*

*To all my friends and colleague at work,*

*We hope this work will deliver on your alleged promises and  
infallible support leads,*

*Thanks for always being there for me.*

## ***FIGURES***

<b>Figure №01:</b>	<i>Culcidae</i> mosquito classification.....	<b>8</b>
<b>Figure№02:</b>	Mosquito morphology.....	<b>9</b>
<b>Figure№ 03 :</b>	<i>Aedes, Culex, Anophele</i> comparison.....	<b>15</b>
<b>Figure№04:</b>	Principal characters for identifying the three genera of medical importance.....	<b>15</b>
<b>Figure №05 :</b>	The shematic diagram of organic NPs.....	<b>25</b>
<b>Figure №06:</b>	The shematic diagram of inorganic NPs.....	<b>25</b>
<b>Figure №07:</b>	The shematic diagram of metal NPs.....	<b>26</b>
<b>Figure№08 :</b>	Inorganic nanomaterials.....	<b>26</b>

## ***TABLES***

<b>Table №01 :</b>	Various NPs with their applicative measures against the different mosquito species.....	<b>28</b>
<b>Table №02:</b>	Advantages and disadvantages of different synthesis methods .....	<b>30</b>
<b>Table № 03 :</b>	Article reviews.....	<b>36</b>
<b>Table №04:</b>	Comparative summary.....	<b>38</b>

## ***ABBREVIATIONS***

<b>NPs</b>	:	Nanoparticles.
<b>CNPs</b>	:	Carbon-nanoparticles.
<b>CNTs</b>	:	Carbonnano-tubes.
<b>LBNPs</b>	:	Lipid-basednanoparticles.
<b>QDs</b>	:	Quantum dots.
<b><i>An.</i></b>	:	<i>Anophele.</i>
<b><i>Ae.</i></b>	:	<i>Aedes.</i>
<b><i>Cx.</i></b>	:	<i>Culex.</i>
<b>RVF</b>	:	Rift vallery fever.
<b>LF</b>	:	Lymphatic filiarisis.
<b>TBE</b>	:	Tick-borne encephalitis.
<b>WNV</b>	:	West Nile virus.
<b>SLEV</b>	:	Saint Louis Encephalitis Virus.
<b>EEE</b>	:	Eastern Equine Encephalitis.

## Abstract:

The aim of this study is to show the enormous danger that mosquitoes represent to the public health and development of several million people in several countries and continents, a variety of diseases are caused by mosquitoes as vectors (*Anopheles*, *Aedes*, *Culex*).

The important ones are Dengue Fever, Malaria, Yellow Fever, West Nile Virus, Rift Valley Fever, Chikungunya, Japanese Encephalitis and some others.

the second aims of the study, is to focus on possible solutions to fight and combat the devastating effect of these mosquitoes while avoiding the use of chemical pesticides very polluting. So we opted for the choice of nanoparticles. An alternative that is less polluting, efficient and opens up very promising prospects.

Keywords: Nanoparticles; mosquitoes; health, alternative; efficient.

## Résumé:

L'objectif de cette étude est de montrer l'énorme danger que représentent les moustiques pour la santé publique et le développement de plusieurs millions de personnes dans plusieurs pays et continents, une variété de maladies sont causées par les moustiques comme vecteurs (*Anopheles*, *Aedes*, *Culex*).

Les plus importants sont la dengue, le paludisme, la fièvre jaune, le virus du Nil occidental, la fièvre de la vallée du Rift, le chikungunya, l'encéphalite japonaise et quelques autres.

Le deuxième objectif de l'étude, est de se concentrer sur les solutions possibles pour lutter contre l'effet dévastateur de ces moustiques tout en évitant l'utilisation de pesticides chimiques très polluants. Nous avons donc opté pour le choix des nanoparticules. Une alternative moins polluante, efficace et qui ouvre des perspectives très prometteuses.

**Mot clés :** Nanoparticules ; moustiques ; santé, alternatif ; efficace.

---

## ملخص

الهدف من هذه الدراسة هو إظهار الخطر الهائل الذي يمثله البعوض على الصحة العامة والتنمية لعدة ملايين من الناس في العديد من البلدان والقارات، وتسبب البعوض مجموعة متنوعة من الأمراض كناقلات (*Anopheles*، *Aedes*، *Culex*).

اهم الأمراض التي تنقلها هذه الأنواع من البعوض حمى الضنك والملاريا والحمى الصفراء وفيروس غرب النيل وحمى الوادي المتصدع وتشيكونغونيا والتهاب الدماغ الياباني وبعض الآخرين.

الهدف الثاني للدراسة هو التركيز على الحلول الممكنة لمكافحة ومكافحة التأثير المدمر لهذا البعوض مع تجنب استخدام مبيدات الآفات الكيميائية الملوثة للغاية. لذلك اخترنا اختيار الجسيمات النانوية. هناك بديل أقل تلويثًا وكفاءة ويفتح آفاقًا واعدة للغاية.

**الكلمات المفتاحية:** الجسيمات النانوية؛ البعوض؛ الصحة؛ البديل؛ الكفاءة.

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- Figures.
- Tables.
- Abbreviations.
- Abstract.

## *SUMMARY*

INTRODUCTION .....	6
<b>CHAPTER I: BIBLIOGRAPHY</b>	
1. Mosquitoes.....	11
1.1 Major type of Mosquitoes.....	11
A. <i>Anopheles</i> Mosquitoes .....	11
A.1. Biology.....	11
A.2 Habitat .....	11
A.3 Distribution.....	11
A.4 Biting behavior.....	12
B. <i>Aedes</i> mosquitoes.....	12
B.1 Biology.....	12
B.2 Habitat.....	13
B.3 Distribution.....	13
B.4 Biting behavior.....	13
C. <i>Culex</i> Mosquitoes.....	13
C.1 Biology.....	14
C.2 Habitat.....	14
C.3 Distribution.....	14
C.4 Biting behavior .....	14
1.2 Mosquitoes-borne diseases.....	16
2. Nanoparticles.....	19
2.1 Major type of NPs.....	19
2.2 Applications of NPs.....	27
A. Toxicity of NPs to insect.....	27
B. Different type of NPs against insect.....	29
C. Different methods of NPs synthesis.....	29
D. Method of action of NPs against vector insect.....	31
E. The safety of the NPs.....	32
<b>CHAPTER II : ANALYSIS AND DISCUSS</b>	
A. Methodology.....	35
A.1 Search strategy .....	35
A.2 Data extraction Process.....	35
A.3 Limitations .....	36
B. Article review .....	36
C. comparative summary .....	48
D. conclusion.....	50

## • INTRODUCTION

Vector-borne diseases pose significant threats to public health globally, accounting for millions of infections and deaths each year. Traditional methods of vector control, such as insecticides and repellents, while effective to some extent, often face challenges such as resistance development and environmental concerns. In recent years, there has been a growing interest in exploring alternative strategies for vector control, particularly the use of nanotechnology. (Mandodan et al, 2023).

Humanity is progressing from the macro to the micro to the nano-world 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. (Mandodan et al, 2023). So, it is necessary to clarify what exactly are nanomaterials here. These are materials with a minimum of one external dimension measuring 100 nanometers (one-millionth of a millimetre) or less or with internal structures of 100 nanometers or less, irregular in shape, more robust, lighter, and with a high surface area-volume ratio which differs from corresponding bulk materials. (Mandodan et al, 2023). 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 with the bulk counterpart. (Mandodan et al, 2023). These properties make them a suitable candidate for use as a bioactive compound and controlled release carrier of active ingredients. (Mandodan et al, 2023). 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). Materials used to make nanomaterials include emulsions, metal oxides, silicates, ceramics, materials with magnetic activity, semiconductor quantum dots, polymers, lipids, and dendrimers. (Mandodan et al, 2023). 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. (Mandodan et al, 2023). 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. (Mandodan et al, 2023).

Nanoscience is a branch of science that comprises the Study of properties of matter at the nanoscale, and particularly focuses on the unique, size-dependent properties of solid-state materials. Nanotechnology is the branch that comprises the synthesis, engineering, and utilization of materials whose size ranges from 1 to 100 nm, known as nanomaterials. The birth of nanoscience and nanotechnology concepts is usually linked to the famous lecture of Nobel laureate Richard Feynman at the 1959 meeting of the American Physical Society, “There’s Plenty of Room at the Bottom”. However, the use of nanotechnology and nanomaterials goes back in history long before that. (Joudeh and Linke, 2022).

Interest in nanomaterials and especially nanoparticles has exploded in the past decades primarily due to their novel or enhanced physical and chemical properties compared to bulk material. These extraordinary properties have created a multitude of innovative applications in the fields of medicine and pharma, electronics, agriculture, chemical catalysis, food industry, and many others. (Joudeh and Linke, 2022).

### • **Properties of nanoparticles**

In 2008 the International Organization for Standardization (ISO) defined a nanoparticle as a discrete nano-object where all three Cartesian dimensions are less than 100 nm. The ISO standard similarly defined two-dimensional nano-objects (i.e., nanodiscs and nanoplates) and one-dimensional nano-objects (i.e., nanofibres and nanotubes). But in 2011 the Commission of the European Union endorsed a more-technical but wider-ranging definition:

*A natural, incidental or manufactured material containing particles, in an unbound state or as an aggregate or as an agglomerate and where, for 50% or more of the particles in the number size distribution, one or more external dimensions is in the size range 1 nm–100 nm.* (King and Dobson, 2022).

Under that definition a nano-object needs only one of its characteristic dimensions to be in the range 1–100 nm to be classed as a nanoparticle, even if its other dimensions are outside that range. (The lower limit of 1 nm is used because atomic bond lengths are reached at 0.1 nm.) (King and Dobson, 2022).

There are three major physical properties of nanoparticles, and all are interrelated: (1) they are highly mobile in the Free State (e.g., in the absence of some other additional influence, a 10-nm-diameter nanosphere of silica has a sedimentation rate under gravity of 0.01 mm/day in water). (King and Dobson, 2022).

(2) they have enormous specific surface areas (e.g., a standard teaspoon, or about 6 ml, of 10-nm-diameter silica nanospheres has more surface area than a dozen doubles-sized tennis courts; 20 percent of all the atoms in each nanosphere will be located at the surface).

(3) They may exhibit what are known as quantum effects. Thus, nanoparticles have a vast range of compositions, depending on the use or the product. (King and Dobson, 2022).

The small size, large surface, and more active area account for the extensive use of NPs in various applications, such as in drug delivery, diagnostics, food science, electronics, and several other biological and nonbiological areas. With the increased interest in nanotechnology in the last decade, the safety of NPs in the environment has also been considered. Therefore, in addition to the toxicity of NPs to vector insects, the impact of NPs on non-target organisms in the environment has become the focus of attention. (Danyue et al, 2023).

- **Mosquitos:**

Mosquitoes are considered as the most fatal and lethal organisms in the world causing millions of deaths annually around the world. Deaths caused by malaria alone reached to 4,38,000 deaths in 2015. A variety of diseases are caused by Mosquitoes as vectors. The important ones are Dengue Fever, Malaria, Yellow Fever, West Nile Virus, Rift Valley Fever, Chikungunya, Japanese Encephalitis and some others. (Shaukat et al 2019).

Acting as vectors (living organisms that can transmit infectious diseases between humans or from animals to humans) for different diseases. Their ability to transmit

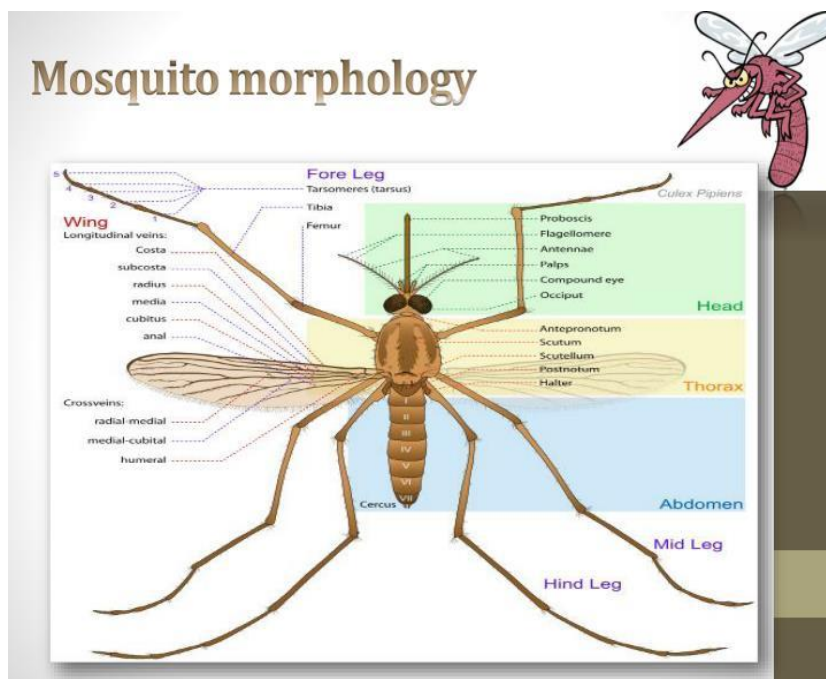
And disseminate disease to humans causes millions of deaths every year. (Shaukat et al 2019).



