"Eco-friendly and Economic approach of Green Synthesized Nanoparticles as *Aedes* Mosquito Control."

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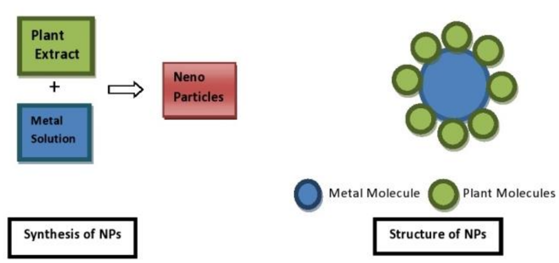
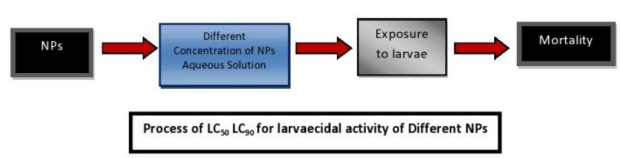
Abstract-

World's 40% population is at risk of dengue which is transmitted by *Aedes aegypti* and *Aedes albopictus*. Many measures for *Aedes* control are taken but still mosquitoes find their way to breed and transmit diseases. Insecticide use is been considered effective for emergency mosquito control and many more insecticides are under trials but mosquitoes usually develop resistance against these chemical formulations. In recent years green synthesized nanoparticles are proved to be potential targets against larvae, pupa and adult form of mosquito. This paper reviews the various developed nanoparticles during and their potentiality in *Aedes* control. Larvicidal activity of nanoparticles is given for I instars, II instars, III instars, IV instars and pupa differently. Nanoparticles are fabricated from many medicinal plants extract and some are very much effective against mosquito control. This is an eco friendly approach for mosquito control with low risk of resistance development.

KEYWORDS: *Aedes aegypti; Aedes albopictus;* Green synthesized Nanoparticles.





Introduction-

Urbanization significantly made modifications in the *Aedes* mosquito ecology by certain environmental changes. The mosquito borne diseases such as Dengue, Zika, and yellow fever are primarily transmitted to the humans by the *Aedes* mosquito and vector control is significant to restrain the transmission of these drastic viral diseases. Studies indicate that 390 million people in the world face dengue infections per year with 96 million infections confirmed clinically (Bhatt *et al.*, 2003). Additionally, the rapid spread of mosquito borne diseases is vitalized by global freight transportation and international travel. For the proper development, the larvae and pupae of mosquitoes necessitate an aquatic environment with standing or flowing water. Larvae of the majority mosquito species generally filter out and feed organic matter, other microorganisms from water. Heterotrophic microorganisms such as bacteria, fungi and protozoan from detritus surfaces or containers are significant for the larval diet. Freshwater swamps, rice fields, borrow pits, marshes, puddles, water-filled tracks, ditches, galleys and drains are tremendous source of mosquito larval habitats. Wide range of 'natural container- habitats' such as, rock-pools, water-filled bamboo stumps, tree holes filled with water, leaf axis in banana, snail shell and coconut husks offer enough requirements for mosquito larval habitat. Man-made container habitats including water storage jars, tins, cans, motor vehicle tyres and discarded kitchen utensils also provide space for breeding of mosquitoes. After the larvae have accomplished their fourth larval molt they develop into pupae (called tumblers). Pupae don't require food and be alive for 1-3 days before the adult form. Male adult mosquitoes primarily feed nectar from plants to get sugar while the female mosquitoes imbibe the blood meal to generate viable eggs. Female mosquitoes usually nourish every 3-5days. *A. albopictus* females are diurnal feeders; they not only give preference to attack large mammals but also imbibe blood meals from birds. The mostly found *Aedes* species are; *Aedes (Stegomyia) aegypti* (Linnaeus), *Aedes (Stegomyia) africanus* (Theobald), *Aedes (Stegomyia) albopictus* (Skuse), *Aedes (Stegomyia) luteocephalus* (Newstead), *Aedes (Stegomyia) opok* (Corbet and Van Someren), *Aedes (Diceromyia) furcifer* (Edwards), *Aedes (Diceromyia) taylori* (Edwards), *Aedes (Stegomyia) cooki* (Belkin), *Aedes (Stegomyia) hebrideus* (Edwards), *Aedes (Stegomyia) hensilli* (Farner), *Aedes (Stegomyia) polynesiensis, Aedes (Stegomyia) rotumae* (Belkin), *Aedes (Stegomyia) scutellaris* (Walker), *Aedes (Gymnometopa) mediovittatus* (Coquillett) (Leopoldo M. and Rueda, 2004). Among all *Aedes* species *Aedes aegypti, Aedes albopictus, and Aedes vittatus* are the dangerous species which carry maximum burden to transmit Vector Borne Diseases such as dengue and chikunguniya.

