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An Overview of Naturally Synthesized Metallic Nanoparticles

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ABSTRACT

Nanotechnology is a powerful technology offers wide spectrum of devices, drugs etc for the welfare of human and other living organisms. Nanoparticles are the tiny molecule in the size of 1-100nm acting as potential antimicrobial, anticancer, Anti-Larvicidal and Antiparasitic Agents. Among the nanoparticles deployed, silver and gold nanoparticles have been greatly used against multidrug resistant microbes like *Staphylococcus aureus*, vector mosquitoes like *Aedes aegypti, Anopheles stephensi* and *Culex quinquifasciatus* as well as wide range of cancer Cell lines like MCF-7, Hep G2, etc. In the recent years, identification of dynamic nanoparticles, possessing antimicrobial, anti-larvicidal and anticancer activity, becomes important for defending the existing multitude of diseases spreading to human beings. In this context, this review was prepared to measure the dynamics of bioactive nanoparticles extremely used against pathogens, cell lines and vectors.

INTRODUCTION

The mosquito vectors are responsible transfer of deadly diseases such as malaria, chickungunia, filariasis and dengue. One of the major economic and health issues in several countries are the vector borne diseases caused by mosquito. The mosquito vector for human diseases like yellow fever and dengue is *Aedes agypti* mosquito (Suganya *et al.*, 2014). Similarly, mosquito-borne viral disease called dengue was found mostly in tropic and sub-tropic region around the world. Estimation by World Health Organization (WHO) states that there are about 50-100 million dengue infection are prevalent worldwide (Suresh *et al.*, 2015). A vector of *Wuchereria* species called *Culex quinquefasciatus* was responsible for causing lymphatic Filariasis which are wide spread in the tropical region with 120 million people infected and 40 million people are under clinical manifestation (Veerakumar *et al.*, 2013). Two million malarial cases were reported annually in India (Gnanadesigan *et al.*, 2011). Due to the development of insecticides resistance, biological magnification, serious effect on environmental quality and destruction of non-target organism, the vector controlling methods involving chemical insecticides are becoming less effective (Suganya *et al.*, 2014). The use of artificial insecticides in order to control mosquito-borne vector especially *Aedes* leads to high cost and harmful non-target effect (Suresh *et al.*, 2015). Cancer, which is grouped as the uncontrolled development of cells, is one of the serious causes of death throughout the world. In the last few years, Increase of cancer patient have been observed (Abbas *et al.*, 2015). The bites of *Aedes agypti* can transmit hamster reticulum cell sarcoma by transfer of tumor cell. They also plays role in changing the human metabolic pathway which lead to viral infection or/and oncogenesis (Benelli *et al.*, 2016). There are several ways in the treatment of cancer by chemotherapy while there are multiple barriers that recently prevent the clinical advantages. Currently, the field of nanotechnology plays a major role in the cancer treatment through drug delivery method because of the good pharmacokinetic activity, better drug solubility, increased the half-life period of drugs. In addition to that they also have less toxic phytochemicals with target-specific nanoparticles which provide a new way of treating cancer (Joseph *et al.*, 2015).

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Benelli, 2016 stated that nanodrugs with multipotency against mosquito-borne diseases and cancers are required. In particular, a focus on effectiveness and non-target effects of metal nanoparticles synthesized using natural products as reducing agents may support the development of novel antiplasmodial, mosquitocidal, and anticancer tools. In this vision we have prepared this review. This review mainly focuses on the pharmacokinetics activity of several nanoparticles such as antiparasitic, anticancer, antimicrobial, antioxidant and anti-inflammation.

AGNPS (AgNps)

Antiparasitic Study

The AgNps (AgNps) synthesised using leaf extract of *Rhizophora mucronata* have excellent larvicidal activity (LC_{50} and LC_{90}) against the larvae of *Aedes aegypti* and *Culex quinquefasciatus* with respect to 0.585 mg/L and 2.615 mg/L and 0.891 and 6.291 mg/mL (Gnanadesigan *et al.,* 2011). The AgNps synthesised through aqueous extract of stem of *Cissus quadrangularis* have excellent adulticidal activity (LC_{50} and LC_{90}) against *Hippobosca maculata* with respect to 37.08, 40.35 and 6.30 mg/L as well as 175.46, 192.17 and 18.14 mg/L. It also revealed larvicidal activity against *Rhipicephalus (Boophilus) microplus* (LC_{50} values of 50.00, 21.72 and 7.61 mg/L; LC_{90} values of 205.12, 82.99 and 22.68 mg/) (Santhoshkumar *et al.,* 2012).

