

Green synthesis of metallic nanoparticles using leaf extract of *Calotropis* species and their applications: A Review.

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Abstract

Biosynthesis of metallic nanomaterials has become an important field of research. The synthesis of metallic nanomaterials using plant extracts is a single-step, simple, rapid, and eco-friendly. The reducing agents involved include the various water-soluble secondary metabolites (Alkaloids, phenolic compounds, terpenoids, carbohydrates etc.) of the plant extracts. Diverse salts of metals of the transition metal series such as Gold (Au), Silver (Ag), Iron (Fe), Zinc (Zn) and Copper (Cu) etc, have been used in the synthesis. This review focused on the use of extracts of *Calotropis* species (spp) in the synthesis of metallic nanoparticles. The methods of synthesis and various applications of the synthesized nanoparticles were also discussed.

Keywords: Metallic nanoparticles, biosynthesis, green synthesis, *Calotropis*, Plant extracts.

10 Introduction

This review focused on synthesis of metallic nanomaterials using plant extracts of *Calotropis* spp. The emerging or potential applications of these nanomaterials in clinical diagnostics, therapy (Azzazy *et al.*, 2012; Chen *et al.*, 2012; Daria *et al.*, 2012; Fortina *et al.*, 2007; Lagunho and Baptista, 2012; Sahoo *et al.*, 2007; Salata *et al.*, 2004; Seil and Webster, 2012; Wagner *et al.*, 2006; Youns *et al.*, 2011; zhang *et al.*, 2008), photovoltaics (Yoon *et al.*, 2010), food storage (Costa *et al.*, 2011), textiles (Perelshtein *et al.*, 2008) as well as in environmental technology (Li *et al.*, 2008) is highlighted.

Green Chemistry is the practice of chemical science and manufacturing in a manner that is sustainable, safe and non-polluting (eco-friendly) and that consumes minimum amounts of materials and energy while producing little or no waste material. It harnesses a vast body of chemical knowledge and applies it to the production, use, and ultimate disposal of chemicals in a way that minimizes consumption of materials, exposure of living organisms, including humans, to toxic substances, and damage to the environment (Mannahan, 2005). The synthesis of nanoparticles via plants is an eco-friendly process that produces no toxic or harmful by-products, as such is a green synthetic process.

Nanomaterials could be synthesized using various physical and chemical methods (CaO, 2004; Sepeur, 2008) but, biosynthesis is more preferred because of its non-toxicity and environment-friendly, and could be used to produce large quantities of nanoparticles that are free of contamination with well defined size and morphology (Hutchinson, 2008). Plants extracts ability to reduce metal ions had been known since 1900' but, the nature of the reducing agents involved was not well understood (Mittal *et al.*, 2013). Within the last 30 years, phytosynthesis of nanoparticles has attracted considerable attention (Amkanwar, 2010; Armendariz *et al.*, 2004; Beattie and Haverkamp, 2011; Gran and Li, 2012; Gardea-Torresdey *et al.*, 2003; Gericke and Pinches, 2006; Haverkamp and Marshall, 2009; Iravani, 2011; Kandasamy *et al.*, 2012; Kumar and Yadav, 2009; Marshall *et al.*, 2007; Park *et al.*, 2011; Parsons *et al.*, 2007).

When compared to whole plant, the use of plant extracts for synthesis of nanoparticles is simpler (Mittal *et al.*, 2013). Plant extract-mediated synthesis is becoming a focus of attention (Ali *et al.*, 2011; Ankamwar, 2010; Babu and Prabu, 2011; Benerjee, 2011; Bankar *et al.*, 2010; Bar *et al.*,

2009; Baskaralingam *et al.*, 2012; Castro *et al.*, 2011; Chandran *et al.*, 2006; Daisy and Sapriye, 2012; Dubey *et al.*, 2009; Kaler *et al.*, 2011; Kesharwani *et al.*, 2009; Lee *et al.*, 2011; Singh *et al.*, 2010; Song *et al.*, 2009). The synthesis processes using plant extracts are readily scalable and may be less expensive (Iravani, 2011) compared to microbial processes of synthesis (Dhillon *et al.*, 2012; Li *et al.*, 2011; Wangpipat *et al.*, 2011; Sastry *et al.*, 2003) and whole plants (Armendariz *et al.*, 2004; Beattie and Haverkamp, 2011; Haverkamp and Marshall, 2009; Kumar and Yadav, 2009; Marshall *et al.*, 2007).

