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REVIEW

Biosynthesis of metallic nanoparticles using plant derivatives and their new avenues in pharmacological applications – An updated report



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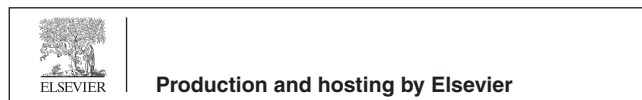
Biological synthesis;
Metallic nanoparticles;
Plants;
Secondary metabolites;
Chronic diseases

Abstract The field of nanotechnology mainly encompasses with biology, physics, chemistry and material sciences and it develops novel therapeutic nanosized materials for biomedical and pharmaceutical applications. The biological syntheses of nanoparticles are being carried out by different macro–microscopic organisms such as plant, bacteria, fungi, seaweeds and microalgae. The biosynthesized nanomaterials have been effectively controlling the various endemic diseases with less adverse effect. Plant contains abundant natural compounds such as alkaloids, flavonoids, saponins, steroids, tannins and other nutritional compounds. These natural products are derived from various parts of plant such as leaves, stems, roots shoots, flowers, barks, and seeds. Recently, many studies have proved that the plant extracts act as a potential precursor for the synthesis of nanomaterial in non-hazardous ways. Since the plant extract contains various secondary metabolites, it acts as reducing and stabilizing agents for the bioreduction reaction to synthesized novel metallic nanoparticles. The non-biological methods (chemical and physical) are used in the synthesis of nanoparticles, which has a serious hazardous and high toxicity for living organisms. In addition, the biological synthesis of metallic nanoparticles is inexpensive, single step and eco-friendly methods. The plants are used successfully in the synthesis of various greener nanoparticles such as cobalt, copper, silver, gold, palladium, platinum, zinc oxide and magnetite. Also, the plant mediated nanoparticles are potential remedy for various diseases such as malaria, cancer, HIV, hepatitis and other acute diseases.

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Contents

1.	Introduction	474
1.1.	Classical approaches of metals	474
1.2.	Different methods for metallic nanoparticle synthesis	475
1.3.	Bio-reduction mechanism.	475
2.	Different parts of plants used to produce metallic NPs	475
2.1.	Stem as source for nanoparticle synthesis	475
2.2.	Fruits mediated synthesis of metallic nanoparticles	476
2.3.	Seeds as source.	476
2.4.	Leaves mediated synthesis of NPs	477
2.5.	Flowers as source for NPs production	477
3.	Pharmacological application of metallic nanoparticles.	477
3.1.	Anti-bactericidal activities of metallic nanoparticles	477
3.2.	Anti-fungicidal activities of metallic nanoparticles	477
3.3.	Antiplasmodial activity of metallic nanoparticles	477
3.4.	Anti-inflammatory action of nanoparticles	479
3.5.	Anticancer studies on plant mediated nanoparticles	479
3.6.	Antiviral effects of metallic nanoparticles	479
3.7.	Antidiabetic management of metallic nanoparticles	479
3.8.	Antioxidant mechanisms of plant derived nanoparticles	479
4.	Secondary metabolites effect in bio-reduction reaction	480
5.	Commercial applications of biosynthesized nanoparticles	481
5.1.	Waste water treatment	481
5.2.	Cosmetics.	481
5.3.	Nanoparticles in food industry.	481
6.	Factors influencing the synthesis of metallic nanoparticles.	481
7.	Conclusion and future prospective of plant derived nanoparticles	482
	Acknowledgements	482
	References.	482

1. Introduction

Nanoparticle has multifunctional properties and very interesting applications in various fields such as medicine, nutrition and energy (Chandran et al., 2006). The biogenic syntheses of monodispersed nanoparticles with specific sizes and shapes have been a challenge in biomaterial science. Also, it has created remarkable advantages in the pharmacological industry to cure various bacterial and viral diseases (Song and Kim, 2009). Biosynthesis methods have more compensation over other classical synthesis procedures due to the availability of more biological entities and eco-friendly procedures. The rich biodiversity and easy availability of plant entities have been highly explored for the nanomaterials synthesis (Monda et al., 2011). Recently, the biosynthesis of nanosized particles, wires, flowers, tubes was reported successfully. These biological synthesized nanomaterials have potential applications in different areas such as treatment, diagnosis, development surgical nanodevices and commercial product manufacturing (Bar et al., 2009). Nanomedicine makes a huge impact in healthcare sector in treating various chronic diseases. Hence, eco-friendly synthesis of nanoparticles is considered as building blocks of the forthcoming generations to control various diseases (Cruz et al., 2010).

Plant crude extract contains novel secondary metabolites such as phenolic acid, flavonoids, alkaloids and terpenoids in which these compounds are mainly responsible for the reduction of ionic into bulk metallic nanoparticles formation

(Aromal and Philip, 2012). These primary and secondary metabolites are constantly involved in the redox reaction to synthesize eco-friendly nanosized particles. Many previous reports are demonstrating that biosynthesized nanoparticle effectively controlled oxidative stress, genotoxicity and apoptosis related changes (Kim et al., 2007). Additionally, nanoparticles have broad application in agriculture industry and plant sciences. For instance, the nanoparticle using bioprocessing technology converts the agricultural and food wastes into energy and useful by-products. Based on that, the review focused on biosynthesized metallic nanoparticles from plant derivatives and its application in medical and commercial sectors including waste water treatment, cosmetics and food industry.