The mesocarp layer extract *Cocos nucifera* coir engineered AgNps have potential larvicidal activity against *Anopheles stephensi* and *C. quinquefasciatus* with an LC_{50} value of 87.24 and 49.89 as well as LC_{90} values of 230.90 and 84.85 mg/L respectively (Roopan *et al.,* 2012). AgNps from bark aqueous extract of *Ficus racemosa* have shown excellent larvicidal activity against *C. quinquefasciatus* (LC_{50}=67.72 and 63.70 mg/L) and *C. gelidus* (LC_{50}=12.00 and 11.21 mg/L) (Velayutham *et al.,* 2012). Similarly, AgNps from aqueous aerial extract of *Ammannia baccifera* represented dynamic activity against mosquito larvae namely *A. subpictus* (LC_{50} = 257.16) and *C. quinquefasciatus* (LC_{50} = 210.88ppm). also have shown toxic (LC_{50}) effect against *A. subpictus* and *C. quinquefasciatus* with respect to 29.54 and 22.32ppm respectively (Suman *et al.,* 2013). Similarly AgNps form *Delphinium denudatum* have excellent anti-mosquito activity against second instar larvae of *A. Aegypti* (LC_{50} : 96ppm (24hrs) and 9.6ppm (48hrs)) (Suresh *et al.,* 2014).

AgNps engineered from extracts of leaf and fruit of *Couroupita guianensis* and revealed broader larvicidal activity against A. aegypti (Leaf: LC_{50} – 44.55 ppm and LC_{90} – 318.39 ppm) and (Fruit: LC_{50} – 49.96 ppm and LC_{90} – 568.84 ppm) when compared to methanol extract (Leaf: LC_{50} – 85.75 ppm and LC_{90} – 598.63 ppm and (fruit; LC50 – 67.78 ppm and LC90 – 714.45 ppm). However colloid synthesis of AgNPs using aqueous extract of the *C. quianensis* by decoction method showed extensive mortiality rate against *A. aegypti* (Leaf: LC_{50} – 2.1 ppm and LC_{90} – 5.59 ppm) and (Fruit: LC_{50} – 2.09 ppm and LC_{90} – 5.7 ppm) (Vimala *et al.,* 2014). AgNps from leaf extract of *Feronia elephantum* (Rutaceae) have revealed potential antiparasitic activity (LD_{50} and LD_{90}) against adult of *A. Stephensi*: 18.041 and 32.575µgmL^{-1}, *A. Aegypti*: 20.39 and 37.53µgmL^{-1}, *C. quinquefasciatus*: 21.79 and 39.59 µgmL^{-1}) (Veerakumar *et al.,* 2014).

Leaf extract of *Leucas aspera* synthesized AgNps portrayed potential larvicidal activity against fourth instar larvae of *A. aegypti* with respect to (LC_{50} and LC_{90} values of 8.56 and 31.30 mg/l) (Suganya *et al.,* 2014). *Aloe vera* originated AgNps showed considerable toxicity against I, II, III, IV and pupae of *A. stephensi* with respect to 48.79, 59.09, 70.88, 83.58 and 152.55ppm (Dinesh *et al.,* 2015).

Leaf extract of *Annona muricata* emerged AgNps exemplified excellent larvicidal activity against *A. aegypti* (LC_{50} and LC_{90} values: 12.58 and 26.46 µg mL^{-1}), *A. stephensi* (15.28 and 31.91 µgmL^{-1}) and *C. quinquefasciatus* (18.77 and 35.72 µg mL^{-1}) (Santhosh *et al.,* 2015). Larvicidal activity of *Euphorbia hirta* leaf extract generated AgNps found highly active against the first and fourth instar larvae and pupae of *Anopheles stephensi* (LC_{50}: 10.14, 16.82, 21.51, and 27.89 ppm; LC_{90}: 31.98, 50.38, 60.09, and 69.94 ppm) (Priyadarshini *et al.,* 2012). Acetone leaf extract of *Morinda tinctoria* synthesized AgNps have greater larvicial activity against third instar larvae of *C. quinquefasciatus* (LC_{50}: 8.088 and 1.442 ppm) (Kumar *et al.,* 2014). The synthesised AgNps from *Chomelia asiatica* (Rubiaceae) has potential larvicidal activity against the mosquito vectors of *A. stephensi*, *A. aegypti*, and *C. quinquefasciatus* (Diptera: Culicidae) with the following LC_{50} and LC_{90} values. *A. stephensi* had 17.95 and 33.03 µg/mL while *A. aegypti* and *C. quinquefasciatus* had 19.32 and 34.87 µg/mL and 20.92 and 37.41 µg/mL respectively (Muthukumaran *et al.,* 2014).

