



ISSN (E): 2320-3862
ISSN (P): 2394-0530
NAAS Rating: 3.53
www.plantsjournal.com
JMPS 2020; 8(6): 26-33
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Received: 16-09-2020
Accepted: 21-10-2020

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A brief review for the development of bio-nanoparticles using some important Indian ethnomedicinal plants

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DOI: <https://doi.org/10.22271/plants.2020.v8.i6a.1226>

Abstract

Nanotechnology are often described as the manipulation of materials by certain conventional and/or natural processes so as to get materials with some specifications which will be utilized in various applications including the fields of drugs, chemistry, climate, electricity, agriculture, information, communication, heavy industry, and commodity. In recent years, the event of efficient green chemistry methods for synthesis of metal nanoparticles has become a serious focus of research to having several strong benefits of biological synthesis protocols over traditionally used physical and chemical methods. They need investigated so as to seek out an eco-friendly technique for production of well-characterized nanoparticles. Among these plants seem to be the simplest candidates and that they are suitable for large-scale biosynthesis of nanoparticles. Nano-conjugates which are developed by green origin are more consistent, stable and therefore the rate of synthesis is quicker than within the case of microorganisms. Moreover, the nanoparticles are more various in shape and size as compared with those produced by other organisms. During this review, role of six different ethnomedicinally important plants: *Phyllanthus amarus*, *Acalypha indica*, *Mentha spicata*, *Limonia acidissima*, *Centella asiatica*, *Murraya koenigii* within the synthesis of metal nano-conjugates has been discussed. The prosperity of employing such plants and plant-derived compounds for the biosynthesis of nanoparticles make the researchers to find accurate yet nontoxic safe research mechanisms of metal ions uptake and thereafter their bio reduction by plants, and to know the possible mechanism of nano-conjugates synthesis.

Keywords: Green synthesis, nano-conjugates, bio-nanoparticles, ethnomedicinal plants

Introduction

Nanotechnology term was used by Norio Taniguchi of Tokyo Science University in the year of 1974. According to him Nanotechnology basically is the process of separation, consolidation, and deformation of materials by atom or molecule. It is the concoction between science, engineering, and technology that is directed at the nanoscale level that is 1 to 100 nanometers^[1]. The sector of nanotechnology is one among the foremost active areas of research in modern sciences^[2]. The utilization of nanoparticles is gaining impetus within the present century as they possess defined chemical, optical and mechanical properties and thus making impression altogether spheres of human life^[3-4]. Metallic nanoparticles, mostly made from noble metals like gold, silver, platinum are of importance in catalysis, optics, phytomedicine, and antimicrobial activity applications^[5-7]. Conventional methods for the synthesis of nanoparticles like attrition and pyrolysis have limitations like defective surface formation, low production rate, high manufacturing cost and better energy requirements^[8]. Methods of chemical synthesis (e.g., chemical reduction, sol gel process) include the utilization of harmful chemicals, the creation of hazardous by-products, and precursor chemical contamination. Therefore, a safe, non-toxic, and ecologically beneficial procedure for the synthesis of nanoparticles is urgently required which is that the biological approach to biosynthesis of metal nano-conjugates^[9-10]. It is well documented that employing a plant derived compound or rather using the plant itself as a bio reducer (Figure 1) acts as a lowering and stabilizing agents that enhances the event of small nanoparticles even in large-scale with none external experimental conditions like high-energy and/or high-pressure, ultimately leading to substantial energy savings^[11]. In a brief sense, the term biosynthesis consists of a wide range of possible applications from nanotechnology approved eco-friendly constructing

processes that lower waste productions; enhances the utilization of nano-materials as catalysts and nano-devices to

scale back pollution for greater efficiency of energy production.