1.1. Classical approaches of metals

Anciently, the gold metal is known as a symbol of power and wealth. The gold metal is used in different forms to improve the human health ever since. Even today, the biological aspects of metallic gold nanoparticles (GNPs) are very useful to human health and cosmetics applications (Alanazi et al., 2010). In the 18th century, Egyptians used gold metal solubilized water for mental and spiritual purification. The restorative property of gold is still honoured in rural villages, where peasants cook their rice with a gold pellet to replace the minerals in the body via food intake. Traditionally, silver metal is used to control bodily infection and prevent food spoilage. Silver is used as wound healer agents and ulcer treatment

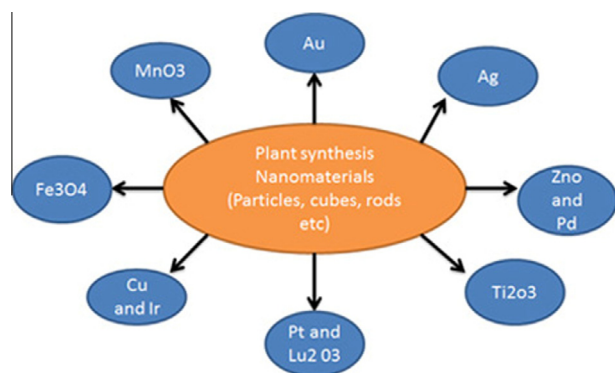


Figure 1 Different types of nanoparticle synthesis from plant resources.

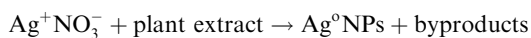
(Singh et al., 2013). In fact, nowadays the colloidal silver nanoparticles have been used as antimicrobial agent, wound dressing material, bone and tooth cement and water purifier as well (Narayanan and Sakthivel, 2011).

1.2. Different methods for metallic nanoparticle synthesis

Several methods are used for synthesis of nanoparticles (NPs) such as physical, chemical, enzymatic and biological. Physical methods are including plasma arcing, ball milling, thermal evaporate, spray pyrolysis, ultra thin films, pulsed laser desorption, lithographic techniques, sputter deposition, layer by layer growth, molecular beam epitaxy and diffusion flame synthesis of nanoparticles (Joerger et al., 2000). Similarly, the chemical methods are used to synthesized NPs by electrodeposition, sol-gel process, chemical solution deposition, chemical vapour deposition (Panigrahi et al., 2004; Oliveira et al., 2005), soft chemical method, Langmuir Blodgett method, catalytic route, hydrolysis (Pileni, 1997), co-precipitation method and wet chemical method (Gan et al., 2012). Physical and chemical methods have been using high radiation and highly concentrated reductants and stabilizing agents that are harmful to environmental and to human health. Hence, biological synthesis of nanoparticles is a single step bioreduction method and less energy is used to synthesize eco-friendly NPs (Sathishkumar et al., 2009). Apart from that, the biological methods are using eco-friendly resources such as plant extracts, bacteria, fungi, micro algae such as cyanobacteria, diatom, seaweed (macroalgae) and enzymes (Irvani, 2011). Fig. 1 shows different types of metallic nanoparticles synthesized from plant resources.

1.3. Bio-reduction mechanism

Silver: the biochemical reaction of AgNO_3 reacts with plant broth leads to the formation of AgNPs by following reaction (Tripathy et al., 2010). Fig. 2 explains the proposed mechanism of biological synthesis of nanoparticles.



Gold: the plant extract contains different biomolecules such as proteins, sugars, amino acids, enzymes and other traces of metals. These metabolites are strongly involved in the bio-reduction process. The proposed reaction was Au^+ ions

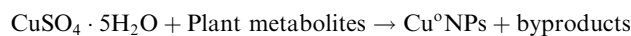
reduction into metallic Au^0 nanoparticles in the presence of metabolites and redox enzymes (Thakkar et al., 2010). The reaction is given below.



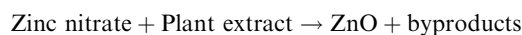
Platinum: platinum is involved in the following reduction process such as



Copper: the copper nanoparticles are synthesized from plant extracts and the reduction mechanism was proposed by Ramanathan et al. (2013)



Zinc oxide: A typical procedure was employed in ZnO nanoparticles production, the zinc nitrate was dissolved in the aloe plant extract to produce the nanosized particles. The method is as follows (Sangeetha et al., 2011):



2. Different parts of plants used to produce metallic NPs

Recently, the plant mediated nanomaterial has drawn more attention due to its vast application in various fields due to their physico-chemical properties. The different metallic nanoparticles such as gold, silver, platinum, zinc, copper, titanium oxide, magnetite and nickel were synthesized from natural resources and have been studied exclusively. The different parts of plant such as stem, root, fruit, seed, callus, peel, leaves and flower are used to syntheses of metallic nanoparticles in various shapes and sizes by biological approaches. Fig. 3 shows different sizes and shapes of the nanoparticles derived from plants resources. Biosynthesis reaction can be altered by wide range of metal concentration and amount of plant extract in the reaction medium, it may transform the shapes and size of the nanoparticles (Chandran et al., 2006; Dubey et al., 2010).

2.1. Stem as source for nanoparticle synthesis

Shameli et al. (2012) *Callicarpa maingayi* stem methanolic extract used for synthesis of silver nanoparticles and formed [Ag (*Callicarpa maingayi*)] + complex. The plant extract contains aldehyde group and it's mainly involved in the reduction of silver ions into metallic Ag nanoparticles. The different functional group $-\text{C}=\text{O}$, $\text{C}=\text{N}$ indicates amide I, polypeptides which are the responsible compounds in the capping of ionic substances into metallic nanoparticles. The molecular studies on biosynthesis of silver crystals are complex and not yet fully understood. But some previous studies are proposed model mechanisms of nanoparticles interaction with pathogenic organisms. The biosynthesized silver NPs binding with protein outer cell wall of bacteria, fungi or viral bodies that breaks the lipoproteins of microbial cell wall. Finally the cell division was stopped and cell leads to death. Phytosynthesis of silver nanoparticles use *Cissus quadrangularis* extracts at room temperature was reported by Vanaja et al. (2013). The stem part of plant extract shows the different functional groups, particularly the carboxyl, amine, and phenolic compounds that are involved in the reduction of silver ions.