The synthesised AgNps from *Feronia elephantum* (Rutaceae) has effective larvicidal activity against the *C. quinquefasciatus, A. stephensi,* and *A. aegypti* with LC_{50} and LC_{90} values of 11.56 and 20.56 µg mL^{-1}, 13.13 and 23.12 µg mL^{-1}, and 14.19 and 24.30 µg mL^{-1} respectively (Veerakumar *et al.,* 2014). AgNps from leaf extract of *Gmelina asiatica* had potent larvicidal activity against larvae of *A. stephensi* (LC_{50}: 22.44 and LC_{90}: 40.65 µg/mL), *Aedes aegypti* (LC_{50}: 25.77 and LC_{90} = 45.98 µg/mL) and *C. quinquefasciatus* (LC_{50}: 27.83 and LC_{90} = 48.92 µg/mL) (Muthukumaran *et al.,* 2015). The AgNps synthesised using aqueous fruit extract of putranjiva, *Drypetes roxburghii* (Wall.) has an effective larvicidal activity against *C. quinquefasciatus* (LC_{50} value: 0.8632, 1.1619 and 1.2814 ppm with respect to second, third and fourth instar larvae while *A. stephensi* had LC_{50} values of 0.7329, 0.8397 and 0.9848 ppm (Haldar *et al.,* 2013). The AgNps synthesised from the crude methanol and aqueous extraction of *Nelumbo nucifera* Gaertn. (Nymphaeaceae) have excellent larvicidal activity against the fourth instar larvae of *A. subpictus* (LC_{50} = 8.89, 11.82, and 0.69ppm; LC_{90} = 28.65, 36.06, and 2.15ppm) and *C. quinquefasciatus* (LC_{50} = 9.51, 13.65, and 1.10ppm; LC_{90} = 28.13, 35.83, and 3.59ppm) (Santhoshkumar *et al.,* 2010).

Table 1: Larvicidal activity of AgNps synthesized from different sources.

BIOLOGICAL SOURCE/ METHOD	SIZE (NM)	NAME OF MOSQUITO SPECIES	LETHAL CONCENTRATION (LC) (MG/L) / PPM		REFERENCES
			LC_{50}	LC_{90}	
Leaf extract of *Rhizophora mucronata*	60-95	*Aedes aegypti*	0.585	2.615	Gnanadesigan *et al.*, 2011
		Culex quinquefasciatus	0.891	6.291	
Stem Aqueous extract of *Cissus quadrangularis*	42.46	*Hippobosca maculata*	37.08, 40.35, 6.30	175.46, 192.17, 18.14	Santhoshkumar *et al.*, 2012
		Rhipicephalus (Boophilus) microplus	50.00, 21.72, 7.61	205.12, 82.99, 22.68	
Mesocarplayer extract of *Cocos nucifera*	23 ± 2	*Anopheles stephensi*	87.24	230.90 ± 17.10	Roopan *et al.*, 2012
		Culex quinquefasciatus	49.89	84.85 ± 6.50	
Bark aqueous extract of *Ficus racemosa*	250.6	*Culex quinquefasciatus*	67.72, 63.70	--	Velayutham *et al.*, 2012
		Culex gelidus	12.00, 11.21	--	
Aqueous aerial extract of *Ammannia baccifera*	10-30	*Anopheles subpictus*	257.16	--	Suman *et al.*, 2013
		Culex quinquefasciatus	210.88	--	
Aqueous root extract of *Delphinium denudatum*	85	*Aedes aegypti*	96,9.6	--	Suresh *et al.*, 2014
Ethyl acetate extract of leaf and fruit of *Couroupita guianensis* Aubl.	Leaf: 10-45 Fruit: 5-15	*Aedes aegypti*	Leaf: 44.55 Fruit: 49.96	Leaf: 318.39 Fruit: 568.84	Vimala *et al.*, 2014
Methanol extract of *Couroupita guianensis* Aubl.		*Aedes aegypti*	Leaf: 85.75 Fruit: 67.78	Leaf: 598.63 Fruit: 714.45	Vimala *et al.*, 2014
Colloid synthesis of aqueous extract of *Couroupita guianensis* Aubl		*Aedes aegypti*	Leaf: 2.1 Fruit: 5.59	Leaf: 2.09 Fruit: 5.7	Vimala *et al.*, 2014
Leafs of *Melia azedarach* using 2,7.bis[2-[diethylamino]-ethoxy] fluorence	3-31	*Aedes aegypti*	4.27	12.61	Ramanibai *et al.*, 2014
		Culex quinquefasciatus	3.43	10.29	
Leaf extract of *Feronia elephantum* (Rutaceae)	18-45	*Anopheles stephensi*	18.041	32.575	Veerakumar *et al.*, 2014
		Aedes aegypti	20.399	37.534	
		Culex quinquefasciatus	21.798	39.596	
Leaf extract of *Leucas aspera*	25-80	*Aedes aegypti*	8.56, 10.03, 14.46, 13.45, 17.41, 27.49	21.5685, 93.0392, 39.6485, 42.2029, 31.3009, 53.2576	Suganya *et al.*, 2014
Leaf extract of *Aloe vera*	35-55	*Anopheles stephensi*	48.79, 59.09, 70.88, 83.58, 152.55	--	Dinesh *et al.*, 2015
Leaf extract of *Annona muricata*	20-53	*Aedes aegypti*	12.58	26.46	Santhosh *et al.*, 2015
		Anopheles stephensi	15.28	31.91	
		Culex quinquefasciatus	18.77	35.72	
Leaf extract of *Euphorbia hirta*	30-60	*Anopheles stephensi*	10.14, 16.82, 21.51, 27.89	31.98, 50.38, 60.09, 69.94	Priyadarshini *et al.*, 2012
Aqueous leaf extract of *Morinda tinctoria* using acetone	60-95	*Culex quinquefasciatus*	8.088, 1.442	--	Kumar *et al.*, 2014
Aqueous leaf extract of *Chomelia asiatica* (Rubiaceae)		*Anopheles stephensi*	17.95	33.03	Muthukumaran *et al.*, 2014
		Aedes aegypti	19.32	34.87	
		Culex quinquefasciatus	20.92	37.41	
Leaf extract of *Feronia elephantum* (Rutaceae)	20-60	*Anopheles stephensi*	11.56	20.56	Veerakumar *et al.*, 2014
		Aedes aegypti	13.13	23.12	
		Culex quinquefasciatus	14.19	24.30	
Leaf extract of *Gmelina asiatica*	32	*Anopheles stephensi*	22.44	40.65	Muthukumaran *et al.*, 2015
		Aedes aegypti	25.77	45.98	
		Culex quinquefasciatus	27.83	48.92	
Aqueous fruit extract of *Drypetes roxburghii*	26.6	*Culex quinquefasciatus*	0.86, 1.16, 1.28	--	Haldar *et al.*, 2013
		Anopheles stephensi	0.73, 0.83, 0.98	--	
Crude methanol and aqueous extraction of *Nelumbo nucifera*	45	*Anopheles subpictus*	8.89, 11.82, 0.69	28.65, 36.06, 2.15	Santhoshkumar *et al.*, 2010
		Culex quinquefasciatus	9.51, 13.65, 1.10	28.13, 35.83, 3.59	
Aqueous leaf extract *of Mukia maderaspatana*	64	*Aedes aegypti*	0.211	0.703	Chitra *et al.*, 2015
		Culex quinquefasciatus	0.094	0.482	
Murraya koenigii leaf extract	25-35	*Aedes aegypti*	13.34, 17.19, 22.03, 27.57, 34.84	36.98, 47.67, 55.95, 67.36, 77.72	Suganya *et al.*, 2012
		Anopheles stephensi	10.82, 14.67, 19.13, 24.35, 32.09	32.38, 42.52, 53.65, 63.51, 75.26	
Leaf aqueous extract of *Nerium oleander*	20-35	*Anopheles stephensi*	20.60, 24.90, 28.22, 33.99	41.62, 50.33, 57.78, 68.41	Roni *et al.*, 2012