**Fig 1:** *Culicidae* mosquito classification. (Almuhanna 2012).

Since the late nineteenth century, when mosquitoes were first associated with the transmission of pathogens to humans and other vertebrates, a number of mosquito species have been intensively studied. The three main mosquito genera, *Anopheles*, *Aedes* and *Culex*, transmit the causative agents of malaria, dengue and filariasis, respectively, as well as a variety of mosquito-borne zoonotic arboviruses, such as West Nile Virus (WNV), Saint Louis Encephalitis Virus (SLEV) and Eastern Equine Encephalitis Virus (EEE). Because of the inherent difficulty of mosquito control and therefore the implantation of surveillance strategies, there still is a significant morbidity and mortality due to these diseases, along with an increase in various other diseases caused by insect-vectorated pathogens of epidemiological importance. (Wilke and Marrelli, 2015).

The increase in the geographic distribution of mosquitoes is followed by the emergence of viruses and diseases in new areas. For example, the number of malaria cases has increased as a result of deteriorating health systems, increased *Anopheline* resistance to insecticides, Plasmodium resistance to antimalarial drugs and the time taken to develop an effective vaccine.(Wilke and Marrelli, 2015).



**Fig 02:** Mosquito morphology. (Almuhanna 2012).

## ***CHAPTER I: BIBLIOGRAPHY***

## **1. Mosquitoes:**

### **1.1 major types of Mosquitoes:**

#### ***A. Anopheles***

*Anopheles* mosquitoes are primarily known for their importance in the transmission of human malaria. Of the more than 450 recognized *Anopheles* species, around 40 have the capacity to transmit human malaria parasites well enough to cause significant human illness (M A P. M M V, 2019). Those species that are effective vectors have a preference for feeding on humans rather than other animals, are able to survive and breed in places close to homes, and can survive long enough after feeding on infected blood to allow the parasite time to develop and travel to the mosquito's salivary glands ready to infect the next person bitten. (M A P. M M V, 2019).

#### **A.1. Biology**

Like all mosquitoes, *anophelines* go through four stages in their life cycle: egg, larva, pupa, and adult. females lay 50-200 eggs per oviposition, each placed singly onto water with a small float on either side. These eggs are not resistant to drying, and typically hatch within 2-3 days (C D C P. M, 2018). The egg, larval and pupal stages are aquatic and last 5-14 days. When the adult ecloses it may live up to a month, but most do not live more than 1-2 weeks. Adults usually mate within a few days after emerging from the pupal stage. In most species, the males form large swarms, usually around dusk, and the females fly into the swarms to mate (CDC P. M, 2018).

#### **A.2. Habitat**

*Anopheles* mosquitoes breed in natural water collections, so breeding increases dramatically in the rainy season when water collects in man-made containers, ponds, water tanks, paddy fields and other places that can serve as breeding grounds. Some species, such as *An. coluzzii*, are more commonly found in puddles, swamps and ditches, while others, including *An. gambiae* (s.s.) are more frequent in drains, construction sites, and others habitats (Mattah et al, 2017).

#### **A.3. Distribution**

*Anopheles* mosquito are found throughout the tropics and sub-tropics. In Africa, a small number of highly dominant malaria vector species cover large areas. *Anopheles fenestus* and *An. gambiae* are distributed across central Africa, and these species are found

along with *An. arabiensis* in sub-Saharan West Africa. In South America, *An. darlingi* is considered to be the most important of the dominant vector species. In Asia there are many dominant vector species, including *An. dirus*, *An. minimus* and *An. punctulatus*, and this complexity increases the problems associated with understanding the vector/transmission environment (Sinka, 2023).

#### **A.4. Biting Behaviours**

Most *Anopheles* mosquitoes are crepuscular (active at dusk or dawn) or nocturnal (active at night), which is why bed nets are such an effective tool for malaria prevention. However, whilst some *Anopheles* mosquitoes feed indoors (endophagic), others have a preference for feeding outdoors (exophagic). Similarly, some *Anopheles* mosquitoes prefer to rest indoors (endophilic), while others prefer to rest outdoors (exophilic) [Centers for Disease Control and Prevention. Malaria, 2018]. There is evidence of changes in biting and resting behaviour of the main malaria vectors as a result of selective pressures by the widespread and long-term use of bed nets and indoor residual spraying (Ferreira et al, 2017).

#### **B. *Aedes* mosquito**

There are over one hundred species of *Aedes* mosquito, of which two are the main vector of disease. *Aedes aegypti* and *Aedes albopictus* both species have a deserved reputation for transmitting viruses of medical importance to humans, including West Nile virus, yellow fever virus, and dengue virus, therefore understanding their life stages can help to target effective control interventions for disease prevention. In addition to being efficient vector, these are two of the most prevalent mosquito species across the world, primarily due to their ability to adapt to new environments. The eggs of both species can survive drying out for long periods of time, thus allowing eggs to be transported and colonize non-native areas (Carvalho et al, 2017).

#### **B.1. Biology**

The *Aedes* life cycle starts with the female taking a blood meal to provide nutrients for the production of eggs. Each female produces 100-200 eggs per batch depending on the size of the blood meal taken. Each female can lay eggs five times during their lifetime, with eggs being laid every 4-5 days. Eggs are smooth, oval shaped and about a millimetre long. These eggs are not laid directly on water, but on damp surfaces that are likely to flood. Egg

development depends on temperature: in warmer climates, eggs may develop in two days, but in colder climates development can take a week. (Knudsen, 1995).

*Aedes* eggs can survive in the dry state for more than a year and will hatch when submerged in water. Upon hatching, larvae will begin to feed on algae and other small organisms. Larvae will spend most of their time at the water's surface, but will also swim to the bottom when feeding and when disturbed. (Knudsen, 1995).

The larvae pass through four stages of development, called instars, at the end of which the larvae moult and grow in size. After the fourth instar, the larvae develop into pupae, which are mobile and respond to stimuli in the water. They do not feed at this stage and need two days to develop into adults. In total, egg to adulthood takes approximately two weeks, but the length of time they spend at each stage is temperature dependent: in colder climates *Aedes aegypti* may stay in the larval state for months. (Knudsen, 1995).

## **B.2. Habitat**

*Aedes aegypti* adults normally occupy urban areas with or without vegetation. *Aedes albopictus* adults normally occupy areas with thickets and arboreal vegetation, but will also make use of man-made containers for laying eggs. (Knudsen, 1995).

## **B.3. Distribution**

*Aedes aegypti* and *Aedes albopictus* are primarily mosquitoes of the tropical and sub-tropical parts of the world. However, both species have taken advantage of human trade and travel to expand their distribution ranges considerably. (Knudsen, 1995). *Aedes aegypti* is concentrated in South America, sub-Saharan Africa, Southern Asia and Australia (Kraemer, 2015).

## **B.4. Biting Behaviours**

*Aedes* mosquitoes are aggressive biters, which often results in a high biting rate. They will feed multiple times from different individuals. *Aedes* are mostly active during the day, so traditional control methods such as sleeping under a bed net, are not normally recommended (Farjana, Tuno, 2013).

*Aedes aegypti* have strong preference for taking blood meals from humans and will often take more than one blood meal for each batch of eggs. *Aedes albopictus* are mostly found outdoors where they feed on animals, they will also feed on humans. (Farjana, Tuno, 2013).

## **C. *Culex* Mosquitoes.**

*Culex* mosquitoes are widely distributed in tropical and temperate parts of the world. Approximately 770 species of *Culex* mosquitoes have been described, several of which serve as vectors of agents that cause disease in birds, humans, and other animals. West Nile virus, Japanese encephalitis, St. Louis encephalitis, filariasis and avian malaria can all be transmitted by *Culex* species (Turell, 2012).

### **C.1. Biology**

Like all mosquitoes, *Culex* go through four stages in their life cycle: egg, larva, pupa, and adult. *Culex* eggs are laid upright in distinct rafts on the surface of the water. Rafts can contain up to 300 eggs. *Culex* larvae have a siphon tube at their posterior end, through which they breathe, and they filter feed on microorganisms at the water surface or scrape biofilms from underwater rocks and vegetation (Roberts, 2014).

### **C.2. Habitat**

The larval habitats of *Culex* mosquitoes include pools, puddles, ditches, borrow pits, rice fields, pit latrines and treeholes. *Culex quinquefasciatus* tends to lay eggs in anaerobic waters, which means their larvae are under less risk from aquatic predators (Roberts, 2014). They are also associated with turbid waters, while *Cx. tritaeniorhynchus* larvae are often found in rice fields, grassy pools and fish ponds [SM.ES. CU P, 2012].

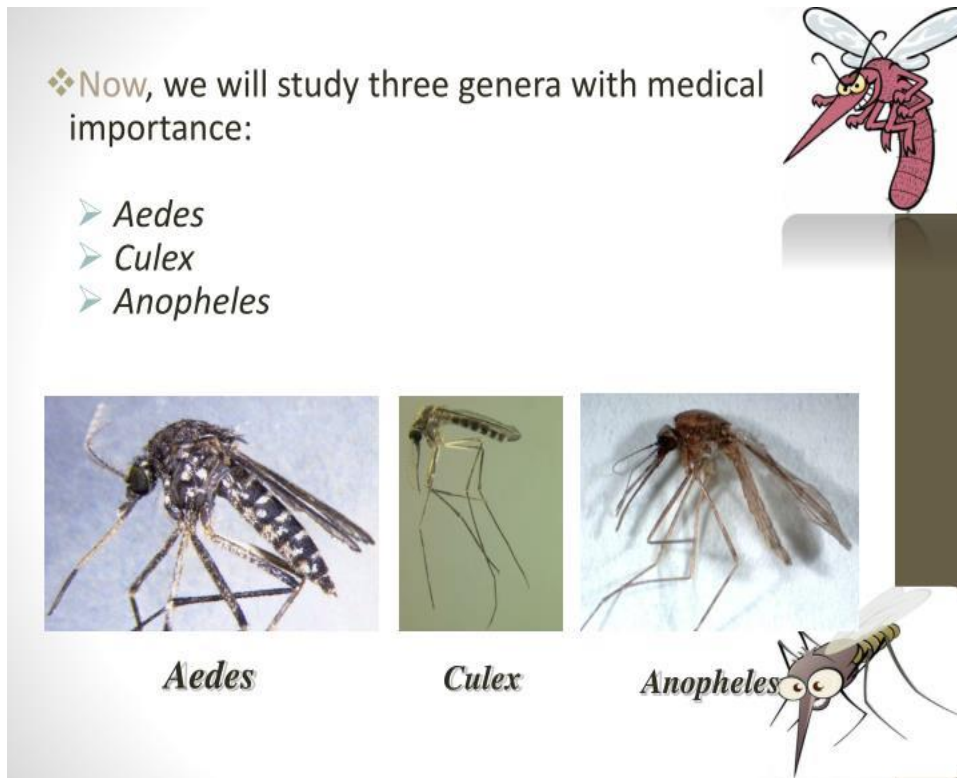
### **C.3. Distribution**

*Culex* species are widely distributed around the world but are absent from extreme northern parts of temperate zones. *Culex quinquefasciatus* is present mainly across tropical and subtropical regions, while *Cx. pipiens* is present across more temperate regions, including parts of North and South America, the Middle East, Africa and Asia. There is some overlap in the distribution of this species with *Cx. quinquefasciatus* in North America (Farajollahi, et al, 2011).