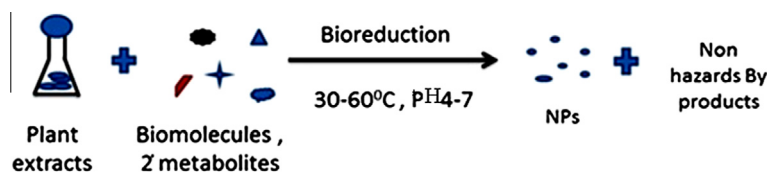


Figure 2 Proposed mechanism of nanoparticle synthesis using plant extracts.

Thus, synthesized silver nanoparticles show more activity against *Klebsiella planticola* and *Bacillus subtilis* pathogenic bacteria. Therefore, the biosynthesized metal nanoparticles acted as good antibacterial agents.

2.2. Fruits mediated synthesis of metallic nanoparticles

Gopinath et al. (2012) used plant fruit bodies *Tribulus terrestris* extract with addition of different molar concentrations of silver nitrate solution in order to synthesize eco-friendly AgNPs with specific morphological features. The extract contains active phytochemical compounds that are liable for the single step reduction reaction. The spherical shapes of silver nanoparticles were produced by the *T. terrestris* extract and substantiated admirable antimicrobial activity against multidrug resistant human pathogens. There is similar report on using of polyphenol from grapes to synthesize palladium nanoparticles and act effectively against bacterial diseases

(Amarnath et al., 2012). In addition, *Rumex hymenosepalus* extract acts as a reducing and stabilizing agent for silver nanoparticle synthesis. The use of optimum physicochemical parameters to synthesize nanomaterial is very effective in pharmacological solicitation to treat various endemic diseases.

2.3. Seeds as source

The fenugreek seed extract contains high flavonoids and other natural bioactive products such as lignin, saponin and vitamins. The reduction of chloroauric acid by using the powerful reducing agents fenugreek seed extract acts as a better surfactant. The COO^- group (carboxylic), $\text{C}=\text{N}$ and $\text{C}=\text{C}$ functional groups are present in the seed extract. The functional group of metabolites acts as a surfactant of gold nanoparticles and the flavonoids can stabilize the electrostatic stabilization of gold NPs (Mittal et al., 2013). The aqueous extract of *Macrotyloma uniflorum* enhanced the reduction rate of silver

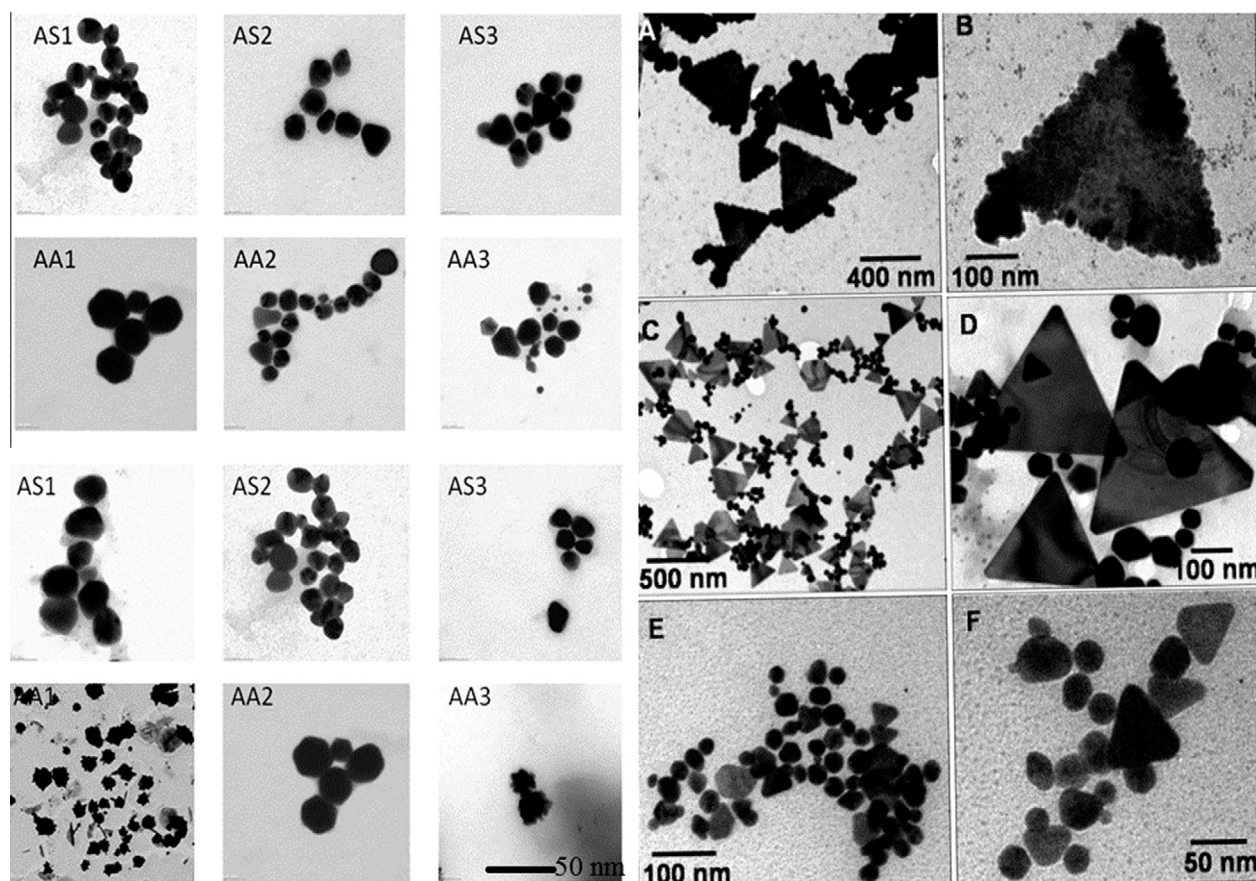


Figure 3 Different size and shapes of the nanoparticle synthesis from plant extracts (derived from Chandran et al., 2006 and Dubey et al., 2010).

ions. This may be owing to the presence of caffeic acid in the extract. Therefore, the presence of caffeic acid reduction reaction was occurred within a minute.