AgNps synthesised using aqueous leaf extract *of Mukia maderaspatana* (Cucurbitaceae) served as a potent larvicidal agent against *A. aegypti* and *C. quinquefasciatus* in which LC_{50} and LC_{90} of *A. aegypti* had 0.211 and 0.703ppm while *C. quinquefasciatus* had 0.094; 0.482ppm (Chitra *et al.,* 2015). The AgNps synthesised from *Murraya koenigii* leaf extract have excellent larvicdical activity against *A. stephensi* (LC_{50} values: 10.82, 14.67, 19.13, 24.35, 32.09ppm and LC_{90} values of 32.38, 42.52, 53.65, 63.51, 75.26ppm) while *A. aegypti* (LC_{50} values of 13.34, 17.19, 22.03, 27.57, 34.84ppm and LC_{90} values of 36.98, 47.67, 55.95, 67.36, 77.72ppm (Suganya *et al.,* 2012). AgNps synthesised from leaf aqueous extract of *Nerium oleander* have effective larvicidal activity against first to fourth instar larvae and pupae of *A. stephensi* with following values: LC_{50} and LC_{90} of instar larvae were 20.60, 24.90, 28.22, and 33.99 ppm and 41.62, 50.33, 57.78, and 68.41 ppm while for pupae it was 39.55 and 79.10 ppm (Roni *et al.,* 2012). The larvicidal activity of AgNps synthesised from different source is tabulated in table 1.

Anticancer Study

The anticancer potential of AgNps synthesised from *Acorus calamus* was evaluated against epidermoid carcinoma cell (A431) (Nayak *et al.,* 2015). The AgNps synthesised from plant polyphenol called caffeic acid through facile mediated process had shown effective anticancer activity against the human hepatoma (HepG2) cells by reducing the tumour cell viability through activating apoptosis (Guo *et al.,* 2015). The AgNps synthesised from *Andrographis echioides* (leaf) through aqueous extract process have been reported with potential anticancer activity against the human breast adenocarcinoma cancer cell line (MCF-7) with an inhibitory concentration (IC_{50}) of 31.5µg/mL at 24h incubation by suppressing its growth (inhibiting the proliferation of tumour cells) (Elangovan *et al.,* 2015). The anticancer activity of AgNps synthesized from different plant is listed in table 2.

The AgNps synthesised from ethanol extract of rose (*Rosa Indica*) petals have exhibited effective anticancer activity against human colon cancer cells (HCT 15 cells) by down regulating the Bcl-2 and Bax level by which upregulates activation of caspase 3 and 9 that finally induce apoptosis (Ramar *et al.,* 2015).

The AgNps synthesised from Mollick et al. (2015) have revealed excellent anticancer activity against the Jurkat cell (human T-cell lymphoma) by reducing the viability at the rate of 52.6%, 85.4%, and 91.6% with respect to the concentration of 10, 25, and 50µg/ml of AgNPs. Citrate coated AgNps (10nm in size) showed overall DNA damages and cytotoxic affect against human lung cells (BEAS-2B) after 24h by the comet assay (Gliga *et al.,* 2014).