### **C.4. Biting Behaviours**







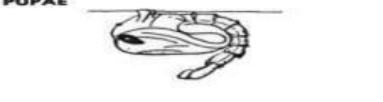


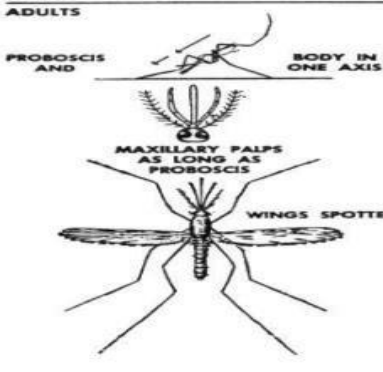
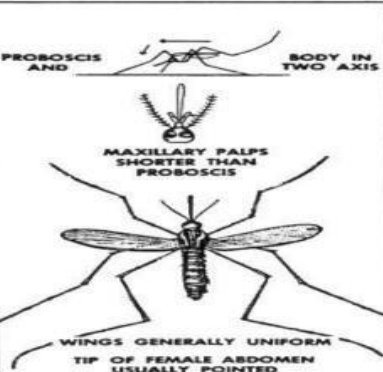
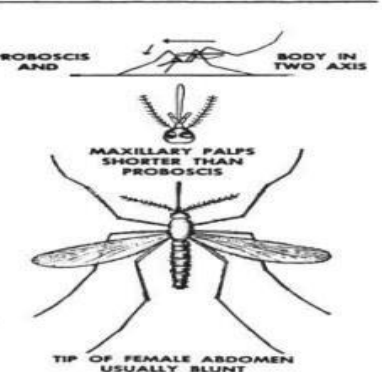
Adult *Culex* mosquitoes feed on a range of hosts, including humans and domestic animals, and birds. Feeding on birds has important implications for the transmission of West Nile virus, as avians can act as reservoir hosts (Julian et al, 2010), (Brugman et al, 2018).

Different species within the genus show different feeding and resting habits. *Culex pipiens* f. *molestus* are endophilic (rest indoors), while *Cx. pipiens* is an exophilic species (rest outdoors). Members of the *Cx. vishnui* subgroup are known to rest and feed outside (Das et al, 2004).



**Fig 03:** *Aedes*, *Culex*, *Anopheles* comparison. (Almuhanna 2012).

**PRINCIPAL CHARACTERS FOR IDENTIFYING  
THE THREE GENERA OF MEDICAL IMPORTANCE**

	ANOPHELES	AEDES	CULEX
<b>EGGS</b>	 <p>LAI D SINGLY HAS FLOATS</p>	 <p>LAI D SINGLY NO FLOATS</p>	 <p>LAI D IN RAFTS NO FLOATS</p>
<b>LARVAE</b>	 <p>REST PARALLEL TO WATER SURFACE RUDIMENTARY BREATHING TUBE</p>	 <p>REST AT AN ANGLE SHORT AND STOUT BREATHING TUBE WITH ONE PAIR OF HAIR TUFTS</p>	 <p>REST AT AN ANGLE LONG AND SLENDER BREATHING TUBE WITH SEVERAL PAIRS OF HAIR TUFTS</p>
<b>PUPAE</b>		 <p>PUPAE DIFFER ONLY SLIGHTLY</p>	
<b>ADULTS</b>	 <p>PROBOSCIS AND BODY IN ONE AXIS MAXILLARY PALPS AS LONG AS PROBOSCIS WINGS SPOTTED</p>	 <p>PROBOSCIS AND BODY IN TWO AXES MAXILLARY PALPS SHORTER THAN PROBOSCIS WINGS GENERALLY UNIFORM TIP OF FEMALE ABDOMEN USUALLY POINTED</p>	 <p>PROBOSCIS AND BODY IN TWO AXES MAXILLARY PALPS SHORTER THAN PROBOSCIS TIP OF FEMALE ABDOMEN USUALLY BLUNT</p>

**Fig 04:** principal characters for identifying the three genera of medical importance (Almuhanna 2012).

## I.2. Mosquito-Borne Diseases:

Mosquito-borne diseases are spread by the bite of infected female mosquitoes. The Main mosquito-borne diseases include malaria, Chikungunya, Zika, Dengue, West Nile, yellow fever, Rift Valley fever, Lymphatic filariasis, and tick-borne encephalitis. Important vectors of the pathogens causing these diseases are mosquitoes belonging to the genera *Aedes*, *Culex*, and *Anopheles*, widely distributed in Africa, Asia, South America, and Europe. Approximately seven hundred million people around the world suffer from mosquito-borne illnesses, resulting in over one million deaths. (Hudson et al, 2023) Of these,

### *malaria*

Which is transmitted to humans by infected female *Anopheles* mosquitoes, poses the most life-threatening conditions. The malaria burden spans from Africa's tropics to Asia and South America. In 2020, an estimated 241 million cases of malaria were reported

worldwide, with 627 thousand people dying, the majority of whom were children in Africa. (Hudson et al, 2023)

### ***West Nile***

Is a mosquito-borne disease caused by the West Nile virus which is an enveloped, positive-strand ribonucleic acid (RNA) flavivirus of the family Flaviviridae.

The virus is primarily responsible for bird infections, especially in crows and blue jays, but it can also infect humans, dogs, horses, and other animals. The mosquito genus *Culex*, especially species such as *Cx. quinquefasciatus*, *Cx. stigmatosoma*, *Cx. thriambus*, *Cx. pipiens*, and *Cx. nigripalpus*, affecting a range of avian and mammalian species are the main vectors

Responsible for the transmission of West Nile virus. However, the virus can also be transmitted by several species of birds. (Hudson et al, 2023).

### ***Dengue (fever)***

Is caused by the Dengue virus, a positive (+)-stranded ribonucleic acid (RNA) virus that also belongs to the genus Flavivirus, and family Flaviviridae.

The virus is mainly transmitted through the bite of an infected female *Aedes aegypti* and *Ae. albopictus*, and zoonotic agents with no known arthropod vector. The disease is the leading cause of morbidity and mortality throughout the tropics and sub-tropics, with an estimated 10,000 deaths and 100 million symptomatic infections per year in over 125 countries. (Hudson et al, 2023).

### ***Yellow fever disease***

Is caused by the yellow fever virus. This flavivirus is endemic in tropical Africa, South America, and North America. Yellow fever can cause extensive epizootics in non-human primates and outbreaks of human cases. Pathogens causing the disease are mainly transmitted in Africa by *Ae. albopictus* and *Ae. Aegypti*. (Hudson et al, 2023).

A component of the sylvatic reservoir system is in the non-human primates. The disease transmission involves urban (human and urban mosquitoes) and sylvatic (non-human primates and forest-dwelling mosquitoes) cycles. Sylvatic cycles account for the majority of the reported cases in South America. By contrast, the intermediate cycle, which involves the transmission of yellow fever virus from monkey to human or from human to human through mosquito bites, is currently only reported in Africa. Chikungunya is caused by an arthropod-

borne alphavirus, Chikungunya virus. This virus is primarily transmitted through the bite of infected *Aedes* (subgenus *Stegomyia*) mosquitoes (e.g., *Ae. aegypti*, *Ae. albopictus*, *Ae. Furcifer*, and other members of the *Ae. furcifer-taylori* group). Chikungunya virus is endemic in tropical and subtropical Africa and Southeast Asia, where transmission cycles between non-human primates and *Aedes* spp. exist. (Hudson et al, 2023).

#### ***Infection with the Rift Valley fever (RVF) virus (Phlebovirus, family Bunyaviridae)***

Is a disease of domestic livestock such as cattle, sheep, and goats, as well as humans. The disease is transmitted by mosquitoes or direct contact with infected animals and their products. Mosquito species, such as *Ae. vexans* (Meigen), *Cx. poicilipes* (Theobald), and *Cx. quinquefasciatus*, are the main vectors responsible for the transmission of RVF. Rift Valley fever is also transmitted by some species of the genus *Mansonia* and. The prevalence of RVF is highest in sub-Saharan Africa but recently the disease has been reported in Arabian Peninsulas and Saudi Arabia. (Hudson et al, 2023).

#### ***The Zika virus disease***

Is caused by a flavivirus. Since 2007, outbreaks of Zika virus have been reported in Micronesia and Brazil. Moreover, from 2015 to 2017, approximately 6000 cases of symptomatic Zika virus disease were reported in the United States of America. Like other flaviviruses, the Zika virus is spread by mosquitoes, primarily the *Aedes* (*Stegomyia*) genus, and species such as *Ae. aegypti*, *Ae. africanus*, *Ae. hensilli*, and *Ae. albopictus* have been implicated. Although viral isolation studies suggest that *Ae. albopictus* was the likely vector in a 2007 Zika virus outbreak in Gabon, the dominant *Aedes* species vector has not been definitively identified in Africa. Other modes of Zika virus transmission include maternal–fetal transmission, sexual transmission, blood transfusions, organ transplantation, and laboratory exposure. (Hudson et al, 2023).

#### ***Lymphatic filariasis (LF)***

Is caused by microfilaria of *Wuchereria bancrofti*, *Brugia malayi*, or *Brugia timori*. Depending on the geographical distribution, different species of the following mosquito genera are vectors of Lymphatic filariasis:

- (i) *Culex* (*Cx. annulirostris*, *Cx. bitaeniorhynchus*, *Cx. quinquefasciatus*, and *Cx. pipiens*).
- (ii) *Anopheles* (*An. arabinensis*, *An. bancroftii*, *An. farauti*, *An. funestus*, *An. gambiae*, *An. koliensis*, *An. melas*, *An. merus*, *An. punctulatus*, and *An. wellcomei*).

- (iii) *Aedes* (*Ae. aegypti*, *Ae. aquasalis*, *Ae. bellator*, *Ae. cooki*, *Ae. darlingi*, *Ae. kochi*, *Ae. polynesiensis*, *Ae. pseudoscutellaris*, *Ae. rotumae*, *Ae. scapularis*, and *Ae. vigilax*); (iv) *Mansonia* (*M. pseudotitillans* and *M. uniformis*); and (v) *Coquillettidia* (*C. juxtamansonia*).

Globally, over 120 million people are affected by Lymphatic filariasis. The disease is endemic in 73 countries, and 1.1 billion people in Asia, Africa, western Pacific, and parts of South America and the Caribbean are at risk of exposure to and contracting the disease. (Hudson et al, 2023).

### ***Tick-borne encephalitis (TBE)***

Is one of the most dangerous infections that can occur in humans. Tick-borne encephalitis virus (TBEV), the causative agent of TBE, is a member of the virus genus *Flavivirus* and the *Flaviviridae* family. Transmitted by the bite of an infected arthropod, specifically mosquitoes and ticks, TBE involves the central nervous system. This disease is very common in Central, Northern, and Eastern European as well as Asian countries. The highest notification rates of TBE in 2020 occurred in Lithuania, Latvia, Slovenia, and the Czech Republic, with incidences of up to 24 cases/100,000 individuals. In these endemic areas, the virus mortality reaches 0.5 to 4%. (Hudson et al, 2023).

## **2. The Nanoparticles (NPs):**

the necessity for more biodegradable and target-specific mosquitocidal treatments, Considering 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. It takes advantage of the material's properties at the nanometric scale through a top-down approach. 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. (Hudson et al, 2023).

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 (Hudson et al, 2023).

### **2.1. Major type of Nanoparticles:**

Nanoparticles are categorized into four groups based on structural morphology: Organic, inorganic, carbon-based, and composite. Some of the most important types of nanoparticles are listed below:

- **Organic nanoparticles**

Organic nanoparticles, derived from compounds like proteins, carbohydrates, lipids, and polymers, encompass micelles, dendrimers, liposomes, nanogels, polymeric NPs, and ferritin. Generally non-toxic and biodegradable, they may have a hollow core, such as liposomes, and are sensitive to thermal and electromagnetic radiation. Formed through noncovalent interactions, these labile organic NPs are easily cleared from the body. Nanospheres or nanocapsules, common polymeric forms, collectively referred to as labeled polymorphic NPs, possess properties like a high surface area to volume ratio, stability, inertness, ease of functionalization, and unique optical, electrical, and magnetic behaviors, making them suitable for applications in drug delivery, imaging, biosensors, and cancer treatment. (Mandodan, et al 2023).

- **Inorganic nanoparticles**

Inorganic nanoparticles, devoid of carbon atoms, are hydrophilic, non-toxic, and biocompatible, providing high mechanical strength and stability. Precise control over size,

shape, and composition allows researchers to design nanoparticles with tailored electrical, optical, and magnetic properties for targeted biomedical applications (Mandodan, et al 2023).