Aedes aegypti and Aedes albopictus are severe pest species and a component vector of many exotic arboviruses. It is a known vector of dengue (Mitchell *et al.*, 1987; Hawley, 1988), Japanese encephalitis (Weng *et al.*, 1997), eastern equine encephalitis (Mitchell *et al.*,1992; Turell *et al.*1994), western equine encephalitis, Venezuelan equine encephalitis (Fernandez *et al.*, 2003), Ross River virus (Kay *et al.*, 1982;Lee at el., 1984), Chikunguniya virus (Tesh *et al.*,1976; Reiter *et al.*, 2006), yellow fever (Mitchell *et al.*, 1987; Johnson *et al.*, 2002), Cache Valley (Mitchell *et al.*, 1998;), West Nile Virus (Tiawsirisup *et al.*, 2005), *Dirofilaria immitis* (dog heartworm) (Chellappah and Chellapph, 1968; Lee *et al.*, 2003a), *Dirofilaria repens* (Cancrini *et al.*, 2003b), *avian malaria* (La Pointe *et al.*, 2005), *St. Louis encephalitis* (Savage *et al.*, 1994) and *La Crosse encephalitis* (Gerhartdt *et al.*, 2001).

Green synthesized nanoparticales as *Aedes* Control-

In 2012, Only 3 studies focused on the toxicity of plant synthesized nanoparticles against *Aedes* mosquito larvae. *Annona squamosa* synthesized AgNP were toxic to IV instar larvae of *Ae. Aegypti* ; LC50 was 0.30 ppm, (Arjunan *et al.* 2012). AgNP produced using *Plumeria rubra* plant latex were toxic to II and IV instar larvae of *Ae. aegypti*; LC50 values were 1.49 (II) and 1.82 ppm (IV) for *Ae. aegypti* (Patil *et al.* 2012a). AgNP synthesized with the *Pergularia daemia* latex were toxic to *Ae. aegypti* larvae; LC50 values were 4.39 (I), 5.12 (II), 5.66 (III), and 6.18 ppm (IV) for *Ae. aegypti*, (Patil *et al.* 2012b).

In 2013, only 3 studies were published against *Aedes* mosquito. AgNP produced using *Pedilanthus tithymaloides* aqueous leaf extract showed anti-developmental activity and acute toxicity towards *Ae. aegypti*, with LC50 values of 0.029 (I), 0.027 (II), 0.047 (III), 0.086 (IV), and 0.018 % (pupa) (Sundara vadivelan *et al.* 2013). AgNP produced with the *Murraya koenigii* leaf extract were toxic to *Ae. Aegypti*, LC50 were 13.34 (I), 17.19 (II), 22.03 (III), 27.57 (IV), and 34.84 ppm (pupa) (Suganya *et al.* 2013). AgNP fabricated with the *Sida acuta* leaf extract were tested against III instar larvae of *Ae. aegypti*, with LC50 values of 23.96, (Veera Kumar *et al.* 2013).