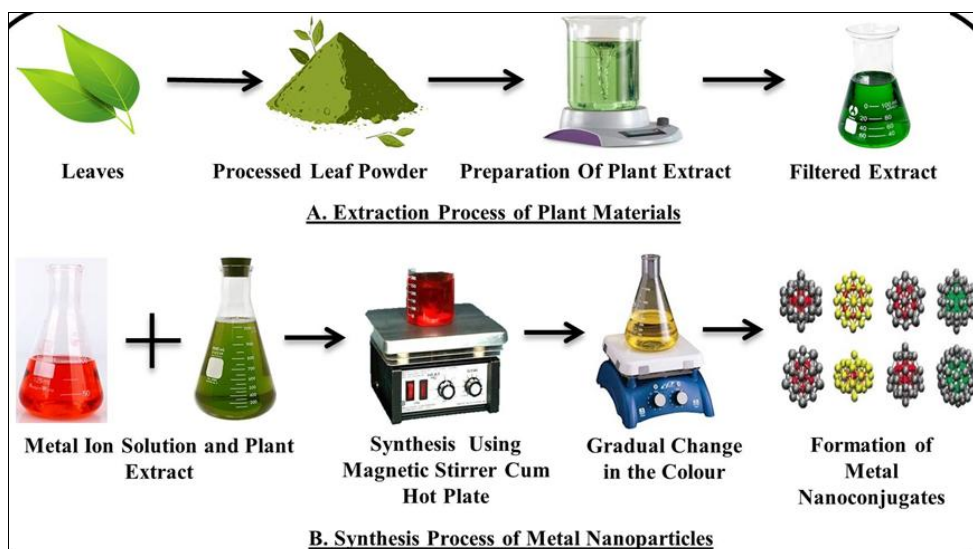


Fig 1: The process of metal nano-particle synthesis using plant as bio reducing agent

A Concise Description of Some Pharmacologically Active Plants used in Metal Nano-conjugates Development

Acalypha indica

Acalypha indica (Figure 2A) belongs to the Euphorbiaceae family, is an annual herb. It is a little erecting herb up to 70 cm tall or little more, with a couple of ascending branches [12]. It consists of catkin like inflorescences with cup-shaped involucre surrounding the minute flowers [13]. The aerial parts contain a cyanogenic glycoside called acalyphin. Also contains flavonoids, kaempferol, glycosides, mauritianin, clitorin, nicotiflorin and biorobin [14, 15]. The chemical analysis of the extracts from the basis and leaf of *Acalypha indica* exhibited the presence of phytochemical constituents like alkaloids, flavonoids, phenolic compounds, saponins and sterols. Ingestion of *Acalypha indica* may cause hemolysis in people affected by glucose-6-phosphate dehydrogenase deficiency. Acalyphin is employed as a substitute for ipecacuanha, a vermifuge, expectorant and emetic [16]. *Acalypha indica* leaves are utilized in the normal medicine of India as a jaundice remedy. A leaf infusion is additionally taken as purgative in India. This plant has antibacterial and antifungal activity. Literature reviews suggested that the gold and silver nanoparticles synthesized by using *Acalypha indica* extracts seem to be a promising cure as an anticancer agent against a number of human cancers cells, however, a very few reports are available in case of breast cancer cells. On the other hand copper nano-particles synthesized by *Acalypha indica* shows a great response of cytotoxicity when evaluated by MTT assay against MCF-7 breast carcinoma cells along with efficient antibacterial and antifungal effect against *Escherichia coli*, *Pseudomonas fluorescens* and *Candida albicans*. Zinc nanoparticles developed from this plant exhibits rapid generation of electron-hole pairs by photo-excitation as well as highly negative reduction potentials of excited electrons have been generated high electron-hole pair when treated under UV-visible light, and thus it increases antimicrobial properties [17-20].

Phyllanthus amarus

Phyllanthus amarus (Figure 2B) is a crucial herb of Indian Ayurveda, belonging to Euphorbiaceae family [21]. It has axillary sort of inflorescence, contains one male and one

female flower in each axil [22, 23]. The active phytochemicals such as flavonoids, alkaloids, terpenoids, lignans, polyphenols, tannins and coumarins, phyllanthin, hypophyllanthin, phyltertralin are identified from various parts of *Phyllanthus amarus* [24, 25]. The plant is of medicinal importance for varied ailments like dysentery, influenza, vaginitis, tumors, diabetes, diuretics, jaundice, urinary calculus, dyspepsia, anti-hepatotoxic, anti-hepatitis-B, anti-hyperglycemic and also as antiviral and antibacterial [26-28]. After studying several literatures, it has been well documented that green synthesized copper nano-conjugates using *Phyllanthus amarus* leaf extract enhances the antimicrobial activity of the plant against both Gram positive and Gram negative as well as various multidrug resistance bacteria. Studies support that presence of various phytochemicals is directly involved in the reduction and development of plant mediated nanoparticles especially the silver ones. Various researches show that silver nanocompound of *Phyllanthus amarus* were found to be good antibacterial agent against multidrug resistant *Pseudomonas aeruginosa*, *Escherichia coli*, *Streptococcus* sp. and *S. pyogenes*. Therefore these metal nano-conjugates may act as ecofriendly antibacterial and antifungal agent and can provide a potent alternative medicine in the health care system to reduce the burden of multidrug resistance [29, 30].