Plant extracts may act as reducing or stabilizing agent or both, in the synthesis of nanoparticles (Kumar and Yadav, 2009). The source of the plant extract is known to influence the characteristics of the nanoparticles synthesized (Kumar and Yadav, 2009). Plant extract-mediated synthesis of nanoparticles is a single-step process involving mixing of the aqueous extract of the plant with an aqueous solution of the metal salt of interest (Mittal *et al.*, 2013). The reaction occurs at room temperature and is completed in a matter of minutes. Since there are various components of the extract involved in the bioreduction, the process tends to be relatively complex (Mittal *et al.*, 2013).

Metallic nanoparticles formation can easily be modified to control the shape, size, composition, structure, assembly and encapsulation, as well as tunability of their optical properties. Metallic nanoparticles have been used for vivo and in vitro diagnostics (Vio Vet., 2017; Baptista *et al.*, 2011; Azzazy and Mansoor, 2009; Radwan and Azzazy, 2009) and drug delivery (Ahmad *et al.*, 2010; Adeyemi and Sulaiman, 2015). The wide application of metallic nanoparticles is due to their large surface area per unit mass, unique thermal, optical and electrical properties.

There are only two species of *Calotropis* (family: Asclepiadaceae) plant widely distributed across Africa, Asia and South America (Mascolo *et al.*, 1988). These are *Calotropis procera* and *Calotropis gigantean*. *C. procera* grows to a height of 3 to 6 ft while *C. gigantean* grows to a height of about 8 to 10 ft. The plant is erect, tall, large, branched and perennial with milky latex throughout. The flowers of *C. procera* are coloured white to pink and are fragrant while those of *C. gigantean* are white to purple and without any fragrance (Lindley, 1985). The different parts of the plant are used in traditional medicine for the treatment of painful muscular spasm, dysentery, fever, rheumatism, asthma and as an expectorant and purgative. A large quantity of latex can be easily collected from its green parts (Irvine, 1961). Local people use it successfully to combat

some cutaneous fungal infections. The abundance of latex (containing alkaloids) in the green parts of the plant reinforces the idea that it produced and accumulated latex as a defence strategy against organisms such as virus, fungi and insects (Lahrsini *et al.*, 1997). The presence of plant defence related proteins such as hevein, an alpha-amylase inhibitor has been described to occur in the latex secretion of other plants (Wititsuwannakul *et al.*, 1998).

2.0 Synthetic methods of nanoparticles

There are two major pathways for synthesizing nanoparticles. These are the “Top-down” and “Bottom-up” approach (Sepeur, 2008).

In “Top-down” synthesis, nanoparticles are produced by size reduction from a suitable starting material (Meyers *et al.*, 2006). The size reduction is achieved by various physical and chemical treatments (Fig.1) (Mittal *et al.*, 2006). Top-down synthesis introduce imperfections in the surface structure of the product, which is a setback since the surface chemistry and other physical properties of nanoparticles are dependent on the surface structure (Thakkar *et al.*, 2010)

Bottom-up synthesis involves building the nanoparticles from smaller entities by joining atoms, molecules or particles (Mukherjee *et al.*, 2001). The building blocks of the nanoparticles are formed first and assembled to produce the final particles (Thakkar *et al.*, 2009) (Fig.2) (Mittal *et al.*, 2013). Bottom-up approach relies on chemical and biological methods of production. The biological method of synthesis based on micro-organisms have been widely reported (Dhillon *et al.*, 2012; Gericke and Pinches, 2006; Kaler *et al.*, 2011; Korbekandi *et al.*, 2009; Li *et al.*, 2011; Mohanpuria *et al.*, 2008). Even though microbial synthesis is readily scalable, environment-friendly and compatible with the use of product for medical applications but, the production of the micro-organisms is often more expensive than the production of plant extracts. Plant extract-mediated synthesis has been widely reported (Gardea-Torresdey *et al.*, 2003; Park *et al.*, 2011; Haleemkhan *et al.*, 2015).