Antimicrobial Study

The AgNPs synthesised from *C. maxima* (petals), *M. oleifera* (leaves) and *A. calamus* (rhizome) have exhibited strong antimicrobial activity against *Bacillus subtilis* (gram positive) and *E. coli, P. aeruginosa* and *Vibrio cholerae* (gram negative) (Nayak *et al.,* 2015).

The AgNps synthesised from *Andrographis echioides* (leaf) through aqueous extract process also had excellent antibacterial activity against *E. coli* (28mm) and *S. aureus* (23mm) and moderate activity against *Salmonella typhi* (18mm), *Micrococcus luteus* (15mm) and *Pseudomonas aeruginosa* (13mm) (Elangovan *et al.,* 2015). The AgNps synthesised from rose (*Rosa Indica*) petals using ethanolic extraction have a potential antibacterial activities against *E. coli (*MTCC-40) and *K. pneumonia* (MTCC-740) (gram negative) than *S. mutans* (MTCC-896) and *Enterococcus faecalis* (MTCC-439) (Ramar *et al.,* 2015).

The antimicrobial activities of AgNps synthesized from different plant were represented in table 3. The AgNps synthesised from *Abelmoschus esculentus* (L.) pulp extract have potential antibacterial activity against *B. subtilis* (MTCC 736), *Bacillus cereus* (MTCC 306), *P. aeruginosa* (MTCC 8158), *Micrococcus luteus* (MTCC 1538) and *E. coli* (MTCC 68) with zone of inhibition (ZoI) of 33, 28, 26, 40 and 19mm respectively (Mollick *et al.,* 2015). Suresh et al. (2014) generated AgNps from root of *Delphinium denudatum* (DdAgNPs) and obtained ZoI of 10 and 8mm against *B. cereus* (NCIM 2106) and *E. coli* (ATCC 8739) respectively which was comparatively lower than the activity rendered by Mollick et al. (2015).

The minimal inhibitory concentration (MIC) and minimal bactericidal concentration (MBC) of citrate stabilized AgNps synthesised using sodium citrate and found 60, 160 mg/mL and 80, 160 mg/mL against *S. aureus* and *B. Megaterium* respetively. Similarly, Borah et al. (2013) reported that the MIC and MBC values of AgNps synthesised from *Ocimum sanctum* was 40, 120 mg/mL and 80, 140 mg/mL against *S. aureus* and *B. megaterium* respectively.

The AgNps from leaf extract of *O. tenuiflorum* exhibited potential antibacterial activity against *E. Coli* (gram negative) and *Corynebacterium* (gram positive) with ZoI of 10, 15, 20mm and 14, 16, 20mm respectively while it was 19, 24, 26mm against *B. substilus* (spore forming) (Patil *et al.,* 2012). AgNps pellets synthesised from seeds of *Elaeocarpus ganitrus* (Rudraksha) and Foliage of *Prosopis spicigera* (Shami) exhibited excellent antibacterial activity against *P. aeruginosa* and *S. aureus* with 25 and 21mm (Dwivedi *et al.,* 2013).

Anti-inflammation Activity

The AgNps synthesised from ethanol extraction of rose (*Rosa Indica*) petals have potent anti-inflammatory activity by attenuating the production of superoxide anion (O^-) and nitric oxide (NO) which was studied in rat peritoneal macrophages (Ramar *et al.,* 2015).

Table 2: Anticancer activity of AgNps synthesized from different sources.

BIOLOGICAL SOURCE/METHOD	SIZE (NM)	SHAPE	CELL TYPE	REFERENCES
Extracts from *Cucurbita maxima* (petals), *Moringa oleifera* (leaves), *Acorus calamus* (rhizome).	30-72	Highly crystalline, roughly spherical and cuboidal	Epidermoid carcinoma cell (A431)	Nayak *et al.*, 2015
Caffeic acid (Plant Polyphenol))	3-10	Spherical	human hepatoma HepG2	Guo *et al.*, 2015
Aqueous extract of leaf of *Andrographis echioides*	--	hexagonal	Human breast adenocarcinoma cancer cell line (MCF-7)	Elangovan *et al.*, 2015
Ethanolic extraction of petals of *Rosa Indica*	23.52-60.83	Crystalline and spherical	human colon cancer cells (HCT 15 cells)	Ramar *et al.*, 2015
Abelmoschus esculentus (L.) pulp extract	3-11	Spherical	Jurkat cell line (human T-cell lymphoma)	Mollick *et al.*, 2015
Citrate coated AgNps	10	--	human lung cells (BEAS-2B)	Gliga *et al.*, 2014

Table 3: Antimicrobial activity of AgNps synthesized from different sources.