2.4. Leaves mediated synthesis of NPs

Plant leaves extract used as a mediator to synthesis of nanoparticles was reported. Leaves of *Centella asiatica*, *Murraya koenigii*, *Alternanthera sessilis* and many plants leaves extract have been studied. Recently, *P. nigrum* leaves were stated to contain an important bioactive compound which is involved in the nanoparticle synthesis by eco-friendly method. The biological mode of synthesized silver nanoparticles of 100 µg/ml concentration was proficient drug concentration on HEp-2 and HeLa cell line to regulate the normal biochemical function in cancer cells. The AgNPs have effective drug in cancer medicine to cure various oncology and dreadful diseases. *P. nigrum* extracts have been longumine and piper longminine, it acts as a capping agent for the formation of silver nanoparticles and may enhance the cytotoxic effects of the tumour cells (Jacob et al., 2012). A green synthesis of silver nanoparticles using the leaves of *Artemisia nilagirica* plant extract has been described by Vijayakumar et al. (2013). It shows a significant tool for antimicrobial agents in present and in a near future. Similarly, silver nanoparticles synthesized from the plant resources possibly control different pathogenic condition in human.

2.5. Flowers as source for NPs production

Noruzi et al. (2011) studied an eco-friendly method synthesis of gold nanoparticles by using rose petals. The extract medium contains abundant sugars and proteins. These functional compounds are the main sources for reduction of tetrachloroaurate salt into bulk GNPs. Likewise, *Catharanthus roseus* and *Clitoria ternatea* diverse groups of flowers are used for the metallic nanoparticle synthesis with desired sizes and shapes. The plant synthesized nanoparticles have been effectively controlling harmful pathogenic bacteria and similarly the medicinal usable *Nyctanthes arbortristis* flowers of gold nanoparticles extract are synthesized via green chemistry method (Das et al., 2011). The aqueous extract of *Mirabilis jalapa* flowers acts as a reducing agent and produced gold nanoparticles with eco-friendly method (Vankar and Bajpai, 2010). Table 1 illustrates the plant metabolites which represent in the bioreduction reaction to synthesis of metallic nanoparticles and its pharmacological applications.

3. Pharmacological application of metallic nanoparticles

3.1. Anti-bactericidal activities of metallic nanoparticles

The AgNPs were effectively disrupting the polymer subunits of cell membrane in pathogenic organisms. The reciprocal action of nanoparticles subsequently breaks the cell membrane and disturbs the protein synthesis mechanism in the bacterial system (Sondi and Salopek-Sondi, 2004). The increasing concentrations of silver nanoparticles have faster membrane permeability than the lower concentrations and consequently rupture the cell wall of bacteria (Kasthuri et al., 2009). The maximum conductivity was observed in *Rhizophora apiculata* reduced silver nanoparticles shown a low number of bacterial

colony in the experimental plate compared with AgNO₃ treated cells, which may be due to the smaller size of the particles and larger surface area which leads to the increase of membrane permeability and cell destruction (Antony et al., 2011). The interactions of bacteria and the metallic silver and gold nanoparticles have been binding with active site of cell membrane to inhibit the cell cycle functions (Kim et al., 2007). The biosynthesized silver nanoparticles were achieved in a single step procedure by using *Citrus sinensis* peel extract as a reducing and a capping agent. *C. sinensis* peel extract reduced silver nanoparticles effectively and the activity against *Escherichia coli*, *Pseudomonas aeruginosa* (gram-negative) and *Staphylococcus aureus* (gram-positive) has been proved (Kaviya et al., 2011). Similarly, Krishnaraj et al. (2010) reported that *Acalypha indica* plant leaf synthesized silver nanoparticles effectively control water borne pathogenic bacteria with lower concentrations of 10 µg/ml.

3.2. Anti-fungicidal activities of metallic nanoparticles

The fungicidal mechanism of biosynthesized metallic nanoparticles has more potential than commercial antibiotics such as fluconazole and amphotericin. The plant derived Ag nanoparticles have clearly showed the membrane damage in *Candida* sp. and damage in fungal intercellular components and finally cell function was destroyed (Logeswari et al., 2012). Most of the commercial antifungal agents have limited applications clinically and in addition, there are more adverse effect and less recovery from the microbial disease. Subsequently, the commercial drugs induce side effect such as renal failure, increased body temperature, nausea, liver damage, and diarrhoea after using the drugs. Nanoparticles were developed for novel and effective drug against microbes. The fungal cell wall is made up of high polymer of fatty acid and protein. The multifunctional AgNPs have a promising activity against spore producing fungus and effectively destroy the fungal growth. The fungal cell membrane structure significant changes were observed by treating it with metallic nanoparticles (Gardea-Torresdey et al., 2002).