- **Metal-based nanoparticles**

Metal-based nanoparticles, derived from various metals through disruptive or constructive methods and typically ranging in size from 10 to 100 nm, including aluminum (Al), cadmium (Cd), cobalt (Co), copper(Cu), gold (Au), iron (Fe), lead (Pb), silver (Ag), and zinc (Zn), exhibit unique optoelectrical properties due to localized surface plasmon resonance. Specifically, alkali and noble metals like Cu, Ag, and Au, when utilized in nanoparticle construction, show significant absorption in the visible region of the solar spectrum. The synthesis of metal nanoparticles with specified facets, sizes, and forms necessitates controlled conditions, and their advanced optical properties make them versatile across various research domains. (Mandodan, et al 2023).

These nanoparticles, distinguished by their small dimensions and surface properties, including pore size, surface charge, etc., find applications in biomedical science, such as cancer treatment, disease diagnostics, radiation enhancement, drug delivery, and gene transport. (Mandodan, et al 2023).

- **Metal oxide based nanoparticles:**

Metal oxide nanoparticles result from modifying the properties of metal-based nanoparticles. These nano-scale metal oxides find diverse applications in fluorescence, optical sensors, catalysts, biomedicine, gas sensors, and fuel cell anode materials. Various synthesis methods, including inert gas condensation, co-precipitation, and lithography, have been used, but traditional methods often lack control over morphological structure, affecting essential nanomaterial properties. (Mandodan, et al 2023).

- **Ceramic nanoparticles:**

Ceramic nanoparticles, resistant to environmental stresses, form with a solid core through heat or a combination of heat and pressure, incorporating metallic or non-metallic elements. Typically composed of inorganic compounds like silica or alumina, they may also include metals and metal oxides, yielding diverse nanomolecules with varying shapes, sizes, and porosities. Engineered to evade the reticulo-endothelial system, ceramic NPs undergo size and surface composition modifications. Widely used in medical applications,

ceramics such as calcium phosphates, alumina, silica iron oxides, carbonates, and titanium dioxide have been found. Ceramics also play an important role in various applications in photocatalysis, dye photodegradation, imaging, and catalysis. Researchers aim to develop advanced ceramics with minimal cytotoxicity and enhanced biocompatibility, addressing challenges through innovative strategies that integrate ceramic nanoparticles with biocompatible materials, considering characteristics like shape, size, and physicochemical attributes. (Mandodan, et al 2023).

- **Lipid-based nanoparticles:**

Lipid-based nanoparticles (LBNPs), typically 10-100 nm in diameter, consist of a lipid core surrounded by lipophilic molecules, finding applications in oncology and biomedicine. Liposomes, a key type of LBNP, use a phospholipid bilayer for enhanced drug solubility and stability, accommodating both hydrophobic and hydrophilic molecules. Incorporating cholesterol improves stability, decreases fluidity, and enhances permeability for hydrophobic drugs in liposomal formulations. Solid lipid nanoparticles, sized between 50-1000 nm, and composed of physiological lipids in a solid state; offer a compelling alternative for drug delivery, featuring a matrix of mono-, di-, or triglycerides, fatty acids, and complex glyceride mixtures, with stability ensured by surfactants or polymers. (Mandodan, et al 2023).

- **Semiconductor nanoparticles:**

Semiconductor nanoparticles, possessing hybrid characteristics of metals and nonmetals, have garnered attention for their versatility in diverse applications. Their crucial broad bandgap, adjustable by researchers, makes them valuable in photocatalysis, photo optics, and electronic devices. Additionally, their nanoscale dimensions provide benefits such as increased surface area-to-volume ratio, enhanced quantum confinement effects, and improved catalytic activity, contributing to exceptional performance in various applications. (Mandodan, et al 2023).

- **Quantum dots:**

Quantum dots (QDs), semiconductor nanoparticles with size- and composition-dependent optoelectronic properties (1.5 to 10.0 nm), play a significant role in the electronic and biomedical industries. Their success is attributed to superior features like photostability, size-dependent optical properties, high extinction coefficient,

brightness, and a large Stokes shift, overcoming limitations of organic dyes. (Mandodan, et al 2023).

QDs, due to their ultra-small size, are well-suited for imaging and biosensing applications. They facilitate the development of multimodal/multifunctional probes with increased surface area for optical trackability in vitro and in vivo, designed to detect pH, metal ions, DNA, and enzyme activity, and deliver various therapeutics. (Mandodan, et al 2023).

- **Carbon-based nanoparticles:**

Carbon-based nanoparticles encompass five main materials: carbon nanotubes, graphene, fullerenes, carbon nanofiber, and carbon black, each with unique structural configurations and diverse applications in nanotechnology. (Mandodan, et al 2023).

- **Graphene:**

Graphene, a two-dimensional carbon allotrope, is a single layer of carbon atoms arranged in a hexagonal lattice with exceptional properties, such as elasticity, mechanical strength, and unparalleled thermal and electrical conductivity. Synthesized in the laboratory, it forms a 1nm-wide honeycomb lattice, exhibiting semiconductor properties without an effective mass and zero band gap. Graphene demonstrates an ambipolar electric field effect, with a breaking strength of 42 Nm<sup>-1</sup> and a Young's modulus of approximately 1.0, making it the strongest material ever tested. These attributes position graphene as a promising material for electrical and photonic devices, sensing platforms, and clean energy applications (Mandodan, et al 2023).

- **Fullerene:**

Fullerenes, a molecular form of carbon allotrope, consists of C<sub>n</sub> clusters (n > 20) arranged on a spherical surface with carbon atoms at pentagon and hexagon vertices. The extensively studied C<sub>60</sub> fullerene, composed of 60 carbon atoms, is highly symmetric and spherical, with a 0.7 nm diameter and sp<sup>2</sup> hybridized carbon atoms. Exhibiting exceptional symmetry and stability, fullerenes have 20 tripled axes, 12 fivefold axes, and 30 twofold axes. These unique properties position fullerenes as promising nanoparticles widely utilized in biomedical sciences, acting as inhibitors for human immunodeficiency virus, contrast agents for magnetic resonance imaging, and sensitizers for photodynamic therapy. (Mandodan, et al 2023).

- **Carbon nanotubes:**

CNTs, unique in carbon-based nanomaterials, possess versatile characteristics like length, diameter, chirality, and layer number, showcasing exceptional properties and widespread applications. Composed of graphite, CNTs, typically with at least two layers and an outer diameter ranging from 3 nm to 30 nm, are divided into two categories: single-walled nanotubes (SWCNTs) and multi-walled nanotubes (MWCNTs). SWCNTs, with a diameter of around 1 nm, exhibit high electrical conductivity, mechanical strength, and thermal conductivity due to their nearly one dimensional structure, indicated by a length-to-diameter ratio of approximately 1000. MWCNTs, robust cylindrical structures with a minimum diameter of 100 nm, demonstrate resilience and diverse structures rooted in grapheme sheets, with an interlayer distance resembling that in graphite, about 3.3 Å. The initial proposal for gram-scale synthesis of double-walled carbon nanotubes in 2003 involved chemical vapor deposition, selectively reducing oxide solid solutions in methane and hydrogen. Applications of CNTs include bicables, AFM tips, hydrogen storage, electrochemical electrodes, nanocomposites, field emission displays, and diverse electrical devices. (Mandodan, et al 2023).

- **Composite nanoparticles:**

Composite nanoparticles are produced via the integration of two or more different components. The components bear different properties at the nanoscale level. This integration of diverse components eliminates the limitation of individual components which enables researchers to produce nanomaterials with specific properties and uses. These NPs exhibit unique physical and chemical properties and each component has strong mutual coupling effects on the other. The chemical properties of composite nanoparticles depend on their composition and structure. The mutual coupling effect between the components of composite NPs can lead to changes in the chemical properties of composite NPs. Composite NPs are used in a variety of applications including electronics, optoelectronics, and biomedical sciences. (Mandodan, et al 2023).

Composite nanoparticles can be classified into three main categories based on their structural features:

**Simple hybrid NPs:**

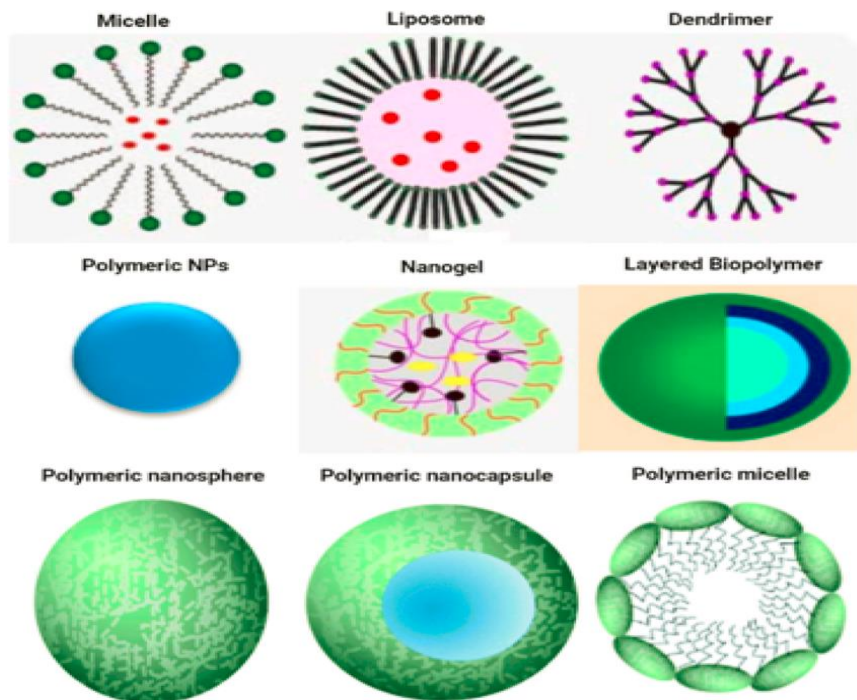
These types of composite NPs formed by combining two or more components without a specific structural hierarchy. They exhibit unique properties due to the combination of different materials. (Mandodan, et al 2023).

- **Core or shell structured composite NPs:**

These NPs are made up of two different regions: an inner core region and an outer shell. These two regions of NPs are composed of two or more different materials. The core and shell structure influences the properties of the nanoparticles, such as electromagnetic wave attenuation capacity, etc (Mandodan, et al 2023).

- **Multifunctional quantum NPs:**

These NPs have multiple functionalities, such as magneto-optical, and electrochemical properties. The specific structure of Multifunctional Quantum Composite NP is used in applications like biosensing, bioassays, catalysis, and separations (Mandodan, et al 2023).