4.0 The use of extracts of *Calotropis* spp in metallic nanoparticles synthesis

In the production of metallic nanoparticles using plant extracts, the extract is simply mixed with a solution of the metal salt at room temperature and the reaction is complete within minutes (Mittal *et al.*, 2013).

Nanoparticles of silver, gold and many other metals have been synthesized this way (Li *et al.*, 2011). The nature of the extract, its concentration, the concentration of the metal salt, the pH, the temperature and contact time are known to affect the rate of production of nanoparticles, their quantity and other characteristics (Dwivedi and Gopal, 2010).

Babu and Prabu (2011) synthesized 35nm silver nanoparticles (AgNPs) using flower extract of *C. procera*. Alkammash (2017) reported the synthesis of AgNPs using leaf extract of *C. procera*. The nanoparticles were spherical and mostly aggregated with size ranges of 8-20nm.

Baskaralingham *et al.* (2012) used a leaf extract of *C. gigantean* to produce AgNPs that showed antibacterial activity against *vibrio alginolyticus* (Baskaralingham *et al.*, 2012). In a study reported by Pavani and Gayathramma (2015), they used flower extract of *C. gigantean* to synthesize AgNPs within 60 minutes. The AgNPs were polydispersed, crystalline and yeast-like with size ranges of 10-50nm. XRD confirmed the face-centred cubic structure of the AgNPs. Nipane *et al.* (2016) synthesized AgNPs using flower extract of *C. procera*. The particles were spherical, with size ranges of 20-35nm, and their surface showed selective adsorption of Fe^{2+} ions in aqueous medium which could be used in quantitative estimation of Fe^{2+} ions in environmental samples.

Chandrasekar (2014) reported that AgNPs synthesized from leaf extract of *C. gigantean*, showed mosquito larvicidal property against *A. aegypti* and *A. stephensis*.

In a study by Sivakumar *et al.* (2011), AgNPs of various sizes were synthesized using leaves extract of *C. gigantean*. Antibacterial activity against similar strains was demonstrated using AgNPs synthesized from latex of *C. gigantean* (Chandrasekaran *et al.*, 2015).

Activity against Gram Positive bacterial strains (*S. subtilis* and *Streptococcus sp.*) were reported (Priyanka *et al.*, 2015) for AgNPs synthesized from leaf extract of *C. gigantean*

Gold nanoparticles with average size of 45nm have been synthesized using aqueous leaf extract of *C. procera*. FTIR indicated that phenolic phytochemicals were responsible for the reduction process as reported by Tamar and Gary (2013). The AuNPs showed inhibitory effect on the growth of MCF-cell line with increase in concentration. In a microwave-mediated synthesis, Ratil Kumar Das *et al.* (2012) used latex of *C. procera* to produce crystalline and spherical, gold nanoparticles (AuNPs), stable at room temperature for a long period (6 months) with size ranges of 5-13nm. The surface of the AuNPs was coated by organic materials.