In 2014, only 5 studies have been conducted to evaluate the toxicity of plant-synthesized nanoparticles against *Aedes* mosquito larvae. *Feronia elephantum* synthesized silver nanoparticles were toxic against *Ae. aegypti*, LC50 of 13.13 µg/ml; (Veera Kumar *et al.* 2014a). AgNP produced using the aqueous leaf extract of *Leucas aspera* were toxic against IV instar larvae of *Ae. aegypti*, with LC50 of 8.563 mg/l (Suganya *et al.* 2014). The aqueous leaf extracts of *Aegle marmelos* have been used to synthesize nickel nanoparticles toxic to *Ae. aegypti*, LC50 were 534.83, ppm, (Angajala *et al.* 2014). AgNP fabricated with the leaf extract of *Heliotropium indicum* have been tested against III instar larvae of *Ae. aegypti*, LC50=20.10 µg/ml (Veera Kumar *et al.* 2014b). AgNP synthesized using the aqueous root extract of *Delphinium denudatum* exhibited toxic activity towards II instar larvae of *Ae. aegypti*, with a LC50 value of 9.6 ppm (Suresh *et al.* 2014).

In 2015, high number of researches was published. *P. niruri*-fabricated AgNP have been reported as toxic to larvae and pupae of *Ae. aegypti*, with LC50 of 3.90 ppm (I), 5.01 ppm (II), 6.2 ppm (III), 8.9 ppm (IV), and 13.04 ppm (pupa) (Suresh *et al.* 2015). C. citratus-produced AuNP were toxic against *Ae. aegypti*; LC50 were 20.27 ppm (I), 23.24 ppm (II), 8.63 ppm (III), 35.09 ppm (IV), and 41.52 ppm (pupa) (Murugan *et al.* 2015b). *Artemisia vulgaris*-synthesized AgNP were highly against *Ae. aegypti* larvae and pupae; LC50 were 4.429 ppm (I), 7.209 (II), 8.273 (III), 10.776 (IV), and 13.089 ppm (pupa) (Murugan *et al.* 2015c). *Crotalaria verrucosa*-synthesized AgNP evoked high mortality rates against *Ae. aegypti* larvae and pupae; LC50 were 3.496 (I), 5.664 (II), 9.112 (III), 11.861 (IV), and 15.700 ppm (pupa) (Murugan *et al.* 2015e). *Bruguiera cylindrica*-synthesized AgNP were toxic against *Ae. aegypti* larvae and pupae, with LC50 of 8.935 (I), 11.028 (II), 13.913 (III), 22.443 (IV), and 30.698 ppm (pupa) (Murugan *et al.* 2015g). AgNP synthesized using *Chomelia asiatica* leaf extract were toxic to *Ae. aegypti*, LC50 was 19.32 µg/ml (Muthukumaran *et al.* 2015a). AgNP obtained with the *Gmelina asiatica* leaf extract appeared to be effective against *Ae. aegypti* LC50 is 25.77 µg/ml (Muthukumaran *et al.* 2015b). AgNP fabricated using leaf and fruit extracts from *Couroupita guianensis* were toxic to IV instar larvae of *Ae. aegypti*, with LC50 of 2.1 ppm (leaf extract) and 2.09 ppm (fruit extract) (Vimala *et al.* 2015). The aqueous leaf extract of neem, *Azadirachta indica*, has been tested against III instar larvae of *Ae. aegypti* LC50 were 0.006 mg/l (Poopathi *et al.* 2015). AgNP biosynthesized using 2,7 bis[2-[diethylamino]- ethoxy]fluorence isolate from *Melia azedarach* leaves have been tested against III instar larvae of *Ae. Aegypti*, LC50 of 4.27 (Ramanibai and Velayutham 2015). Extremely stable AgNP have been synthesized using the leaf aqueous extract of *Mukia maderaspatana*; LC50 values against *Ae.aegypti* IV instar larvae were 0.211 (Chitra *et al.* 2015). AgNP synthesized with *Avicennia marina* leaf extract have been tested against I–IV larvae of *Ae. aegypti*, with LC50 values of 4.374 (Balakrishnan *et al.* 2015). Green-synthesized AgNP produced using the *Annona muricata* leaf extract were toxic to III instar larvae of *Ae. aegypti* LC50=12.58 µg/ml (Santhosh *et al.* 2015a, b). Low doses of *Mimusops elengi*-synthesized AgNP showed larvicidal and pupicidal toxicity against the arbovirus vector *Ae. albopictus*. AgNP LC50 against Ae. albopictus ranged from 11.72 ppm (I) to 21.46 ppm (pupa) (Subramaniam*et al.* 2015). In acute toxicity experiments, the aqueous extract of *Hypnea musciformis* was toxic against larvae and pupae of *Ae. aegypti*. LC50 were 246.59 ppm (I), 269.05 ppm (II), 301.66 ppm (III), 319.30 ppm (IV), and 342.43 ppm (pupa) (Roni *et al.* 2015). *Annona muricata*-synthesized AgNP achieved good LC50 against several mosquito vectors, including *Ae. Aegypti* LC50=12.58 µg/ml (Santhosh *et al.* 2015a, b). AgNP were successfully synthesized from aqueous silver nitrate using the extracts of *Arachis hypogaea* peels and achieved LC50 against IV instar larvae of *Ae. Aegypti* of 1.85 mg/l (Velu *et al.* 2015). *Cassia roxburghii*-synthesized AgNP showed high toxicity against *Ae. aegypti*, s with LC50 values of 28.67 (Muthukumaran *et al.* 2015c). *Berberis tinctoria*-synthesized AgNP were highly effective against *Ae.albopictus* young instars, with LC50 of 4.97 ppm (I), 5.97 ppm (II), 7.60 ppm (III), 9.65 ppm (IV), and 14.87 ppm (pupa) (Mahesh Kumar *et al.* 2015). *Bauhinia variegata*-synthesized AgNP were toxic to *Ae. albopictus* third instar larvae, with LC50 of 46.16 µg/ ml (Govindarajan *et al.* 2015) Recently, AgNP synthesized from the seed extract of *Moringa oleifera* have been reported as toxic towards *Ae. aegypti* young instars, with LC50 of 10.24 ppm (I), 11.81 ppm (II), 13.84 ppm (III), 16.73 ppm (IV), and 21.17 ppm (pupae). In addition, these AgNP were able to inhibit the growth of dengue virus, serotype DEN-2 (Sujitha *et al.* 2015).