3.3. Antiplasmodial activity of metallic nanoparticles

Currently, the most common diseases are spreading everywhere by vectors. Vector control is a serious requirement in epidemic disease situation. The advanced antiplasmodial species specific control method is less effective. This method has been more economical but less effective to control the target organisms in the health care sector (Gnanadesigan et al., 2011). Hence, effective and affordable antimalarial drugs are urgently required to control the plasmodial activity. In last few decades, plants have been used as traditional sources of natural products and having enough sources for drug development for antimalarial disease. The plant derived chemical constituents such as quinine, artemisinin and aromatic compound have been successfully used against resistant strains of malaria parasites (Jayaseelan et al., 2011). Due to that high resistance of parasites, the alternative drug is needed for controlling the resistance strains. The plants developed metallic nanoparticles such as silver, platinum and palladium nanoparticles are effectively control the malarial population in the environment. Also, the biogenic synthesis of metallic silver nanoparticles

Table 1 Summary of plant derived metallic nanoparticles and its biomedical applications.

Plants used	Nanoparticles	Parts of plant	Size (nm)	Shapes	Plant metabolites involved in bioreduction	Pharmacological applications	Cited
<i>Acalypha indica</i>	Ag, Au	Leaves	20–30	Spherical	Quercetin, plant pigment	Antibacterial	Krishnaraj et al. (2010)
<i>Aloe vera</i>	In ₂ O ₃	Leaf	5–50	Spherical	Biomolecules	Optical properties	Maensiri et al. (2008)
<i>Alternanthera sessilis</i>	Ag	Whole	40	Spherical	Amine, carboxyl group	Antioxidant, antimicrobial	Niraimathi et al. (2012)
<i>Andrographis paniculata</i>	Ag	Leaves	67–88	Spherical	Alkaloids, flavonoids	Hepatocurative activity	Suriyakalaa et al. (2013)
<i>A. mexicana</i>	Ag	Leaves	20–50	Spherical	Protein,	Antimicrobial	Singh et al. (2010)
<i>Artemisia nilagirica</i>	Ag	Leaves	70–90	Spherical	Secondary metabolites	Antimicrobial	Song et al. (2009)
<i>Boswellia serrata</i>	Ag	Gum	7–10	Spherical	Protein, enzyme	Antibacterial	Kora et al. (2012)
<i>Caria papaya</i>	Ag	Fruit	15	Spherical	Hydroxyl flavones, catechins	Antimicrobial	Jain et al. (2009)
<i>Cassia fistula</i>	Au	Stem	55–98	Spherical	Hydroxyl group	Antihypoglycemic	Daisy et al. (2012)
<i>Cinnamon zeylanicum</i>	Ag	Leaves	45	Spherical	Water soluble organics	Antibacterial	Sathishkumar et al. (2009)
<i>Citrullus colocynthis</i>	Ag	Calli	5–70	Triangle	Polyphenols	Antioxidant, anticancer	Satyavani et al. (2011)
<i>Citrus sinensis</i>	Ag	Peel	35	Spherical	Water soluble compounds	Antibacterial	Kaviya et al. (2011)
<i>Dillenia indica</i>	Ag	Fruit	11–24	Spherical	Biomolecules	Antibacterial	Singh et al. (2013)
<i>Dioscorea bulbifera</i>	Ag	Tuber	8–20	Rod, triangular	Diosgenin, ascorbic acid	Antimicrobial	Ghosh et al. (2012)
<i>Euphorbia prostrata</i>	Ag	Leaves	52	Rod, spherical	Protein, polyphenols	Antiplasmodial	Zahir and Rahman (2012)
<i>Gelsemium sempervirens</i>	Ag	whole	112	Spherical	Protein, amide, amine group	Cytotoxicity	Das et al. (2011)
<i>Lippia citriodora</i>	Ag	Leaves	15–30	Spherical,	Isoverbascoside compound	Antimicrobial	Cruz et al. (2010)
<i>Mentha piperita</i>	Au, Ag	Leaves	90–150	Spherical	Menthol	Antibacterial	MubarakAli et al. (2011)
<i>Mirabilis jalapa</i>	Au	Flowers	~100	Spherical	Polysaccharides	Antimicrobial	Vankar et al. (2010)
<i>H. canadensis</i>	Ag	Whole	113	Spherical	Phenolics, protein	Cytotoxicity	Das et al. (2011)
<i>Iresine herbstii</i>	Ag	Leaves	44–64	Cubic	Biomolecules phenolic compound	Biological activities	Dipankar et al. (2012)
<i>Melia azedarach</i>	Ag	Leaves	78	Irregular	Tannic acid, polyphenols	Cytotoxicity	Sukirtha et al. (2012)
<i>Tinospora cordifolia</i>	Ag	Leaves	34	Spherical	Phenolic compound	Antilarvicidal	Jayaseelan et al. (2011)
<i>Trigonella-foenum graecum</i>	Au	Seed	15–25	Spherical	Flavonoids	Catalytic	Aromal et al. (2012)
<i>Withania somnifera</i>	Ag	Leaves	5–40	Irregular, spherical	Methyl 7-oxooctadecanoate	Antimicrobial	Nagati et al. (2012)

from plant extract have been used to suppress the number of malarial productions.

3.4. Anti-inflammatory action of nanoparticles

Anti-inflammatory is an important wound healing mechanism. Anti-inflammation is a cascade process that produces immune responsive compound such as interleukins and cytokinins which can be produced by keratinocytes including T lymphocytes, B lymphocytes and macrophages (Jacob et al., 2012). Various inflammatory mediators such as enzymes, antibodies are secreted from the endocrine system. Other potential anti-inflammatory agents such as cytokines, IL-1, IL-2 are secreted from the primary immune organs. These anti-inflammatory mediators induce the healing process (Satyavani et al., 2011). Also, the inflammatory mediators are involved in biochemical pathways and control the expansion of diseases. Biosynthesized gold nanoparticles achieved positive wound repair mechanisms and tissue regeneration in inflammatory function (Gurunathan et al., 2009). The studies proved that biosynthesized gold and platinum nanoparticles are alternative sources for treating inflammation in a natural way.