Centella asiatica

Centella asiatica, (Figure 2C) a clonal, perennial herbaceous creeper belonging to the family Umbellifere (Apiaceae) is found throughout India growing in moist places up to an altitude of 2000 m [31]. It is a tasteless, odorless plant grows in and around the water. It has small green leaves and white flowers and it bears small oval fruit [32, 33]. The main principles within the plant are the triterpenes, asiatic acid and madecassic acid and their derived triterpene ester glycosides, asiaticoside and madecassoside. From the underground parts of the plant, many polyacetylenic compounds were isolated, the main compound being 8-acetoxycarinalin [34]. The roots are rich in amino acids, specially aspartic, glutamic, serine, threonine, alanine, lysine and histidine [35]. Besides wound healing, the herb is suggested for the treatment of varied skin conditions like leprosy, lupus, varicose ulcers, eczema,

psoriasis, diarrhea, fever, amenorrhea, diseases of the feminine genitourinary tract and also for relieving anxiety and improving cognition [36-40]. The presence of several above mentioned bioactive constituents of *Centella asiatica* act as a good reducing, conjugating and stabilizing materials in the synthesis of nano-conjugates. Developed biogenic silver nano-particles using *Centella asiatica* phenolic extract were used for the analysis of its antibacterial property against some notable foodborne pathogenic bacterial strains. These nanoparticles show prominent catalytic effectively in case of environmental pollutants also. One of the most outdated benefit of utilizing such nano-particles is it offers a potential path towards wastewater treatment involving the transformation of toxic dye pollutants into less harmful components as well as control of pathogenic bacterial strains [37-42].

Murraya Koenigii

Murraya koenigii (Figure 2D) Spreng (curry-leaf tree), a small aromatic tree belonging to the family of Rutaceae. It is a tropical to sub-tropical tree native to India. It is a shrub or tree up to 6-8 m tall. The *Murraya koenigii* has grey color bark. Leaves are bipinnately compound 2.5-3.5 cm long ovate lanceolate with an oblique base having bisexual white funnel shaped. Fruits are ovoid to sub-globose, wrinkled or rough with glands. The preliminary phytochemical screening of varied polar, non-polar solvent extract was performed. The presence of alkaloids, flavonoids, carbohydrates, and sterols in various extracts were observed [43]. Leaves are aromatic and contain proteins, carbohydrates, fiber, minerals, carotene, niacin and vitamin C [44]. The leaves contain high amount of ethanedioic acid. Leaves also contain crystalline glycosides, carbazole alkaloids, koenigin and resin. It also contains girinimbic, iso-mahanimbic, koenine, koenigine, koenidine and koenimbine [45]. Mahanimbicine, bicyclomahanimbicine, phebalosin, coumarine as Murrayoneimperatoxin, cyclomahanimbicine and tetrahydromahanimbicine are also present within the leaves [46]. *Murraya koenigii* is employed as a stimulant, anti-dysenteric and for the management of diabetes mellitus [47]. The plant is very valued for its leaves a crucial ingredient in an Indian cuisine to market appetite and digestion. Plant leaves used in dysentery, vomiting, stomachic, purgative, febrifuge and anti-anemic, cooling, swellings, itching and blood diseases [48-52]. It has been demonstrated that the extract of plant *Murraya koenigii* is capable of producing quite stable silver nano-conjugates through an efficient, eco-friendly and simple process. These silver nano-compounds in combination with commercially available antibiotics show synergistic activity against multi-drug resistant (MDR) bacteria, and therefore could be used as an antimicrobial agent after further trials on experimental animals. Curry leaf mediated silver nanoparticles having the remarkable antibacterial activity against human pathogens. Curry leaf extract having different bioactive compounds. Silver nanoparticles become a natural drug against human pathogens. According to a report in the year 2011, suggests the rapid synthesis of silver and gold nano-particles using *Murraya koenigii* leaf extract and its therapeutic approaches. The antibacterial activities of the nano-particles have been investigated using a number of bacteria including clinical pathogens like *E. coli* and *P. aeruginosa* and the results seem to be very encouraging. It has been demonstrated that the particles were found to be effective against such pathogens due to their hydroxyl bonds present and can be further used in antibiotic drugs. The *Murraya Koenigii* leaf extract mediated

synthesis for titanium nano-particles has also been reported. Furthermore, this process can be extended for the synthesis of other metal nano-particles [53-56].