Adulticidal and ovideterrent activity

AgNP synthesized using *F. elephantum* leaf extract were toxic against adults of *Ae. aegypti* LD_{50} and LD_{90} were 20.399 and 37.534 μg/ml. (Veera Kumar and Govindarajan 2014). The adulticidal activity of AgNP synthesized using *H. indicum* leaf extract has been evaluated against adults of *Ae. aegypti*, LD_{50} 29.626 μg/ml (Veerakumar *et al.* 2014c). *P. niruri*-synthesized AgNP tested against *Ae. aegypti* adults achieved LC_{50} and LC_{90} values of 6.68 and 23.58 ppm, respectively (Suresh *et al.* 2015). For instance, *M. elengi*-synthesized AgNP showed 14.7 ppm against *Ae. albopictus* (Subramaniam *et al.* 2015). Notably, exposure to doses ranging from 100 to 500 ppm of *H. musciformis*-fabricated AgNP strongly reduced *Ae. aegypti* longevity in both sexes, as well as female fecundity (Roni *et al.* 2015). Little information is available on the impact of metal nanoparticles on oviposition behavior of mosquito vectors. Barik *et al.* (2012) investigated the oviposition behavior of three mosquito species in the presence of different types of nanosilica. Complete ovideterrence activity of hydrophobic nanosilica was observed at 112.5 ppm in *Ae. aegypti*, *An. stephensi*, and *C. quinquefasciatus*, while there was no effect of lipophilic nanosilica on oviposition behavior of the three vectors (Barik *et al.* 2012). Later on, Madhiyazhagan *et al.* (2015) showed that 10 ppm of AgNP synthesized using *S. muticum* reduced oviposition rates of more than 70 % in *Ae. aegypti*.