3.5. Anticancer studies on plant mediated nanoparticles

Cancer is an uncontrolled cell proliferation with hysterical changes of biochemical and enzymatic parameters, which is universal property of tumour cells. The overexpression of cellular growth will be arrested and regulated with systematic cell cycle mechanisms in cancerous cell by using bio-based nanoparticles as novel controlling agents (Akhtar et al., 2013). Also the plant mediated nanoparticles have great effect against various cancer cell lines such as Hep 2, HCT 116 and Hela cell lines. Recently, many studies reported that plant derived nanoparticles have potential to control tumour cell growth. The improved cytotoxic effect is due to the secondary metabolites and other non-metal composition in the synthesizing medium (Raghunandan et al., 2011; Das et al., 2013).

The plant derived silver nanoparticles regulate the cell cycle and enzymes in bloodstream (Alt et al., 2004). Moreover, the plant synthesized nanoparticles relatively control the free radicals formation from the cell. Free radicals commonly induce cell proliferation and damage the normal cell function. The moderate concentration of gold nanoparticles induces the apoptosis mechanism in malignant cells (Dipankar and Murugan, 2012). Similarly, Ag nanoparticles treated MCF-7 cancer cell line has retained the biomolecules concentration in the cells, and subsequently the cell metabolism was regulated (Das et al., 2011). The metallic nanoparticles have proved their novel applications in medical field to diagnose and treat various types of cancer and other retroviral diseases. The bio-based nanoparticles are new and revolutionized to treat malignant deposit and without interfering the normal cells. Suman et al. (2013) reported that the green synthesis of silver nanoparticles exhibited a significant cytotoxic effect in HeLa cell lines compared to other chemical based synthetic drugs.

3.6. Antiviral effects of metallic nanoparticles

Plants mediated nanoparticles are the alternative drugs for treating and controlling the growth of viral pathogens. The

entry of viruses into a host is very reckless and it involved in faster translational process to multiply their colony numbers. Biosynthesis of AgNPs nanoparticles can act as potent broad-spectrum antiviral agents to restrict virus cell functions. Suriyakalaa et al. (2013) studied the bio-AgNPs that have persuasive anti-HIV action at an early stage of reverse transcription mechanism. The metallic NPs are strong antiviral agents and inhibit the viral entry into the host system. The biosynthesized metallic nanoparticles have multiple binding sites to bind with gp120 of viral membrane to control the function of virus. The bio-based nanoparticles are acting as effective virucidal agent against cell-free virus and cell-associated virus (Sun et al., 2005). In addition, the silver and gold nanoparticles are constantly inhibiting post-entry stages of the HIV-1 life cycle. Therefore, the metallic nanoparticles will act as promising antiviral drug against retro viruses.

3.7. Antidiabetic management of metallic nanoparticles

Diabetes Mellitus (DM) is a group of metabolic dysfunction in which person has uncontrolled sugar level in blood. Certain foods and balance diet or synthetic insulin drugs can be prevent the diabetes at certain levels, but the complete treatment of DM is a big challenge. However, the biosynthesized nanomaterials could be alternative drug to cure the diabetes mellitus. Daisy and Saipriya's (2012) results showed that gold nanoparticles have good therapeutic effects against diabetic models. Gold nanoparticles significantly reduce the level of liver enzymes such as alanine transaminase, alkaline phosphatase, serum creatinine, and uric acid in treated diabetes mice. The gold nanoparticles treated diabetic model showed a decrease of HbA (glycosylated haemoglobin) level which is maintaining the normal range. Swarnalatha et al. (2012) explored the *Sphaeranthus amaranthoides* biosynthesized silver nanoparticles inhibited α -amylase and acarbose sugar in diabetes induced animal model. It is mainly α -amylase inhibitory components are present in ethanolic extract of *S. amaranthoides* (Manikanth et al., 2010). Likewise, Pickup et al. (2008) studied that the nanoparticles are potent therapeutic agent to control diabetes with few side effects. The clinical studies in mice successfully control the sugar level of 140 mg/dl in silver nanoparticles treated group.

3.8. Antioxidant mechanisms of plant derived nanoparticles

Antioxidant agents including enzymatic and non-enzymatic substances regulate the free radical formation. Free radicals are causing cellular damage including brain damage, atherosclerosis and cancer. The free radicals are generated by reactive oxygen species (ROS) such as superoxide dismutase, hydrogen peroxides and hydrogen radicals. Biomolecules such as proteins, glycoprotein, lipids, fatty acids, phenolics, flavonoids and sugars strongly controlled the free radical formation (Marambio-Jones and Hoek, 2010). The scavenging power of enzymatic and non-enzymatic antioxidants is useful for the management of various chronic diseases such as diabetes, cancer, AIDS, nephritis, metabolic disorders and neurodegenerative. The antioxidant effect of silver nanoparticles was stronger than other synthetic commercial standards e.g. ascorbic acid and so on. The nanoparticles showed higher antioxidant activity whereas the tea leaf extract possesses higher