BIOLOGICAL SOURCE/METHOD	SIZE (NM)	SHAPE	MICROBES NAME	ZONE OF INHIBITION (MM)	REFERENCES
Extract from *Cucurbita maxima* (petals), *Moringa oleifera* (leaves) *Acorus calamus* (rhizome)	30-72	Highly crystalline, roughly spherical and cuboidal	*Bacillus subtilis*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Vibrio cholera*	--	Nayak *et al.*, 2015
Aqueous extract of leaf of *Andrographis echioides*	-	Hexagonal	*Escherichia coli*, *Staphylococcus aureus* *Salmonella typhi* *Micrococcus luteus* *Pseudomonas aeruginosa*	28, 23, 18, 15, 13	Elangovan *et al.*, 2015
Ethanolic extraction of petals of *Rosa Indica*	23.52-60.83	Crystalline and spherical	*Escherichia coli (*MTCC-40) *Klebsiella pneumonia* (MTCC-740) *Streptococcus mutans* (MTCC-896) *Enterococcus faecalis* (MTCC-439)	--	Ramar *et al.*, 2015
Abelmoschus esculentus (L.) pulp extract	3-11	Spherical	*Bacillus subtilis* (MTCC 736) *Bacillus cereus* (MTCC 306) *Pseudomonas aeruginosa* (MTCC 8158) *Micrococcus luteus* (MTCC 1538) *Escherichia coli* (MTCC 68)	33 28 26 40 19	Mollick *et al.*, 2015
Aqueous root extract of *Delphinium denudatum*	85	Spherical	*Bacillus cereus* NCIM 2106 *Escherichia coli* ATCC 8739	10 08	Suresh *et al.*, 2014
leaf extract of *Ocimum tenuiflorum*	25-40	Spherical	*Escherichia coli* *Corynebacterium* *Bacillus substilus*	10,15,20 14,16,20 19,24,26	Patil *et al.*, 2012
Seeds of *Elaeocarpus ganitrus* (Rudraksha) and Foliage of *Prosopis spicigera* (Shami)	--	--	*Pseudomonas aeruginosa* *Staphylococcus aureus*	25,25 21,21	Dwivedi *et al.*, 2013

Table 4: Anticancer activity of gold nanparticles synthesized from different sources.

BIOLOGICAL SOURCE/METHOD	SIZE (NM)	SHAPE	CELL TYPE	REFERENCES
Areca catechu nut	22.2	Spherical	He La cell lines	Rajan *et al.*, 2015
Kaempferol mediated	16.5	Spherical	MCF-7 (breat cancer cells)	Raghavan *et al.*, 2015
Gold nanopraticles modified with alpha-tocopheryl and arginine–glycine–aspartic acid	4	Spherical	U8MG – human primary glioblastoma cell line	Zhu *et al.*, 2015

GNP

Anticancer Study

The biosynthesized gold nanopraticles (GNps) showed anticancer activity against He La cell lines and caused 66 % of cell death at 100 µL concentration. (Rajan *et al.*, 2015). The anticancer activity of gold nanoparticles synthesized from different plant sources were represented in table 4. The GNps synthesised using a flavanol source, Kaempferol (3, 5, 7, 4 - tetrahydroxyflavone) have potential anticancer activity against MCF-7 by inducing apoptosis by increasing in sub-G1 (hypodiploid) population. By inducing angiogenesis process they also inhibited vascular endothelial growth factor (VEGF) which was confirmed through chorioallantoic membrane assay (CAM). It also reduces the viability of cells of MCF-7 based on the dose and time depended manner (Raghavan *et al.*, 2015). Multifunctional dendrimer-entrapped GNps (Au DENPs) modified with alpha-tocopheryl succinate (α-TOS) and arginine–glycine–aspartic acid (RGD) peptide have potential targeting towards the cancer cells which over express the $\alpha_v\beta_3$ integrin and inhibits the proliferation of cancer cell (U8MG – human primary glioblastoma cell line) by inducing apoptosis (Zhu *et al.*, 2015).

Antimicrobial Study

The biosynthesized GNps showed antibacterial activity against *E. coli, K. Pneumonia, P. aeruginosa, Enterobacter* sp. and *S.aureus* with respect to ZoI of 10, 11, 12,10 and 14mm respectively (Rajan *et al.,* 2015). The antimicrobial activity of gold nanoparticles synthesized from a plant is given in the table 5.

Antioxidant study

The GNps have showed potent free radical scavenging activity against the nitric oxide (NO) and 2,2-diphenyl-1-picrylhydrazyl (DPPH) (Rajan *et al.,* 2015).

Catalytic Activity

The GNps showed an excellent catalytic activity (reduction activity) of organic dye such as MB, MO, EY and 4-NP and this can be used in removing hazardous environmental pollutants (Rajan *et al.,* 2015).

Larvicidal Activity

GNps synthesised from *Cymbopogan citratus* have excellent antiparasitic activity against the *C. quinquefasciatus* (filaraial vector) (LC_{50} and LC_{90}: 1.08 and 2.76ppm) while leaf extract of *Anthocephalus cadamba* exhibited 21.82 and 79.52ppm of LC_{50} and LC_{90} against third instar larvae of *C. quinquefasciatus* (Naresh Kumar *et al.,* 2012). The larvicidal activity of gold nanoparticles synthesized from a plant is given in the table 6.