Limonia acidissima

Limonia acidissima (Figure 2E) belonging to the family Rutaceae and it is moderate in size, deciduous, erect tree with a couple of upward reaching branches bending outward near the summit and subdivided into slender, branchlets drooping at the tips throughout India [57]. It is a slow growing tree up to 10 m tall, grows everywhere India in dry and warm areas up to 450m elevation, Often tree with rough, spiny bark. The spines are axillary, short, straight, 2-5 cm long on a number of the zigzag twigs [58]. The leaves of *Limonia acidissima* are deciduous, alternate, dark-green, leathery, 3 to 5 inch long; minutely toothed, blunt or notched a dull-red or greenish, born in small, loose, terminal or lateral panicles. The fruit is round to oval 5-13 cm wide with a woody, amazingly hard rind which may be difficult to crack. The fruit is grayish-white, scurfy rind about 6 mm thick. The pulp of *Limonia acidissima* is sticky, brown, and aromatic [59]. The preliminary phytochemical analysis of plant parts showed the presence of alkaloids, flavonoids, phenols, terpenoids, tannins, fats, steroids, saponins, glycosides, gum, mucilage and glued oils [60, 61]. The unripe fruits contain stigmaterols. Fruit pulp contains great quantity of acid and other fruit acids, mucilage and minerals. Alkaloids, coumarins, fatty acids and sterols are detected within the pericarp. It also contains umbelliferone, dictamnine, xanthotoxol, scoparone, xanthotoxin, isopimpinellin, isoimperatorin and marmin [62]. Leaves contain stigmaterol, psoralen, bergapten, orientin, vitedin, saponarin, tannins and important oil. Marmesin, feronolide and feronone are isolated from the bark. Roots contain feronia lactone, geranylumbelliferone, bargapten, osthol, isopimpinellin, marmesin and marmin [63, 64]. All the plant parts are prescribed in indigenous system of drugs for the treatment of varied ailments. Fruits are refrigerant, stomachic, stimulant, astringent, aphrodisiac, diuretic, cardiotoxic, tonic to liver and lungs, cures cough, hiccup and good for asthma, consumption, tumors, ophthalmic and leucorrhoea [65]. Unripe fruit is astringent while seeds are utilized in heart diseases. The plant fruits are used as a prominent substitute for bael (*Aegle marmelos*) in diarrhea and dysentery [66]. Leaves are astringent and carminative, good for vomiting, indigestions, hiccup and dysentery. The leaves have hepato-protective activity [67]. The gum is demulcent and constipating, and is beneficial in diarrhea, dysentery, gastropathy, hemorrhoids and diabetes [68-70]. The biosynthetic approaches for the green synthesis of silver nano-conjugates using the aqueous extract of *Limonia acidissima* were found to be extremely effective against different bacterial and fungal pathogens such as *Escherichia coli*, *Bacillus subtilis*, and *Pseudomonas aeruginosa* colonies. Due to presence of several potential phytochemicals in *Limonia acidissima* different parts controllable stable, uniform size silver nanoparticles were easily produced under mild conditions. In future, more studies on the anti-cancer and anti-HIV activity of silver nanoparticles colloidal suspension, in addition with both theoretical and experimental investigation of other nanoparticles will be conducted [71-73].

Mentha spicata

Spearmint (*Mentha spicata*) (Figure 2F) belongs to the Labiatae. It is a creeping rhizomatous and perennial herb. Spearmint is indigenous to northern England and is cultivated in areas with climate starting from tropical to temperate, like

America, Europe, China, South Africa and Brazil [74-75]. The leaves are broad and sharply serrate. The trademark of Labiatae is that the stem which is in square-shaped. Spearmint leaves possess a characteristic aromatic odor and its constituents found in spearmint are carvone, a phenolic compound is the main constituent found in flavored, followed by limonene [76-79]. Except carvone, Menthone, Dihydrocarveol, β -bourbonene, α -amorphene and lots of other compounds also are found in spearmint. It is also reported that spearmint possesses antioxidant activity [80-83]. The great antimicrobial activity is attributed to the high concentration of carvone. Spearmint is taken into account as an herbal medicine in folkloric remedies for treating of colds and flu, tract problems, gastralgia, hemorrhoids, and stomachache [84, 85]. Due to the antioxidant and chelating properties it possesses, the incorporation of spearmint in food and it has redox status in organism to improve the safety and effect on human well-being [86] and it also used as toothpaste, breath