**Fig05:** the schematic diagram of organic nanoparticles (Alshammari et al, 2023).

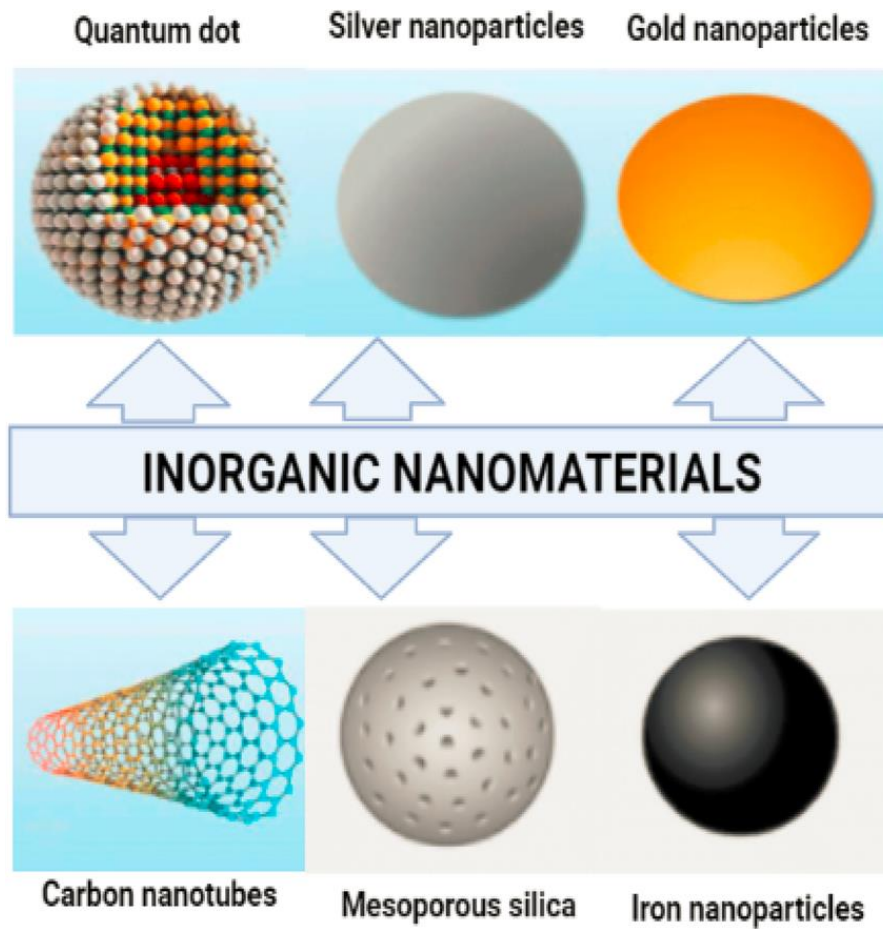
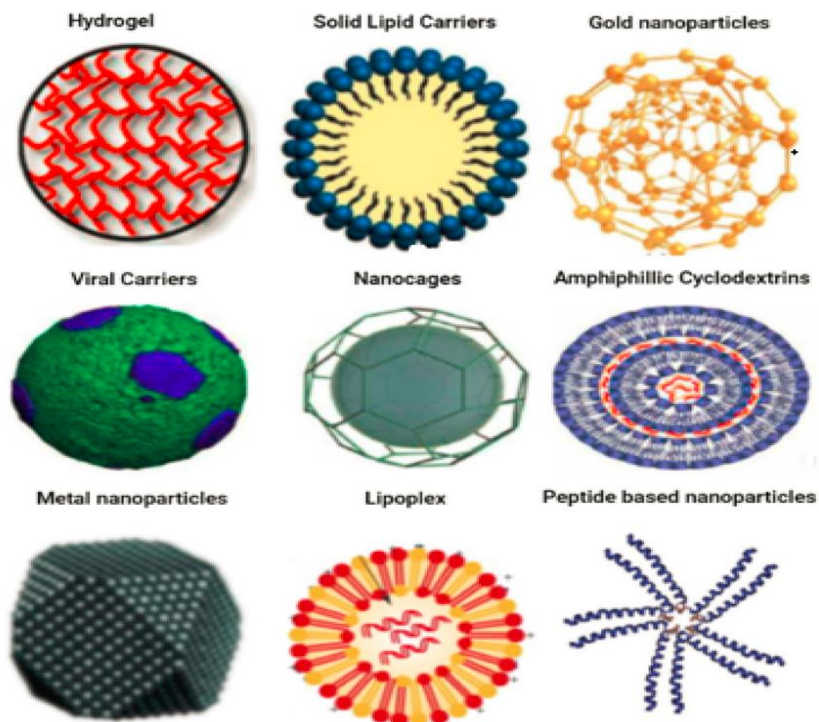


Fig 06: the schematic diagram of inorganic nanoparticles.(Alshammari et al, 2023).



**Figure 07:** the schematic diagram of metal nanoparticles.(Alshammari et al, 2023).



**fig08:** Inorganic nanomaterials.(Alshammari et al, 2023).

## 2.2 Application of NPs in Vector-Insects:

### A. Toxicity of NPs to Insects.

The application of NPs obtained through various synthetic pathways as new pesticides has attracted more attention recently. In the last 5 years, more than 600 studies outlining the toxicity of NPs towards various vector-insects have been published. These NPs including gold, silver, titanium oxide, semiconductors, and silica-based nanomaterials have been tested against a wide range of vectors, covering mosquito, lice, and fly. Among all, the large majority of the researchers focused on mosquito vectors due to their huge ecological and physiological plasticity. According to research, most of NPs have obvious acute toxicity against mosquito (table1). (Danyue et al, 2023).

For example; the effectiveness of *Nelumbonucifera* synthesized Ag NPs against larvae of *An.Subpictus*(LC50 = 0.69 mg/L) and *Cx. Quinquefasciatus*(LC50 =1.10 mg/L).

Palanisamy describes the toxicity of Ag NPs biosynthesized using cheap leaf extract of *Berberis tinctoria* against larval instars (I–IV) of *Ae. Albopictus* with LC50 of 4.97 ppm (I instar), 5.97 ppm (II), 7.60 ppm (III), and 9.65 ppm (IV). (Danyue et al, 2023).

Notably, the NPs obtained as described above showed different toxicity against mosquitoes, even if they are the same NPs. (Danyue et al, 2023).

Barik tested the three types of silica NPs, including lipophilic, hydrophilic, and hydrophobic, to assess the larvicidal properties of different mosquito species. (Danyue et al, 2023).

In *Ae. aegypti*, the LC50 was 5-fold less than hydrophilic when treated with hydrophobic silica NPs. (Danyue et al, 2023).

Besides, a recent review by Benelli pointed out that NPs could not only be used as mosquito larvicides, ovicides, and adulticides but also reduce mosquito longevity and fecundity. In Thelma’s work, the synthesized Ag NPs exhibited significant ovicidal activity. (Danyue et al, 2023).

**Table 1**

**Various NPs with their applicative measures against the different mosquito species [Danyue Nie et al, 2023]**

Nanoparticles	Source	Target species	Lethal indices (LC <sub>50</sub> )
Ag		<i>Ae. aegypti</i>	13.96 ppm
Ag	<i>Bacillus marisflavi</i>	<i>Cx. quinquefasciatus</i>	24.54 ppm
Ag		<i>An. stephensi</i>	29.14 ppm
Ag		<i>Ae. aegypti</i>	17.578 µg/mL
Ag	<i>Ipomoeabatatas</i>	<i>Cx. quinquefasciatus</i>	10.069 µg/mL
Ag		<i>An. stephensi</i>	12.568 µg/mL
Ag		<i>Ae. aegypti</i>	26.35 µg/mL
Ag	<i>Cassia roxburghii</i>	<i>Cx. quinquefasciatus</i>	28.67 µg/mL
Ag		<i>An. stephensi</i>	31.27 µg/mL
Au	<i>Parmelia sulcata</i>	<i>Ae. aegypti</i>	70.16 ppm
ZnO	<i>Cucurbita</i>	<i>Cx. tritaeniorhynchus</i>	39.007 ppm

Nanoparticles	Source	Target species	Lethal indices (LC <sub>50</sub> )
ZnO	Chemical method	<i>Cx. quinquefasciatus</i>	291.0 mg/L
ZnO	<i>Pseudomonas aeruginosa</i>	<i>Culex pipiens</i>	75 ppm
ZnO	<i>Cucurbita</i>	<i>Cx. tritaeniorhynchus</i>	44.68 ppm
MgO	<i>Penicillium chrysogenum</i>	<i>An. stephensi</i>	12.5–15.5 ppm
MgO	Chemical method	<i>Cx. quinquefasciatus</i>	83.4 mg/L
CuO	Chemical method	<i>Cx. quinquefasciatus</i>	100.8 mg/L
CuO	<i>Tridaxprocumbens</i>	<i>Ae. aegypti</i>	4.209 mg/L
SiO <sub>2</sub>	Chemical method	<i>Cx. quinquefasciatus</i>	27.81 mg/L
Se	<i>Nilgirianthusciliatus</i>	<i>Ae. aegypti</i>	0.92 mg/L

### B. Different type of Nanoparticles against Insects:

The analyse of many journal articles which adopted to search the following keywords initially: “nanoparticles against insect,” “NPs against insect,” and “metal nanoparticles against insect,” in PubMed. The three major types of nanoparticles (NPs) were identified (Danyue et al, 2023) :

**Type 1:** are metal-based NPs (for example, Ag, Cu, and Ti) which is the most widely used to resist insect.

**Type 2:** are nonmetal-based NPs (for example, Si and Ca).

**Type 3:** include some complex polymers (for example, chitosan and plant extract). For Type 1 reagents, the element with the largest proportion is Ag, due to its significant impact on insect antioxidant and detoxifying enzymes, leading to ROS-mediated apoptosis, DNA damage, and autophag. In Type 1, most metals work in this way. (Danyue et al, 2023). However, the main insecticidal principle is different in Type 2; for example, the toxicity of SiO<sub>2</sub> NPs is due to desiccation, body wall abrasion, and spiracle blockage, followed by physical sorption of waxes and lipids, leading to insect dehydration. (Danyue et al, 2023). In addition, nanomaterials used as insecticides can be classified according to different functions.

Type 1 mainly includes NPs for directly using as insecticides, and metal-based NPs are the most widely applied in this type. (Danyue et al, 2023). In Type 2, NPs serve as carriers to encapsulate active ingredients to control insects. The first nanoabamectin pesticide recently approved in China adopts the three-dimensional reticulated nanomaterials as the carrier and uses the reticulated nanoscale drug-loading space inherent in the structure of nanomaterials to achieve encapsulation of raw materials without agglomeration.(Danyue et al, 2023).

### **C. Different Methods of NPs Synthesis:**

According to the discipline classification of synthesizing NPs, it can be divided into physical, chemical, and biological methods.

The physical method refers to slicing bulk material to get nanosized particles, which mainly includes vacuum condensation, the evaporation-condensation method, and the mechanical ball grinding method. (Danyue et al, 2023).

Conversely, the chemical method creates nano-structures by controlling the deposition and growth of atoms and molecules, including solvo-thermal, sol-gel, and microemulsion methods. As the most widely used chemical method, the superior advantage of the solvothermal method is the use of no catalysts, but the synthesis mostly prefers toxic solvents to fabricate required materials. (Danyue et al, 2023). However, with the development of synthetic technology, many simpler methods without the use of harsh chemicals to prepare NPs were presented. (Danyue et al, 2023). Li reported a novel solvo-thermal approach to synthesizing carbon nanoparticles (CNPs), in contrast with previous methods, this synthesis process uses glucose and ammonium oxalate as the carbon source and glycol as the solvent, and neither strong acid treatment nor further surface modification was necessary. The current advancements in solvo-thermal synthesis methods for NPs indicate that there are many chemical synthesis research opportunities (Danyue et al, 2023).

Nevertheless, the latest research proposal is the biological method. Nowadays, 1917 articles have been published on PubMed in 2021 (keywords: bio nanoparticle). As an emerging green-synthesis strategy in nanotechnology, the biological method uses living templates that include plants and microorganisms such as plant extracts, viruses, bacteria, and other biomolecules for the synthesis of NPs. (Danyue et al, 2023). Recently, products approach to synthesizing NPs has focused on the use of plant components. These plant-derived nanopesticides can also be subdivided into different types based on their usage, such as plant-derived NPs and nano-emulsions prepared with essential oils extracted from plant

parts. For example, iron oxide (Fe<sub>3</sub>O<sub>4</sub>) NPs are synthesized by a *RhusCoriaria* extract and possess better and enhanced properties than the chemical method, and Copa Plunano-emulsion also showed great antibacterial activity against *Paracoccidioides*. (Danyue et al, 2023). In addition, plants such as *Melia azedarach* leaf, *Azadirachtaindica* leaf, and *Nasturtium officinale* are also explored for the synthesis of Cu-ZnO, CuO, and MoO<sub>3</sub> NPs. (Danyue et al, 2023).

Generally speaking, bioderived NPs are regarded as safe, biocompatible, and environmentally friendly particles that cause less harmful effects to human health. (Table 2).

**Table 2 [Danyue Nie et al, 2023]**

Advantages and disadvantages of different synthesis methods.

	<b>Advantages</b>	<b>Disadvantages</b>
Physical methods	Simple methodology	The lower yield of NPs Higher energy-consuming Higher input cost
Chemical methods	Homogenous NPs with high accuracy The consumption of less energy	The usage of toxic chemicals
Biological methods	Do not involve toxic chemicals in the preparation protocols	Highly demanding Time-consuming Requiring technology and practical microbiological experience to ensure cell culture and nanoparticle purification under aseptic conditions

**D. Mode of Action of NPs against Vector Insects:**

Studies have shown that the insecticidal effect of NPs on vector insects occurs in the following ways:

- Due to the scale effect of NPs, the adhesion of pesticides in the environment can be improved, increasing the possibility of insect exposure to NPs in the environment. After that, NPs could dehydrate cells through stratum corneum adsorption, leading to several morphological and histological abnormalities in insects. (Danyue et al, 2023).

Among different NPs, silica and aluminum are represented to bind with the cuticle layer of ticks, leading to physical uptake of lipids and waxes, cell dehydration, and eventual cell death. Experiments by Sultana found that the carbon-dotted silver NPs had high toxicity to *Anopheles stutzeri* and *Culex quinquefasciatus*. SEM analysis in this experiment showed that the above carbon-dotted silver NPs caused deformation of larvae, while X-ray analysis proved nanohybrids in the treated. (Danyue et al, 2023). The presence of Ag in mosquito tissues suggests that their death may be due to the toxicity of nano-Ag at the cellular level. In addition, HR-TEM also showed stratum corneum and cellular tissue damage. Third-instar *Aedes aegypti* larvae exposed to ZnO NPs (1.57 mg/mL, 24 hours) prepared from Lobelia were found to have abdominal contractions, altered thorax shape, midgut lesions, and loss of lateral hairs, anal gills, and brushes, while the accumulation of ZnO NPs was observed in the chest and abdomen(Danyue et al, 2023).