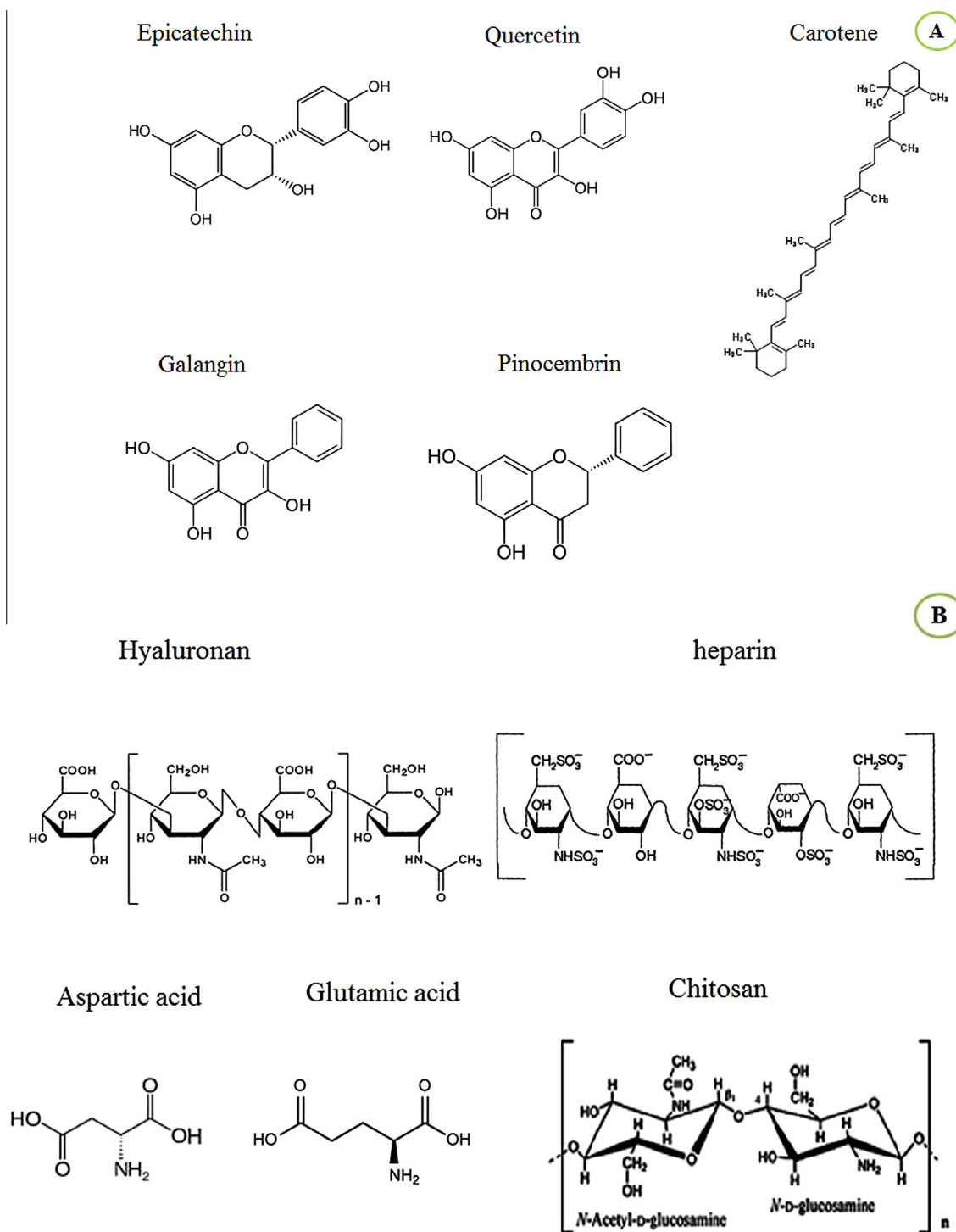


Figure 4 (a-c) Examples of different secondary metabolites are synthesized metallic nanoparticles.

phenolic and flavonoids content in the extract (Reichelt et al., 2012).

4. Secondary metabolites effect in bio-reduction reaction

Several secondary metabolites and enzymes have relatively promoted the formation of metallic nanoparticles from the corresponding ionic compounds. The reduction reaction mainly involved plant biomolecules (secondary metabolites)

such as sugars (polysaccharides), proteins, organic compounds, pigments, and plant resins. Plant natural products are involved in the reduction reaction to synthesize green nanoparticles. Plants are particularly participating in defence mechanisms to produce various chemical compounds such as polyphenols, saponins, antioxidant enzymes, terpenoids and alkaloids. These secondary metabolites are known as key sources for controlling the various acute diseases (Dubey et al., 2010). The proposed reduction reaction proved that

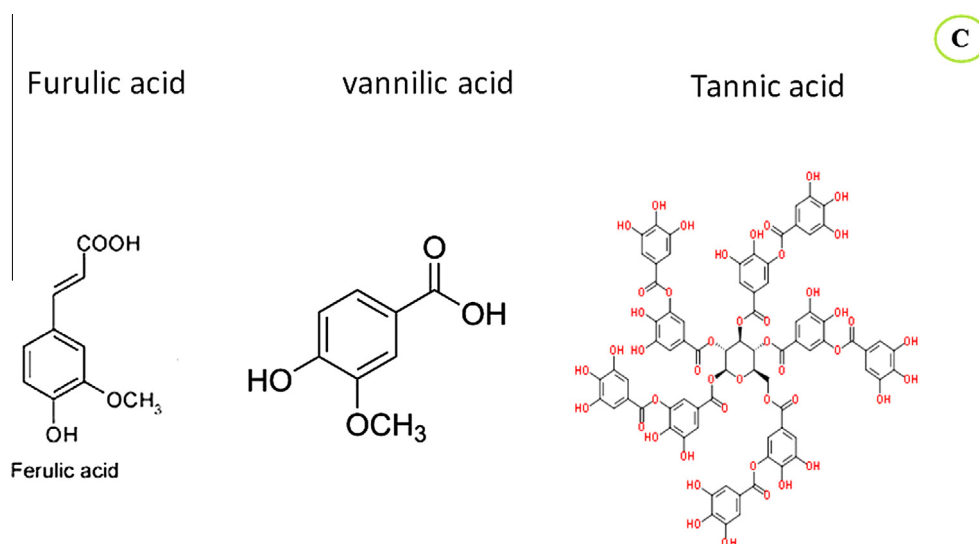


Figure 4 (continued)