freshener and antiseptic mouth rinse [87]. Taking account from a report in the year of 2018, synthesis of silver nanoparticles by aqueous leaf extract of *Mentha spicata* as reducing and stabilizing agent is possible and it shows an efficient antifungal and antioxidant activity, although a relatively low of concentration of silver nanoparticles has no effect on the red blood cell. The antibacterial activity of developed silver nanoparticles were tested against multidrug resistance *Staphylococcus aureus*, *Escherichia coli*, *Enterococcus faecalis*, *Proteus mirabilis* and *Acinetobacter baumannii* (isolated from urinary tract infections in a previous study). The antimicrobial activity of *Mentha spicata* extract may be caused due to the presence of high content of carvone-rich oils. The *in vitro* cytotoxic and anticancer activities to those of silver nanoparticles capped with citrate ions and thereafter the cell death induced by synthesized nanoparticles may be through a mechanism different from apoptosis [88, 89].



Fig 2: The Plant Samples (2A: *Acalypha indica*, 2B: *Phyllanthus amarus*, 2C: *Centella asiatica*, 2D: *Murraya Koenigii*, 2E: *Limonia acidissima*, 2F: *Mentha spicata*)

Future Prospects of Plant-mediated Metal Nano-conjugates

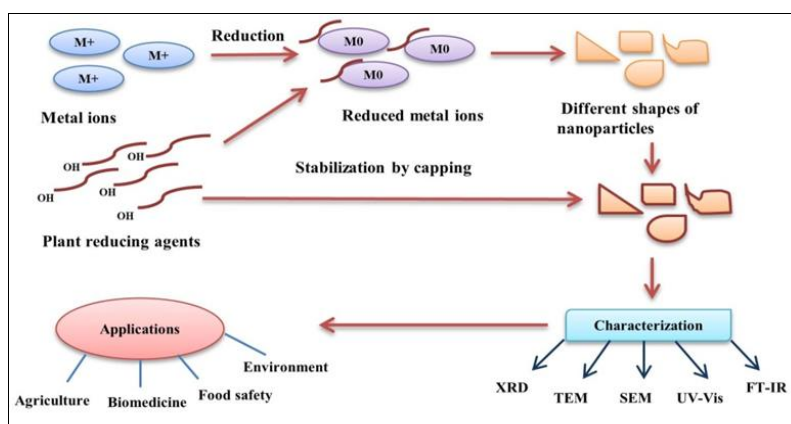


Fig 3: The overall mechanism behind the metal nano-conjugates development, stabilization, characterization and applications

Recent studies showed that the biogenic or green-synthesized metallic nano-particles using plants themselves or their bioactive derivatives without hazardous chemicals are promising in control plant pathogens including bacteria, fungi, and viruses. On the other hand, the biogenic metallic nano-particles have sometimes toxicity to human beings. So, before applying to agriculture, medical sciences and environments it should be kept in mind. Some important parameters must be noticed and these are:

1. Silver nano-particles are the major metallic nano-conjugates that are tested on plant pathogens and show toxicities to plants and plant-associated microbes.
2. Minimum inhibitory concentration of metallic nano-particles on pathogens should be determined *in vitro* and *in vivo*.
3. Metallic nano-product effects on plant growth and development at the working concentration should be determined.
4. Metal nano-conjugates effects on plant and microbes should be determined first.
5. The metal nano-conjugates and its effects on soil microbes should be pay attention.

Future research is recommended to determine the mode of action and efficiency of metal nano-conjugates in applications with the risks to agriculture, environments and humans ^[90-92].

Conclusions

The easy and cost-effective procedures of generating the nano-conjugates are very toxic product and so the proper precautions are required in these aspects. The alternative methods are green chemistry approaches. The present review focused on the biological methods to synthesize nano-conjugates such as microbes and plants are included. The green nano-conjugates have various applications in different fields (Figure 3). Most of the plant derived products can be generated in the native resources in developing countries where important and required materials can occur. The review shares the information on the green synthesis of metal nano-conjugates and their practical applications in the various fields ^[93-102].

Acknowledgement

The authors are grateful to Dr. Madhusudan Mondal, Former Additional Director, Botanical Survey of India, Howrah, and West Bengal for identifying the plant and giving valuable taxonomical inputs.

Authors Contributions

"#" Marked authors contributed equally in the study.

Conflict of interest

The authors declare that there are no conflicts of interest regarding the publication of this review article.

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