- NPs enter the insect body, causing oxidative stress in the insect, destroying the protein in the insect body, and disturbing the normal physiological function of the insect. *In vivo* studies, DNA damage and oxidative stress have been found when cellular uptake NPs. Previous research studies have shown that NPs have insecticidal activity due to its cytotoxicity. Some NPs, such as TiO<sub>2</sub>, can absorb UV in the environment, the electrons are excited to become highly active after absorbing energy, and holes are generated in the valence band. (Danyue et al, 2023). The oxygen in the air combines with the e<sup>-</sup> to produce O<sub>2</sub><sup>-</sup>. H<sub>2</sub>O undergoes oxidation reaction with produced holes to generate reactive oxygen species (ROS), such as H<sub>2</sub>O<sub>2</sub>, O<sub>2</sub><sup>-</sup>, and H<sub>2</sub>O<sub>2</sub> reacting with glycosides, unsaturated fatty acids, proteins, and other substances in the cell, resulting in the death of cells. Besides, the metal ions contained in the material enter the cell during the process of outward release and bind to the amino acids S and P in proteins, reducing cell membrane permeability. (Danyue et al, 2023). Once inside cells, NPs may cause damage to DNA and inhibit the activity of intracellular enzymes. Very recently, Chimkhan outlined that Ag NPs ingested by *Bacillus thuringiensis* led to mortality and detrimental effects on *Aedes aegypti* larvae. The results showed that six protein expressions in *A. aegypti* larvae were involved in DNA and protein damage, inhibition of cell proliferation, and cell apoptosis, indicating that NPs can affect basic physiological regulation in insects (Danyue et al, 2023).
- The expression of target genes in insects is affected after NPs enter the body of the insect. The effect of NPs on gene expression in insects was published in 2011, and

Nair and Choi evaluated the expression of GST genes, which are linked with the occurrence of oxidative stress after *Chironomus riparius* had been exposed to the different concentrations of Cd and Ag NPs for various time (Danyue et al, 2023). The result shows that all GST genes have up-down regulation to varying levels; among them Delta3, Sigma4, and Epsilon1 GST classes have the highest expression levels. (Danyue et al, 2023). However, the expression of genes is not static. Studies have shown that after short-term (24 h) exposure to nanoinsecticides, the expression of detoxification-related genes decreases, but after long-term (48 h) exposure, the expression of detoxification-related genes (*P-gp* and *hr96*) increases significantly. Expression of reproductive system-related genes (*cyp314*, *vtg*, and *dmrt93*) varies with concentration and time. Recently, Zhang analyzed the effect of lufenuron/SPnano-complexes on insect gene expression by RNA-seq technology and found that it not only significantly downregulated insect cuticle-related genes (*cut*) and inhibited the formation of insect cuticles but also upregulated endocytosis-related genes, promoting drug intake. This suggests that NPs can improve insect toxicity by affecting insect gene expression (Danyue et al, 2023).

#### **E. The Safety of the NPs:**

The small size, large surface, and more active area account for the extensive use of NPs in various applications, such as in drug delivery, diagnostics, food science, electronics, and several other biological and non-biological areas. With the increased interest in nanotechnology in the last decade, the safety of NPs in the environment has also been considered. (Danyue et al, 2023). Therefore, in addition to the toxicity of NPs to vector insects, the impact of NPs on nontarget organisms in the environment has become the focus of attention. In a study, Chakraborty et al. used zebrafish as a model organism to investigate the toxic effects of silver NPs, gold NPs, and several metal oxide NPs (TiO<sub>2</sub>, Al<sub>2</sub>O<sub>3</sub>, CuO, NiO, and ZnO) on it. The correlation between successful hatching efficiency and embryotoxicity is an important parameter for evaluating nanotoxicity. (Danyue et al, 2023). The researchers learned about embryotoxicity by assessing the relationship between hatching success and hours after exposure to TiO<sub>2</sub> NPs. (Danyue et al, 2023). The study found that titanium dioxide NPs can cause premature hatching of zebrafish embryos in a dose-dependent manner. (Danyue et al, 2023). Through gene ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) enrichment analyses, Lu et al. found that silver NPs caused the

accumulation of reactive oxygen species (ROS) and malondialdehyde (MDA) in zebrafish embryos, inhibiting the superoxide dismutase (SOD), catalase (CAT), and mitochondrial complex I-V activity, and down regulated the expression of SOD, CAT, and mitochondrial complex I-IV chain-related genes, ultimately leading to zebrafish embryotoxicity. However, some studies have also shown that TiO<sub>2</sub> NPs can reduce the toxicity of pesticides to zebrafish. To study the bioconcentration and cardiotoxicity mechanism of azoxystrobin (AZ) under the action of TiO<sub>2</sub> NPs, zebrafish embryos were exposed for 72 h after fertilization. (Danyue et al, 2023). The results showed that the presence of TiO<sub>2</sub> significantly reduced AZ accumulation in larvae compared with AZ alone and thus notably decreased AZ-induced cardiotoxicity, including changes in gene expression of heart rate, pericardium edema, venous thrombosis, sinus venosus, (Danyue et al, 2023).

and bulbus arteriosus distance. This suggests that insecticides mixed with NPs help to slow the release of active molecules, thereby helping to reduce the toxic effects of insecticides. (Danyue et al, 2023). The effects of Ag NPs synthesized by *T. asiatica* aqueous extract on the predation rate of *Culex quinquefasciatus* by zebrafish were also evaluated in indoor and field experiments. (Danyue et al, 2023). It was found that the predation of mosquito larvae was slightly higher than in normal laboratory conditions in the silver-exposed environment, indicating that Ag NPs can be used at low doses to reduce the number of mosquito vectors without adversely affecting the predation of natural enemies. (Danyue et al, 2023). In addition to acute toxicity, whether NPs have long-term toxicity to organisms has also been investigated. Al<sub>2</sub>O<sub>3</sub> NPs and ZnO NPs are fed uninterrupted daily to rats for 75 days, and the result found that NPs caused hepato-renal toxicity at all parameter levels and inhibited the expression of mitochondrial transcription factor A gene and peroxisome proliferator-activated receptor gamma coactivator. (Danyue et al, 2023). Chronic exposure of the Northern Pike (*Esox lucius*) and their primary prey species Yellow Perch (*Perca flavescens*) to Ag NPs caused the length- and weight-at-age (indices of growth rate) of the Northern Pike decline and the per capita availability of Yellow Perch declined by over 30%. Despite considerable efforts to understand the toxicity and safety of these NPs, many of these questions are not yet fully answered. (Danyue et al, 2023). The differences in the toxicity of these NPs may depend on their biophysical properties, including size, surface area, surface charge, and aggregation state, which have been shown to influence the distribution and deposition of NPs in different organ systems and alter their molecular interactions with various proteins and other macromolecules. (Danyue et al, 2023).

**Chapter II:**  
**Analysis and discuss**

## **A. Methodology:**

### **A.1 Search strategy:**

Five reviews articles were selected for inclusion in this comparative study through a purposive sampling method. The articles were sourced from a variety of databases including PubMed/MEDLINE, Scopus, frontieres, to ensure a large representation of perspectives and findings. The selection process was guided by the relevance of the articles to the topic of vector-borne diseases and the use of nanoparticles, as well as their availability in english language and accessibility.

*"Purposive sampling" is a non-probability sampling method where researchers deliberately select certain elements that they believe will best serve the purpose of the study. In our context of methodology, it means that we intentionally chose specific review articles that we believe they are relevant and important for our research objectives.*

*Instead of randomly selecting articles from the available pool, purposive sampling allows us to target specific sources that are expected to provide valuable insights or represent particular perspectives on the topic.*

*In our study, we used purposive sampling to handpick 5 review articles from different databases, aiming to ensure diversity in perspectives and coverage of important outcomes related to vector-borne diseases and the use of nanoparticles. This deliberate selection process allows us to focus on certain relevant literature and extract key insights for comparison and analysis.*

### **A.2 Data Extraction Process:**

Data extraction was performed iteratively to capture key information and outcomes from each review article. A standardized data extraction form was not used due to the exploratory nature of the study. Instead, special focus was placed on identifying and synthesizing the most pertinent findings and insights from the selected articles.

Key outcomes and themes from each review article were extracted, including but not limited to:

- 1- Types of vector-borne diseases discussed
- 2- Nanoparticle interventions and their mechanisms of action
- 3- Efficacy and limitations of nanoparticle-based approaches
- 4- Future directions and recommendations for research and application

### A.3 Limitations:

It is important to acknowledge the limitations inherent in this methodology. The selection of review articles was not based on strict inclusion/exclusion criteria, which may introduce bias and limit the generalizability of the findings.

### B. Reviews articles:

**Table :03**

<u>Title</u>	<u>Author</u>	<u>Year</u>	<u>Journal</u>	<u>Objective</u>	<u>Method</u>
1. Efficacy of metal nanoparticles as a control tool against adultmosquito vectors.	Indra Vythilingam University of Malaysia	2022	Frontiers	analyze the current literature on green synthesized metal nanoparticles and their effect on adult mosquitoes.	Literature review
2. Nanoparticles: A Potential and Effective Method to Control Insect-Borne Diseases	Demetrio Milea University of Italy	2023	Hindawi	analyzed 425 works, focus on application and development of nanoparticles (NPs) for vector control, discussing the mechanism of action.	Literature review
3. A Review on Nanoparticles in Mosquito Control - A Green Revolution in Future	Priya S University of India	2015	ResearchGate	Assesment of green synthesis nanoparticles in mosquito control.	Literature review.
4. Insecticidal efficacy of nanomaterials used to control mosquito, <i>Culex quinquefasciatus</i> Say, 1823 with special reference to their hepatotoxicity in rats		2022	PortlandPress	evaluate different nanoparticles (silver, chitosan and lavender) as an effective method for controlling the mosquito <i>Culex Quinquefasciatus</i> . Assessing the hepatotoxicity in rats as a non-target mammalian model.	Research article
5. Mosquito-borne diseases and their control strategies: An overview focused on green synthesized plant-based metallic nanoparticles.	Guido Favia University of Camerino_ ITALY	2023	Insects MDPI	Present the different mosquito vector control approaches with a focus on greenly synthesized nanoparticles.	Review article

**1. Review article N°1:title:** Efficacy of metal nanoparticles as a control tool against adult mosquito vectors: A review

- **Summary of key finding :**

- The majority of studies have been limited larvicidal efficacy.
- Synthesizing of metal NPs requires 3 main components: source of metal ion, reducing and stabilizing agent.
- Efficacy proven of green NPs biosynthesis on mosquitos larvae, even though, most of the studies focused on metal choice, probably due to the low cost and availability of such materials.
- Green biomaterials can incorporate compounds which can have demonstrated toxic effects against mosquitos at different stages of mosquito life cycle, and can have a diversity of mode of actions at different level ex: nervous system, reproduction system, enzyme synthesis...
- Increasing levels of insecticide resistance across mosquito population globally have also diminished the potency of current insecticides and new active ingredient are needed to maintain effectiveness of mosquito control.

- **Discussion of NPs application:** nanoparticles has grown as apotential tool in insecticide application due to their unique properties, such as a high surface area-to-volume ratio, enhanced reactivity...

Increasingly, plants are being used in the production of NPs because of the use of their natural stabilizing and reducing agents. It comprised different phytochemicals, metabolites and volatile bioactive compounds which have demonstrated toxic effects against mosquitos, acting as lavicides, pupicides, adulticides and repellents throught different mechanisms such as: disruption of receptor sites of the nervous system.

- **Larvicides approach:**

**1. Selenium nanoparticles:** exhibited LC50 of 99.6, 104.13 and 240.7 µg/mL when administered to larvae of *Anopheles stephensi* (List.), *Aedes aegypti* (Linn.), and *Culex quinquefasciatus* (Say) respectively.

**2. Gold nanoparticles:** has demonstrated slightly stronger toxicity with LC50 of 25.92 and 28.64 µg/mL against *An. stephensi* and *Ae. aegypti* respectively.