Conclusion-

The world health organization (WHO) had already declared that more than 2.5 billion people (over 40% of the world's population) are now at risk of Dengue. WHO estimates there may be more than 100 million dengue infections worldwide every year. An estimated 500,000 people with severe dengue require hospitalization each year, a large proportion of who are children. About 2.5% of those affected die. The primary vector of Dengue is *Ae. aegypti*, but urbanization, deforestation , transportation and more other factors emerged an another dominant vector *Ae. albopictus.*

The present study is about the control of *Aedes* mosquito hence the literature has reviewed that *Ae. aegypti* and *Ae. albopictus* are the dominant vector of Dengue , Chikanguniya, Zika and other arbovirus diseases. Recently high number of Zika cases are reported in Jaipur, Rajasthan. On the Dated 13th November 2018 a local newspaper had published that in that particular week 4 positive cases are reported in that 3 cases are from urban area and one from rural, In the year up to that date total 56 positive cases are reported in which 35 are from urban area and 21 are rural (epaper, 13-Nov-2018, Rajasthan Patrika, Udaipur).

Aedes mosquito is a vulnerable threat to human society, it is very crucial to control this mosquito. There are lots of mosquito control methods like Environmental management (Reducing vector habitats and breeding sites, Solid waste Management and Modification of man-made breeding sites), Biological control (Predators, Parasitoids and Pathogens), Chemical Control **(**Fenitrothion, Fenthione Malathione, Cypermethrin, Deltamethrin and Permethrin) and many more but these all patterns are either naturally placed for a particular session or they are highly economic . Chemical control provides frequent resistance if used regularly.

Nanoparticales are also having a positive potential for mosquito control. Several of research scholars and laboratories are working in this filed. In this study we are focusing on the study of nanoparticles as *Aedes* control from 2012 to 2015. The literature had reviewed and resulting that most of the study had done on *Aedes aegypti*. For the IV instar of *Ae. aegypti* the maximum effect is reported 0.211 ppm of *Mukia mwaderaspatana* AgNPs followed by 534.83 ppm of NiNPs of *Aegle marmelos* minimum, for III instar of *Ae. aegypti* maximum effect was reported 0.006 ppm of *Azadirachta indica* AgNPs followed by 301.66 ppm of *Hypnea musciformis* minimum, for II instar of *Ae. aegypti* 1.49 ppm of *Plumeria rubra* AgNPs effect was maximum followed by 269.05 ppm of *Hypnea musciformis* minimum, for I instar of *Ae.aegyti* 3.496 ppm of *P.niruri* AgNPs was maximum followed by 246.59 ppm of *Hypnea musciformis* minimum.

A few study was citrated for *Ae.albopictus* in those AgNPs of *Berberis tinctoria* for I,II III and IV instars shows maxmimum efficacy 4.97, 5.97, 7.60 and 9.65 respectively. More study on different NPs is required to estimate the proper efficacy of NPs as *Aedes* Control. This study is suggested for synthesis of different NPs and their effect on *Aedes* mosquito control.