Table1. Summary of synthesis of metallic nanoparticles from *Calotropis spp*

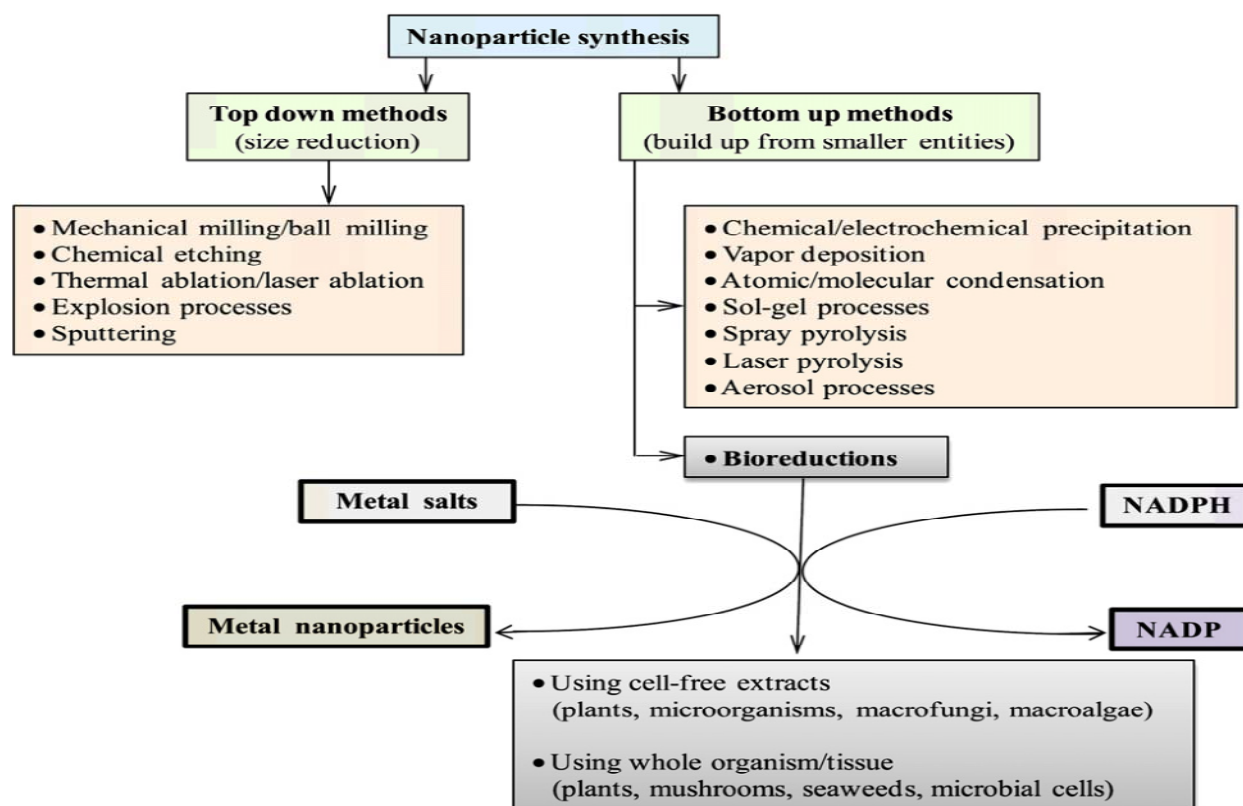


Fig. 1. Various approaches for making nanoparticles and cofactor dependent bioreduction (Mittal *et al.*, 2013).

The summary of the various reports of synthesis of metallic nanoparticles using the extracts of the two species of *Calotropis* (*C. procera* and *C. gigantean*) is given in (Table 1).

Gawade *et al.* (2017) used leaves of *C. procera* to produce spherical ZnO nanoparticles which associated to hexagonal wurtzite structure with sizes ranging from 15-25nm. The nanoparticles were utilized for the degradation of methyl orange. Vidya *et al* (2013) were able to produce ZnO

nanoparticles with sizes of between 30-35nm. Poovizhi and Krishnaveni (2015) reported that ZnO nanoparticles exhibited high bactericidal efficacy against some bacterial strains (*E. coli*, *P.aeruginosa*, *K. pneumonia* and *S. aureus*).

ZnONP synthesized from leaf extract of *C. gigantean* were shown to significantly enhance growth of seedlings of Neem and Milkwood-pine trees when sprayed at nursery stage (Sadhankumar and Lalit, 2017).