the secondary metabolites are the main factors for the biosynthesis of metallic nanoparticles. The plant extracts contain numerous functional groups such as C=C (Alkenyl), C=N (amide), O=H (phenolic and alcohol), N-H (amine), C-H and COO- (carboxylic group). It is mainly symbolized as plant secondary metabolites and might be micro- and macromolecules (Jha et al., 2009). These chemical substances are fully participating for the nanoparticle production. For instance *R. hymenosepalus* plant extract promotes the nanoparticle syntheses at room temperature with fast reaction kinetics. Therefore, the solvent extract of *R. hymenosepalus* is rich in polyphenols such as catechins and stilbenes molecules that act as reducing and stabilizing agents for silver nanoparticles production (Awwad et al., 2013). The plants derived secondary metabolites such as phenolics (Moulton et al., 2010), proteins (Sanghi and Verma, 2009), polysaccharides (Huang and Yang, 2004; Wei and Qian, 2008), flavonoids and tannins (Nam et al., 2008) were synthesized nanoparticles in eco-friendly method. Fig. 4a-c shows different plant metabolites are used for the synthesis of nanoparticles in green chemistry method.

5. Commercial applications of biosynthesized nanoparticles

5.1. Waste water treatment

Recently, nanoproducts have immense applications in day to day life. There are also various eco-friendly nanoproducts available in commercial market with high efficiency such as water purifier, bone and teeth cement, facial cream and home-made products (Kouvaris et al., 2012). For instance, silver, silica and platinum nanoparticles have various applications in personal care and cosmetics and they are used as ingredients in various products such as sunscreens, anti-ageing creams, toothpastes, mouthwash, hair care products and perfumes (Kumar and Yadav, 2009). The silica nanomaterials are used as ingredients in various commercial products. Also, the modified silica nanomaterials are used as excellent pesticide control and it is used in a variety of non-agricultural applications.

5.2. Cosmetics

The metal nanoparticles are used as a preservative agent in food and cosmetic industries. New dimension of metallic nanoparticles is used for different commercial applications mainly cosmetics, pharma coating materials and food preservatives (Songand and Kim, 2009; Kokura et al., 2010). The nanosized metal nanoparticles such as gold, silver and platinum are broadly being applied for various commercial products such as shampoo, soap, detergent, and shoes. The chemical ingredients are mostly synthetic, and it causes side effects to human being. As a result, the green metallic nanoparticles are alternative for preservative agents in healthcare and food industries.

5.3. Nanoparticles in food industry

Silver metal is a highly heat conducting material because of that, nano-Ag is used in various mechanical devices. It is mainly used in heat liable instrumentation such as PCR lid and UV-spectrophotometer. The parts of instrumentation are made by nanosilver which is used as coated materials. It is highly stable in high temperature and without interference to the samples (Weiss et al., 2006). In food industries, the food products gets high microbial contamination due to their various open scale processes such as in manufacturing, processing and shipping of raw materials. Therefore, there is a need to develop a cost effective biosensor to evaluate the quality of the products. The metallic nanoparticles have been developed as biosensors and it effectively detects pathogen and monitors the different stages of contaminant with low cost.

6. Factors influencing the synthesis of metallic nanoparticles

The different hydrogen ion concentration is responding to the different size and shapes of nanoparticles formation. Shankar et al. (2003) reported that *Aloe vera* extract produced Au-Ag core nanoparticles in various sizes and shapes by fluctuating the pH of the solvent medium. Similarly, biosynthesis of nanoparticles by *alfalfa* plant extract of the pH is retort for the size

variation in the nanoparticles production. On the other hand, temperature is also one of the stimulating factors for the nanoparticles biosynthesis with different size and shapes. However, the study on AuNPs formation using leaf extract of *Cymbopogon flexuosus* Raju et al. (2011) revealed that at high temperatures, it will lead to the formation of higher spherical NPs and nanotriangles, whereas lower reaction temperature mostly increases the nanotriangle formation. The difference in morphology is mainly percentage/amount of the salt solution in the reaction mixture. The concentration of salt could be altered with the reduction ability and sizes. Some environmental factors such as physical and chemical parameters controlled metallic crystal structure using the plant biomass as substrates (Marchiol, 2012). In addition, the reduction reaction time (minutes–hours) is one of the factors to reduce the ions into bulk metal with variant shapes. The optimum time period produces high absorbance peak value to identify the higher concentration NPs in the medium. It determined the employment of growth conditions and obvious formation of different size of NPs such as spherical, triangular, hexagonal and rectangular (Rai et al., 2006).

7. Conclusion and future prospective of plant derived nanoparticles

Biosynthesis of metal nanoparticles using plant derivatives is extremely studied in the last two decades. The plant metabolites induce the production of metallic nanoparticles in ecofriendly manner. As a prospect, the ecofriendly synthesis of nanoparticles using plant crude extracts and purified metabolites is novel substrates for the large scale production. The plant mediated nanoparticles have the potential to be used in various fields such as pharmaceuticals, therapeutics, sustainable and renewable energy and other commercial products. The plant derived metallic nanoparticles have projected impact on diagnosis and treatment of various diseases with controlled side effects. In future, the plants have wide perspective for the synthesis of metallic nanoparticles in healthcare and commercial products. Even though, there are two reasons to be explored in the biological production of nanoparticles, they are:

- i. To identify the phytochemical compounds (active metabolites) which is involved partially/fully in the reduction reaction?
- ii. Laboratory scale production of metallic nanoparticles to the extent of large scale production, and need to elucidate their functional mechanism against the pathogenic organisms.

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