**3. Silver nanoparticles (AgNP)** synthesized via plant extracts have demonstrated a wide range of larvicidal efficacy against multiple species with LC50 values between 0.3 to 130.3 µg/mL

- **Adulticides approach:**

Most of the nanoparticles (NPs) discussed in the article were predominantly biosynthesized using plant extracts, bacteria, and fungi. Among these, silver nanoparticles were the most commonly synthesized and tested. There were also instances of gold and zinc nanoparticles being utilized, even these were less frequent.

The gold nanoparticles evaluated against the malaria vector *An. stephensi* were demonstrated to have an LC50 at 11.23 µg/mL whereas zinc nanoparticles were shown to reduce longevity in the same mosquito species when exposed to concentration between 2-10 ppm

- **Strengths and limitations:**

- **Strengths:**

Nanoparticles offer precise targeting of mosquito larvae and adults, minimizing non-target effects and environmental contamination. The biosynthesized AgNPs were effective against specific mosquito species without harming other organisms.

The use of biosynthesized NPs, such as those derived from plant extracts, offers an environmentally friendly alternative to chemical synthesis, reducing the ecological footprint of vector control measures.

The amplification and synergistic effects of various types of nanoparticles when combined with existing pesticides can significantly reduce the need for frequent applications and lower overall usage.

- **Limitations :**

Increasing insecticide resistance in mosquito populations worldwide has reduced the effectiveness of current insecticides, necessitating the development of new active ingredients (AIs) to sustain mosquito control efforts.

There is no consistent methodology for evaluating the toxicity of nanoparticles. According to WHO guidelines, novel insecticides must undergo three testing phases:

(1) inherent toxicity evaluations,

- (2) smallscale studies and outdoor semi-field applications and
- (3) operational trials against field populations with before and after measurements of mosquito population abundance.

But metal nanoparticles in mosquito control research have only reached the first phase.

One hypothesis suggests that metal nanoparticles disrupt cellular membranes and detoxification enzymes, leading to cell dysfunction and death. However, the exact mechanism of nanoparticle-induced mortality is not fully understood and requires further research.

**2. Review article N°2: title:** Nanoparticles: A Potential and Effective Method to Control Insect-Borne Diseases.

- **Summary of key finding:**

- There are no effective vaccines or drugs for most VBDs due to the amazing rate of mutation of the virus.
- Researchers found that where more than 113 residue of pesticides in drinking water samples from 31 countries worldwide.
- Gold nanoparticles are not the only kinds of nanoparticles effective against insect Victor it was found that TiO<sub>2</sub>, Ag, CuO, and Pd displayed also insecticidal activity against vectors.
- The latest review mentioned that the toxicity of the particles is not followed according to their physical- chemical properties such as, shape,size, surface area, surface charge, solubility and others. They provided a hypothesis that the number of atoms/ ions /molecules per nanoparticles is the source of toxicity.
- Nanoparticles can be add as a new composition for pesticides. They can play a protective role for pesticides active ingredients against hydrolysis and photolysis which can be beneficial to the environment.
- Nanoparticles synthesis using biological resources as precursors such as plants, plants extract, bacteria, fungi... shows low toxicity and high compatibility.
- According to the analyzing review article, 3 major types of NPs were identified:  
Metal-based NPs ex: Ag, Cu, Ti.  
Non-metal basic NPs ex: Si, Ca.  
Complex polymers ex : chitosan, plant extract.
- Three types of synthesizing method: physical, chemical, biological

- The use of NPs as carriers for drug delivery can protect drug, delay drug release, improved drug utilization, and reduce side effects.
- **Discussion of NPs application :**
  1. Most of NPs exhibit significant acute toxicity against mosquitoes. Studies have specifically investigated the effectiveness of Ag NPs synthesized from *Nelumbo nucifera*, against mosquito larvae. These studies revealed that Ag NPs were effective against *Anopheles subpictus* larvae with an LC50 of 0.69 mg/L and *Culex quinquefasciatus* larvae with an LC50 of 1.10 mg/L.
  2. Besides, the use of NPs as mosquito larvicides, ovicides, and adulticides, they can also reduce mosquito longevity and fecundity.
  3. NPs Act as transport agents against vector insert. Pesticide microencapsulation technology is to encapsulate liquid or solid pesticides in capsule materials and prepare tiny capsule preparations with a particle size of 0.1–10.0  $\mu\text{m}$ , to protect the active ingredients of pesticides from light, air, and other external factors.
- **Strengths and limitations :**
  - **Strengths:**
    - We can use NPs with different approaches and concepts.
    - Regarding different methods of synthesizing, we can produce a variety of NPs molecules, which will probably gives us more flexibility when facing different situation of combating vectors.
    - BioNPs offer innovative solutions to address the limitations of traditional pesticides, such as chemical synthesis NPs.
    - Detailed exploration of the insecticidal mechanisms and efficacy of NPs, along with their ability to carry and release pesticides, focusing on their potential for enhancing vector control.
  - **Limitations :**
    - The high cost of biosynthesizing nanoparticles (NPs) limits their widespread adoption and application in vector control.
    - Understanding how the number of atoms, ions, molecules per nanoparticles influence their ability to effectively be toxic, is yet to be explored.

- Determining the acute and long-term toxicity of different types of NPs at various doses (correlation) on target and non-target organisms, is a key step and must be fully revealed.

**3. Article N°3: title: A Review on Nanoparticles in Mosquito Control -A Green Revolution in Future**

- **Summary of key finding:**

- Silver nanoparticles (Ag NPs) are less likely to cause ecological damage compared to synthetic chemical insecticides.
- Ag NPs have been identified as potential replacements for conventional insecticides due to their eco-friendly nature.
- Green synthesis of silver (Ag) and gold (Au) nanoparticles using biological organisms offers a rapid and eco-friendly method for mosquito control.
- The synthesized Ag NPs have been tested specifically against mosquito larvae, exhibiting significant bioactivity. This suggests their effectiveness in controlling mosquito populations.
- There is a predominance of plant extracts, especially leaves, in green nanoparticle synthesis for mosquito control, with a strong focus on silver nanoparticles. The research is concentrated in India, with significant contributions from specific regions and researchers.

- **Discussion of nanoparticles application :**

In this section, the discussion is about the application and testing of nanoparticles (NPs) synthesized from three different sources. The first pathway involves the use of plant extracts for NP synthesis, the second utilizes fungi, and the third employs bacterial resources.

1. Most studies focused on synthesizing silver nanoparticles (Ag NPs) using aqueous plant extracts and testing them on various mosquito larvae species. The results were significant, demonstrating a real and effective impact on mosquito control.

For example: The larvicidal activity of synthesized Ag NPs using aqueous extract from *Eclipta prostrata*, was observed against fourth instar larvae of *Cx. quinquefasciatus* (LC50=27.49mg/L), (LC90=70.38mg/L), and against *An. subpictus* (LC50=27.85 mg/L),(LC90=71.45 mg/L)(Rajakumar *et al.*, 2011).

2. Fungi are being used in nanotechnology for nanoparticle production. Fungi have proven to be an environmentally friendly and renewable source, effectively serving as reducing agents for synthesizing silver and gold nanoparticles.

Example: Synthesized Ag NPs using filamentous fungus *Cochliobolus lunatus* and tested against second, third, and fourth instar larvae of *Ae. Aegypti* give the result: (LC50=1.29, 1.48, and 1.58 ppm), (LC90=3.08, 3.33, and 3.41 ppm) respectively, and about *An. stephensi*: (LC50=1.17, 1.30, and 1.41; LC90 =2.99, 3.13, and 3.29 ppm) (Salunkhe et al., 2011).

3. Bacterial sources offer unique advantages in nanoparticle synthesis for mosquito control. Two insecticidal bacteria have been used as larvicides in many countries, *Bacillus thuringiensis ssp. Israelensis* and *Bacillus sphaericus*.

Example: Dhanasekaran and Thangaraj (2013) found that biogenic nanoparticles from *Agaricus bisporus* achieved a *Culex* larvae mortality rate of 100% at 5 mg/L, 81% at 2.5 mg/L, 62% at 1.25 mg/L, 28% at 0.625 mg/L, and 11% at 0.312 mg/L.

The investigation of the larvicidal activities of cobalt nanoparticles (Co NPs) synthesized using the biocontrol agent *Bacillus thuringiensis* against the malaria vector *Anopheles subpictus* and the dengue vector *Aedes aegypti* (Diptera: *Culicidae*) revealed effectiveness and demonstrate significant potential as eco-friendly mosquito control agents. (Marimuthu et al. 2013)

- **Strengths and limitations:**

- The green synthesis of nanoparticles (NPs) using biological organisms like plant extracts, fungi, and bacteria offers an environmentally friendly alternative to chemical methods. This reduces the ecological footprint and minimizes harm to non-target species.
- The use of biological synthesis for NPs is a relatively new approach, opening up innovative pathways for research and application in mosquito control.
- Research indicates that a variety of biological organisms can be used for NP synthesis, providing flexibility and adaptability in the approach.

- **Limitations:**

- There is a need for standardized protocols in the synthesis and application of these NPs to ensure consistent and reliable results across different studies.

- The research demonstrated a wide range of results even when using the same type of nanoparticles. This variability could be due to differences in particle size, **surface coating, and test mediums.**

**4. Article N°4: Title:** Insecticidal efficacy of nanomaterials used to control mosquito, *Culex quinquefasciatus* Say, 1823 with special reference to their hepatotoxicity in rats.

- **Summary of key finding:**

- Insecticide resistance is a widespread and urgent global issue, leading to increased use of insecticides, and so, harming non-target species and agricultural workers.
- chitosan and silver nanoparticles, when used individually, have more lethal effects on the fourth instar mosquito larvae compared to their composite.
- Lavender nanoemulsion was less effective than chitosan and silver nanoparticles, both as individual nanoparticles and as a nanocomposite.
- Same results when talking about pupal mortality, Silver nanoparticles were the most lethal against mosquito larvae and pupae, followed by chitosan nanoparticles and chitosan-silver nanocomposites. Lavender nanoemulsion had the least lethal effect.
- Significant morphological impacts of the tested nanomaterials on mosquito larvae, indicating their effectiveness in causing physical damage and abnormalities, which can contribute to the control of mosquito populations.
- Higher concentrations of chitosan, silver nanoparticles, and their combinations significantly increase ALT and AST enzyme levels, suggesting potential hepatotoxicity. Lavender nanoemulsion, especially and only at lower concentrations (500 ppm), appears to have the same effect, reducing both ALT and AST levels.
- Higher concentrations of chitosan and silver nanoparticles, as well as their composites, significantly increase the levels of IL-1 $\beta$  and IL-6 in the liver of treated rats, suggesting an inflammatory response. Lavender nanoemulsions caused a slight increase in both IL-1 $\beta$  and IL-6 levels, but the increase was much less pronounced compared to chitosan and silver nanoparticles.

- Varying degrees of liver tissue damage and inflammatory responses induced by different concentrations and types of nanomaterials. Chitosan and silver nanoparticles, particularly at higher concentrations, caused significant histopathological changes, while lavender nanoemulsion induced only moderate changes.
- Potential action of nanoparticles, especially silver and chitosan, in mosquito control while also raising concerns about their hepatotoxicity at higher concentrations. Lavender nanoemulsions appear to be a safer alternative with moderate effects on liver tissues.
- **Discussion of nanoparticles application assessment:**

Against the last instar larvae of *Culex quinquefasciatus*:

  - **Chitosan** Nanoparticles:
    - LC50: 140.98 ppm
    - LC90: 461.39 ppm
  - Silver Nanoparticles:
    - LC50: 130.87 ppm
    - LC90: 389.01 ppm
    - Demonstrated higher lethal effects than chitosan nanoparticles.
  - Chitosan-Silver Composite:
    - LC50: 450.45 ppm
    - LC90: 860.43 ppm
    - Required higher concentrations to achieve the same lethal effects, indicating lower efficacy compared to individual nanoparticles.
  - Lavender Nanoemulsion:
    - LC50: 455.67 ppm
    - LC90: 950.00 ppm
    - Exhibited the lowest bioinsecticidal effect among all tested nanomaterials.

Pupal mortality:

Highest pupal mortality was observed at 400, 800, and 1000 ppm concentrations for all nanomaterials. Lowest pupal mortality (17%) was recorded at 100 ppm for chitosan nanoparticles.

Larval pupation percentage:

Pupation percentages decreased with increasing concentrations of nanomaterials as follow:

At 100 ppm: Chitosan (60%), Chitosan-Silver (84%), Silver (88%), Lavender (90%),

At 1000 ppm: Chitosan-Silver (8%), Lavender (4%), Chitosan (0%), Silver (0%).