Year of Public -ation	Name of Plant	Type of NPs	LC_{50} I instars	LC_{50} II instars	LC_{50} III instars	LC_{50} IV instars	Type of Aedes of Mosquito
2012	*Annona squamosa*	AgNP	0	0	0	0.3 ppm	*Ae. aegypti*
2012	*Plumeria rubra*	AgNP	0	1.49 ppm	0	1.82 ppm	*Ae. aegypti*
2012	*Pergularia daemia latex*	AgNP	4.39pp mm	5.12 ppm	5.66 ppm	6.18 ppm	*Ae. aegypti*
2013	*Pedilanthus tithymaloides*	AgNP	0.029	0.027	0.047	0.086	*Ae. aegypti*
2013	*Murraya koenigii*	AgNP	13.34 ppm	17.19 ppm	22.03pp m	27.57 ppm	*Ae. aegypti*
2013	*Sida acuta*	AgNP	0	0	23.96 ppm	0	*Ae. aegypti*
2014	*Feronia elephantum*	AgNP	0	0	0	13.13 µg/ml	*Ae. aegypti*
2014	*Leucas aspera*	AgNP	0	0	0	8.563 mg/l	*Ae. aegypti*
2014	*Aegle marmelos*	NiNPs	0	0	0	534.83 ppm	*Ae. aegypti*
2014	*Heliotropium indicum*	AgNP	0	0	20.10 µg/ml	0	*Ae. aegypti*
2014	*Delphinium denudatum*	AgNP	0	9.6 ppm	0	0	*Ae. aegypti*
2015	*P. niruri*	AgNP	3.90 ppm	5.01 ppm	6.2 ppm	8.9 ppm	*Ae. aegypti*
2015	*C. citratus*	AuNP	20.27 ppm	23.24 ppm	8.63 ppm	35.09 ppm	*Ae. aegypti*
2015	*Artemisia vulgaris*	AgNP	4.429 ppm	7.209 ppm	8.273 ppm	10.776 ppm	*Ae. aegypti*
2015	*Crotalaria verrucosa*	AgNP	3.496 ppm	5.664 ppm	9.112 ppm	11.861 ppm	*Ae. aegypti*
2015	*Bruguiera cylindrica*	AgNP	8.935 ppm	11.028p pm	13.913p pm	22.443 ppm	*Ae. aegypti*
2015	*Chomeliaasiatica*	AgNP	0	0	0	19.32 µg/ml	*Ae. aegypti*
2015	*Gmelina asiatica*	AgNP	0	0	0	25.77 µg/ml	*Ae. aegypti*
2015	*Couroupita guianensis*	AgNP	0	0	0	2.1 ppm	*Ae. aegypti*
2015	*Azadirachta indica*	AgNP	0	0	0.006 mg/l	0	*Ae. aegypti*
2015	*Melia azedarach*	AgNP	0	0	4.27 ppm	0	*Ae. aegypti*
2015	*Mukia maderaspatana*	AgNP	0	0	0	0.211 ppm	*Ae. aegypti*

2015	*Avicennia marina*	AgNP	0	0	0	4.374 ppm	*Ae. aegypti*
2015	*Annona muricata*	AgNP	0	0	12.58 µg/ml	0	*Ae. aegypti*
2015	*Mimusops elengi*	AgNP	11.72 ppm	0	0	0	*Ae. albopictus*
2015	*Hypnea musciformis*	AgNP	246.59 ppm	269.05 ppm	301.66 ppm	319.30 ppm	*Ae. aegypti*
2015	*Annona muricata*	AgNP	0	0	0	12.58 µg/ml	*Ae. aegypti*
2015	*Arachis hypogaea*	AgNP	0	0	0	1.85 mg/l	*Ae. aegypti*
2015	*Cassia roxburghii*	AgNP	0	0	0	28.67 ppm	*Ae. aegypti*
2015	*Berberis tinctoria*	AgNP	4.97 ppm	5.97 ppm	7.60 ppm	9.65 ppm	*Ae.albopictus*
2015	*Bauhinia variegata*	AgNP	0	0	46.16 µg/ ml	0	*Ae. albopictus*
2015	*Moringa oleifera*	AgNP	10.24 ppm	11.81 ppm	13.84 ppm	16.73 ppm	*Ae. aegypti*

Table: List of nano particles developed against *Aedes aegypti* and *Aedes albopictus* from 2012-2015. For *Aedes aegypti* Ist instar *P.niruri* , IInd Instar *Plumeria rubra* , for IIIrd Instar *Azadirachta indica* and for IVth Instar *Mukia mwaderaspatana* AgNPs are most effective and for *Ae.albopictus* AgNPs of *Berberis tinctoria* for I,II III and IV instars.

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