IRON NANOPARTICLES (INPs)

Anticancer Study

The in vitro cytotoxicity of non-toxic β-cyclodextrin assemblied magnetic Fe_3O_4 nanoparticles (β-CD-MNPs) had shown greater anticancer activity against MCF-7 and it was also used as drug delivery system in Cancer therapy (Wang *et al.,* 2015). The anticancer activity of iron nanoparticles synthesized from different plant is tabulated in table 7. A nanocomposites synthesized through layer-by-layer technique called multifunctional peptide-fluorescent-magnetic nanocomposites (Fe_3O_4@PEI@Cy5.5@PEG@HCBP-1 NPs, HPCPMNPs) have strong influence on the the cell viability of human embryonic lung fibroblast cell line (HLF) and human mesenchymal stem cell (MSC) at the concentration of 0.5 mg/mL and 1 mg/mL($p < 0.01$) treatment. HPCPMNPs also have the capability of targeting or detecting the human lung cancer cell line (H460) of about 80%. This indicates that these nanocomoposites can be used in cancer diagnostic agent by modifying diverse fluorescence dyes and targeting ligands on its surface (Zhou *et al.,* 2015). Semkina et al. (2015) reported the anticancer activity of Doxorubin (Dox-anticancer drug) loaded superparamagnetic iron oxide (Fe_3O_4) magnetic nanoparticles (MNPs) with Bovine Serum Albumin (BSA) and Polyethylene Glycol (PEG) called MNP-BSA@Dox-PEG against Dox-resistance (C6 - rat glial tumour cells induced by N-nitrosomethylurea) and Dox-sensitive (HEK293-human embryonic kidney cells) by inhibiting the cell viability.

OTHER NANOPARTICLES

Anticancer Study

The anticancer activity of nickle doped cerium oxide ($Ni_x Ce_{1-x}O2$) had shown that there was 55% reduction of neuroblastoma cancer cell line viability without exhibiting harm to the normal healthy human embryonic kidney 293 cell-HEK293) (Abbas *et al.,* 2015).

PST-Dox (Galactoxyloglucan, PST001-conjugated Dox) nanoparticle showed a potential anticancer activity against lung adinocarcinoma (A549) and metastatic melanoma (A375) by inducing apoptosis. A PST-Dox nanoparticle was reported with non-toxic to normal lymphocytes up to certain dosage (Joseph *et al.,* 2015).

DPM@PL (DTX loaded methoxy polyethylene glycol-s-s-vitamin E succinate (PSV) micelles (DPM) @ PPV-based liposomes) have shown inhibition of *in situ* tumour growth and pulmonary metastasis formation by DTX- inducing the apoptosis and decreased level of metastasis-promoting protein formation. They also have 81% and 92% inhibition rate against the tumour volume and lung metastasis. It doesn't show any systemic toxicity. This indicates that the DPM@PL nanoparticle which can be used as a delivery systems for breast cancer therapy (Xu *et al.,* 2015).

Silica nanopraticles (Dual-SiNPs) which was synthesised using dual aptamer modifier have excellent sensitive detection against two breast cancer cell such as mucin 1 (MUC1) (+) and human epidermal growth factor receptor 2 (HER2) (+) cell lines at the concentration of 1cell/100µL. This indicates its role in diagnosis and prognosis of breast cancer (Jo *et al.,* 2015).

In vitro study with DTX-loaded Gal-pD-TPGS-PLA/NPs (galactosamine conjugated polydopamine-modified NPs synthesized using D-α-tocopherol polyethylene glycol 1000 succinate-poly(lactide) showed potent anticancer activity against HepG2 on heptoma-bearing nude mice by decreasing the tumour size. It also had the higher efficiency of uptaking liver cancer cell line HepG2 which was confirmed by flow cytometry and confocal laser scanning microscopy. It reveals its drug delivery system in liver cancer (Zhu *et al.,* 2015).

By nab technology, human serum albumin loaded with lapatinib (Tykerb – tyrosine kinase inhibitor of HER2 and EFGR) was developed called LHNPs which has excellent anti-tumour efficiency by ceasing the proliferation of HER2 by over expressing SKBr3 (human breast cancer cell line) in tumour-bearing mice. They also suggested that it doesn't have hepatic or kidney toxicity (Wan *et al.,* 2015). LFC/CMC NPs (LFC131 peptide surface conjugated O-carboxymethyl chitosan nanoparticles (O-CMC NP)] have capability of increasing cancer cell death through selective delivery of DTX.

It also has higher efficiency of uptaking tumour cell by receptor mediated interaction of LFC131 with the CXCR4 which is over expressed in cancer cell and by inducing caspase-3 activity in A549 cancer cells. They have also suggested that the NPs have greater cell apoptosis by inducing apoptotic and necrotic cell death (Wang *et al.,* 2015).

Table 5: Antimicrobial activity of gold nanoparticles synthesized from different sources.