Adult emergence reduction:

Significant reduction in adult emergence was observed even at the lowest concentration of 100 ppm:

- Chitosan-Silver: 45%
- Chitosan: 60%
- Silver: 80%
- Lavender: 90%

- **Strengths and limitaions:**

- **Strengths:**

- Plant-mediated synthesis of nanoparticles is emphasized as a cost-effective and environmentally friendly approach, this method avoids the use of toxic compounds, high pressure, and temperature, making it a sustainable alternative.
- The study provides robust data on the bioinsecticidal effects of different nanoparticles against *Culex quinquefasciatus* larvae.
- Silver nanoparticles were particularly noted for their high efficacy, with low LC50 values indicating strong larvicidal activity.
- Detailed histopathological and immunohistochemical analyses, along with investigations into liver enzyme levels and gene expression, provide comprehensive insights into the mechanisms of nanoparticle toxicity.

- **Limitations:**

- Dose dependent toxicity, pose a significant limitation.
- Both chitosan and silver nanoparticles showed dose-dependent hepatotoxicity, with high concentrations causing severe liver damage (non-target toxicity concern), as well as oxidative stress induced, leading to tissue damage and inflammation.
- More research is needed to elucidate the pathways involved in nanoparticle-induced toxicity.

- While the study provides valuable laboratory data, the generalizability of these results to field conditions remains uncertain. Real-world applications may face challenges such as environmental variability and potential resistance development.

## **5. Article N°5: title: Mosquito-Borne Diseases and Their Control Strategies: An Overview Focused on Green Synthesized Plant-Based Metallic Nanoparticles**

- **Summary of key finding:**

- highlighting the major mosquito-borne diseases, including malaria, dengue, chikungunya, yellow fever, Zika, and West Nile virus, emphasizing their significant public health impact worldwide.
- The use of green synthesized-nanoparticles from plant-based materials is considered eco-friendly, biodegradable, and alternatives to chemical insecticides.
- The effectiveness of green synthesized-nanoparticles in controlling mosquito populations. The focus is on various life stages of mosquitoes, including eggs, larvae, pupae, and adults.
- The nanoparticles primarily target the larval stage of mosquitoes, with their mode of action involving toxic effects and disruption of larval growth. Plant-derived nanoparticles can be further explored for their potential against resistant mosquitoes.
- The nanoparticles exhibit repellent properties, which can inhibit mosquitoes from biting humans and animals.

- **Discussion of nanoparticles applications :**

- Some of the plant been used for sythesizing NPs Neem (*Azadirachta indica*), Eucalyptus (*Eucalyptus globulus*), Ocimum sanctum (Holy Basil).
- Plant-based nanoparticles have been successfully applied as larvicidal agents. They target the larval stage of mosquitoes, which is crucial for reducing the mosquito population before they mature and start transmitting diseases. For instance, neem-based nanoparticles have been particularly effective against *Ae. Aegypti* larvae.

- Plant-based nanoparticles also exhibit adulticidal properties, effectively killing adult mosquitoes. This dual action enhances the overall impact on mosquito populations.
  - Certain plant-based nanoparticles have been found to possess strong repellent properties. For example, eucalyptus and holy basil nanoparticles can repel mosquitoes, thereby reducing the incidence of mosquito bites and the spread of diseases.
  - Nanoparticles synthesized from plant extracts can disrupt the normal growth and development of mosquito larvae. They interfere with different growth stages processes, leading to the death of larvae before they become adults.
  - Silver Nanoparticles (AgNPs): Highly effective with broad-spectrum antimicrobial properties.
  - Gold Nanoparticles (AuNPs): Biocompatible and effective, particularly in combination with other metals.
  - Copper Nanoparticles (CuNPs): Known for their strong larvicidal properties.
  - Zinc Oxide Nanoparticles (ZnONPs): Effective against both larvae and adult mosquitoes, with low toxicity to non-target organisms.
- **Strengths and limitation :**
    - **Strengths :**
      - Sustainability: Nanoparticles synthesized from plant extracts, reduce reliance on harmful chemicals and promoting sustainable practices.
      - Biocompatibility: Safer for humans, animals, and the environment compared to traditional chemical insecticides.
      - Demonstrating significant effectiveness against mosquito larvae and adults. At lower concentrations, can reduce overall usage and potential side effects.
      - Multiple mechanisms of action: NPs can disrupt mosquito biology in various ways, making it harder for mosquitoes to develop resistance.
      - Wide range Spectrum effectiveness: effective against a wide range of mosquito species, including those resistant to conventional insecticides.

- Specificity: Potential for targeted application, minimizing the impact on non-target organisms and beneficial insects.
- Degradability: Green synthesized NPs are more likely to be biodegradable, further reducing environmental risks.

○ **Limitations :**

- Difficulties in scaling up the synthesis process to produce large quantities of NPs efficiently and cost-effectively.
- Standardization: variability in plant extract compositions can lead to inconsistencies in NP quality and effectiveness.
- Initial costs for developing and producing green synthesized NPs may be higher compared to conventional insecticides.
- Long-Term Effects: Limited understanding of the long-term environmental and health impacts of NPs.

**C. Comparative Summary:**

	<b>Review Article N°1</b>	<b>Review Article N° 2</b>	<b>Review Article N°3</b>	<b>Review Article N° 4</b>	<b>Review Article N° 5</b>
<b>Title</b>	Efficacy of Metal Nanoparticles as a Control Tool Against Adult Mosquito Vectors: A Review	Nanoparticles: A Potential and Effective Method to Control Insect-Borne Diseases	A Review on Nanoparticles in Mosquito Control - A Green Revolution in Future	Insecticidal Efficacy of Nanomaterials Used to Control Mosquito, <i>Culexquinquefasciatus</i> with Special Reference to Their Hepatotoxicity in Rats	Mosquito-Borne Diseases and Their Control Strategies: An Overview Focused on Green Synthesized Plant-Based Metallic Nanoparticles
<b>Key Findings</b>	<ul style="list-style-type: none"> <li>- Majority studies on larvicidal efficacy</li> <li>- Green NPs biosynthesis effective</li> <li>- Increasing insecticide resistance requires new active</li> </ul>	<ul style="list-style-type: none"> <li>- No effective vaccines/drugs for most VBDs</li> <li>- 113 pesticide residues found in drinking water</li> <li>- Metal-based, non-metal based, complex polymers as NPs</li> <li>- NPs can</li> </ul>	<ul style="list-style-type: none"> <li>- AgNPs less ecologically damaging</li> <li>- Green synthesis eco-friendly</li> <li>- Significant larvicidal activity of AgNPs</li> </ul>	<ul style="list-style-type: none"> <li>- Insecticide resistance is a global issue</li> <li>- Chitosan and AgNPs effective individually</li> <li>- Potential hepatotoxicity at higher concentrations</li> </ul>	<ul style="list-style-type: none"> <li>- Focus on major mosquito-borne diseases</li> <li>- Eco-friendly, biodegradable plant-based NPs</li> <li>- Effective in targeting larval stage</li> </ul>

	ingredients	protect pesticides from degradation			
<b>Application</b>	<ul style="list-style-type: none"> <li>- NPs have unique properties</li> <li>- Plant-based NPs contain bioactive compounds</li> <li>- Various modes of action such as enzyme synthesis disruption</li> </ul>	<ul style="list-style-type: none"> <li>- NPs exhibit acute toxicity</li> <li>- Act as transport agents for pesticides</li> <li>- NPs can reduce mosquito longevity and fecundity</li> </ul>	<ul style="list-style-type: none"> <li>- Synthesis using plant extracts, fungi, bacteria</li> <li>- Significant bioactivity in controlling mosquito populations</li> </ul>	<ul style="list-style-type: none"> <li>- Effective against larvae and pupae</li> <li>- Detailed morphological impacts</li> <li>- Histopathological and immunohistochemical analyses</li> </ul>	<ul style="list-style-type: none"> <li>- Effective larvicidal agents</li> <li>- Repellent properties</li> <li>- Disrupt mosquito growth and development</li> </ul>
<b>Larvicides</b>	<ul style="list-style-type: none"> <li>- SeNPs: LC50 values of 99.6, 104.13, and 240.7 µg/mL</li> <li>- AuNPs: LC50 values of 25.92 and 28.64 µg/mL</li> <li>- AgNPs: LC50 values between 0.3 to 130.3 µg/mL</li> </ul>	<ul style="list-style-type: none"> <li>- AgNPs: LC50 of 0.69 mg/L for <i>An. subpictus</i> and 1.10 mg/L for <i>Cx. quinquefasciatus</i></li> </ul>	<ul style="list-style-type: none"> <li>- AgNPs: LC50=27.49 mg/L for <i>Cx. quinquefasciatus</i>, LC50=27.85 mg/L for <i>An. subpictus</i></li> <li>- AgNPs synthesized using fungi: LC50=1.29-1.58 ppm for <i>Ae. aegypti</i>, LC50=1.17-1.41 ppm for <i>An. stephensi</i></li> </ul>	<ul style="list-style-type: none"> <li>- Chitosan NPs: LC50=140.98 ppm</li> <li>- AgNPs: LC50=130.87 ppm</li> <li>- Chitosan-Ag composite: LC50=450.45 ppm</li> </ul>	<ul style="list-style-type: none"> <li>- Neem, eucalyptus, holy basil NPs effective against larvae</li> <li>- Neem-based NPs effective against <i>Ae. aegypti</i> larvae</li> </ul>
<b>Adulticides</b>	<ul style="list-style-type: none"> <li>- Gold NPs: LC50=11.23 µg/mL for <i>An. stephensi</i></li> <li>- Zinc NPs: 2-10 ppm reduced longevity</li> </ul>	<ul style="list-style-type: none"> <li>- AgNPs act as adulticides</li> </ul>	<ul style="list-style-type: none"> <li>- AgNPs synthesized using fungi and bacteria</li> </ul>	<ul style="list-style-type: none"> <li>- Silver NPs showed high efficacy</li> <li>- Chitosan NPs showed moderate efficacy</li> </ul>	<ul style="list-style-type: none"> <li>- AgNPs, AuNPs, CuNPs, ZnONPs effective against adults</li> </ul>
<b>Strengths</b>	<ul style="list-style-type: none"> <li>- Precise targeting</li> <li>- Environmentally friendly</li> <li>- Synergistic effects with existing insecticides</li> </ul>	<ul style="list-style-type: none"> <li>- Multiple synthesis methods</li> <li>- Enhanced vector control</li> </ul>	<ul style="list-style-type: none"> <li>- Environmentally friendly synthesis</li> <li>- Flexibility in approach</li> </ul>	<ul style="list-style-type: none"> <li>- Effective against specific species</li> <li>- Detailed toxicological data</li> </ul>	<ul style="list-style-type: none"> <li>- Eco-friendly and biodegradable</li> <li>- Significant effectiveness at low concentrations</li> <li>- Multiple mechanisms of action</li> </ul>

Each article provides unique insights into the potential of metal nanoparticles for mosquito control, highlighting both the promising aspects and the challenges that need to be addressed for effective implementation.

**1. Distinctive Features:**

- Article 1 emphasizes larvicidal efficacy and insecticide resistance.
- Article 2 discusses the protective role of NPs in pesticide formulations.
- Article 3 focuses on green synthesis using plant extracts, fungi, and bacteria.
- Article 4 provides detailed data on hepatotoxicity and histopathological effects.
- Article 5 highlights the eco-friendly nature of plant-based NPs and their wide range spectrum effectiveness.

**2. Common Strengths:**

- Environmental friendliness and biocompatibility.
- Effectiveness against multiple mosquito species.
- Potential for synergistic effects with existing insecticides.

**3. Common Limitations :**

- High costs and challenges in large-scale synthesis.
- Need for standardized protocols and methodologies.
- Limited understanding of long-term environmental and health impacts.

**Conclusion:**

The reviewed articles collectively highlight the promising potential of metal nanoparticles, especially those synthesized through green methods, as effective and eco-friendly tools for controlling mosquito vectors. These nanoparticles have demonstrated significant larvicidal, pupicidal, and adulticidal effects against various mosquito species, illustrating their potential to reduce mosquito populations and mitigate the spread of mosquito-borne diseases. However, despite these encouraging findings, several challenges remain.

Issues related to the toxicity of nanoparticles to non-target organisms, the cost of large-scale production, and the need for comprehensive environmental impact assessments must be addressed. Moreover, real-world application strategies need to be developed and tested to ensure practical and sustainable use. Therefore, while metal nanoparticles offer a promising avenue for mosquito control, continued research is essential to fully realize their potential and ensure their safe and effective deployment.

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