BIOLOGICAL SOURCE/METHOD	SIZE (NM)	SHAPE	MICROBES NAME	ZONE OF INHIBITION (MM)	REFERENCES
Areca catechu nut	22.2	Spherical	*Escherichia coli*	10	Rajan *et al.*, 2015
			Staphylococcus aureus	14	
			Enterobacter	10	
			Pseudomonas aeruginosa	12	
			K.pneumonia	11	

Table 6: Larvicidal activity of gold nanoparticles synthesized from different sources.

BIOLOGICAL SOURCE/METHOD	SIZE (NM)	NAME OF MOSQUITO SPECIES	LETHAL CONCENTRATION (LC) (MG/L) / PPM		REFERENCES
			LC_{50}	LC_{90}	
Leaf extract of *Cymbopogan citratus*		*Culex quinquefasciatus*	1.08	2.76	Naresh kumar *et al.*, 2012

Table 7: Anticancer activity of Iron Nanoparticles.

BIOLOGICAL SOURCE/METHOD	SIZE (NM)	SHAPE	CELL TYPE	REFERENCES
Non-toxic β-cyclodextrin assemblied magnetic Fe_3O_4 nanoparticles	12	Spherical	Michigan Cancer Foudation-7 (MCF-7- a breast cancer cell line)	Wang *et al.*, 2015
Multifunctional peptide-fluorescent-magnetic nanocompositesusing layer by layer method	22.3	Spherical	Human embryonic lung fibroblast cell line (HLF), human mesenchymal stem cell (MSC) and human lung cancer cell line (H460)	Zhou *et al.*, 2015
Doxorubin loaded Superparamagnetic iron oxide magnetic nanoparticles with Bovine Serum Albumin and Polyethylene Glycol	85	--	Rat glial tumour cells and HEK293-human embryonic kidney cells	Semkina *et al.*, 2015

Table 8: Anticancer and larvicidal activity of nanoparticles of different origin.

BIOLOGICAL SOURCE/METHOD	SIZE (NM)	SHAPE	CELL TYPE	REFERENCES
Nickle doped cerium oxide using Co-precipitation method	22	Spherical	H-SY-5Y neuroblastoma cancer cell line	Abbas *et al.*, 2015
Galactoxyloglucan, PST001-conjugated Dox	10	Spherical	Lung adinocarcinoma (A549) and metastatic melanoma (A375)	Joseph *et al.*, 2015
DTX loaded methoxy polyethylene glycol-s-s-vitamin E succinate (PSV) micelles (DPM) @ PPV-based liposomes	113.3	Shrapnel	*in situ* tumour growth and pulmonary metastasis	Xu *et al.*, 2015
Gold Nanoparticle synthesised using Dual aptamer modifier	70	--	breast cancer cell such as mucin 1 (MUC1) (+) and human epidermal growth factor receptor 2 (HER2) (+) cell lines	Jo *et al.*, 2015
galactosamine conjugated polydopamine-modified NPs synthesized using D-α-tocopherol polyethylene glycol 1000 succinate-poly(lactide)	209.4	Spherical	HepG2 - heptocellular carcinoma cell	Zhu *et al.*, 2015
Human serum albumin loaded with lapatinib	145.2 ± 4.55	--	human breast cancer cell line - HER2	Wan *et al.*, 2015
LFC131 peptide surface conjugated O-carboxymethyl chitosan	189 ± 3.6	Spherical	A549 lung cancer cells	Wang *et al.*, 2015
Cobalt acetate solution and *Bacillus thuringiensis*	85.3	LC_{50}: 29.16, 8.12, 3.59	*Anopheles subpictus*	Marimuthu *et al.*, 2013
		LC_{50}: 34.61, 6.94, 2.87	*Aedes aegypti*	

Larvicidal activity

Cobalt nanoparticles (CoNps) synthesised using cobalt acetate solution and *B. thuringiensis* (bio control agent) have potential larvicidal activity against fourth instar larvae of *A. subpictus* (malaria vector) and *A. aegypti* (dengue vector) (LC_{50} values of 29.16, 8.12, 3.59 mg/L; 34.61, 6.94, and 2.87 mg/L) (Marimuthu *et al.*, 2013). The anticancer and larvicidal activity of other nanoparticles synthesized in different sources is represented in the table 8.

CONCLUSION

In this review, a summary of various nanoparticles synthesised from different different biological and non biological

sources. Based on the bioactivity, they were listed under different categories such as larvicidal agents, anti-cancer, anti-bacterial, anti-inflammatory, antioxidant and catalytic activity which were discussed in detail. In search of novel biomolecules for the welfare of human beings, active metal of nanosized materials of different sources have been extensively implemented and studied for biological activities against wide range of pathogenic agents and carriers/vectors. This review addressed the prosperous role of nanoparticles in different health sectors of human beings such as vector borne disease, cancer and infectious diseases. As anticipated by Benelli (2016), wide range of research has been executed by the researchers for the benefit of human beings and was observed in this complete review on nanoparticles. Hence nanoparticles playing a dynamic role in treatment and diagnostic of various threatening diseases and soon will occupy an inevitable role in healthcare development than now.

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