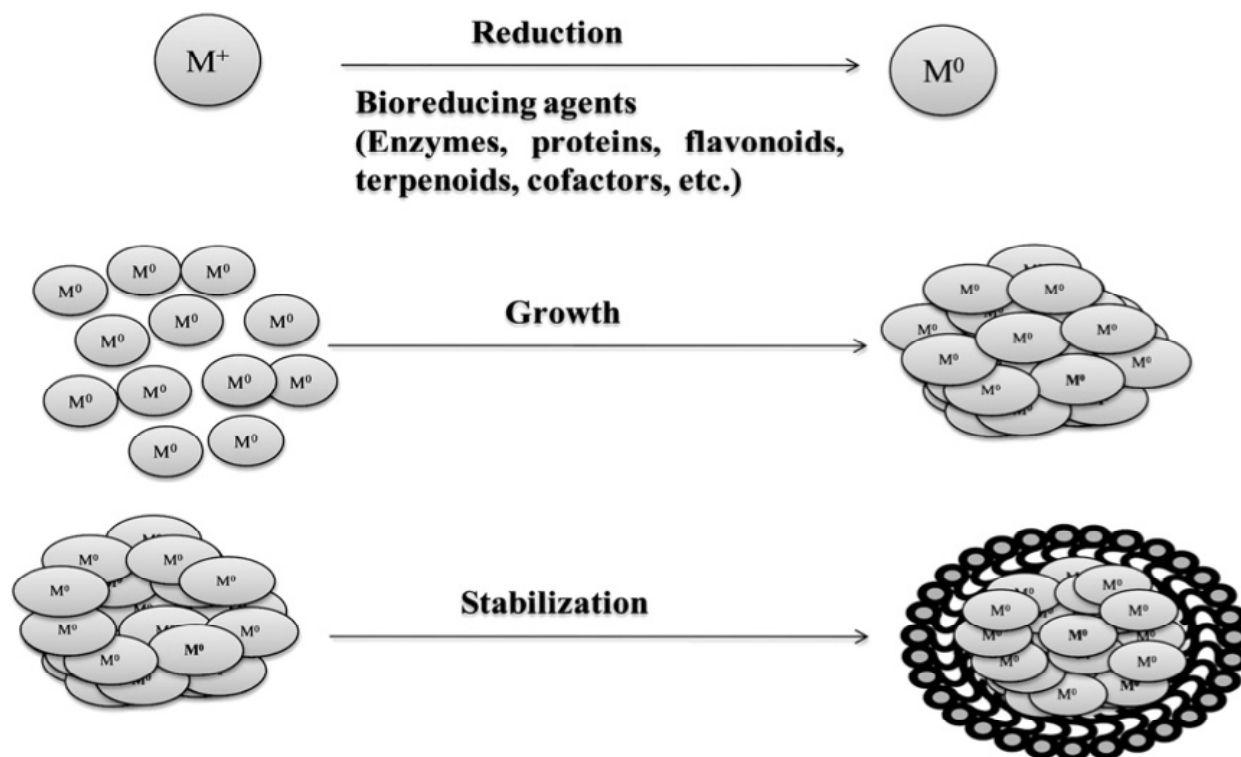


Fig.2. Schematic of biosynthesis of nanoparticles

Plant/Part	Nanoparticles	Method	size/Application	Reference
<i>C. procera</i> flower	AgNPs	LT	35nm	Babu & Prabu, 2011.
<i>C. procera</i> latex	AgNPs	LT	antibacterial activity.	Nadia Hussein Mohamed, 2014.
<i>C. procera</i> leaf	AgNPs	LT	8-20nm	Alkammash, 2017.
<i>C. procera</i> flower	AgNPs	LT	20-35nm	Nipane <i>et al.</i> , 2016.

<i>C. procera</i> leaf	AgNPs	LT	55nm	Nipane <i>et al.</i> , 2016; Vinothkumar & Udayasoorian, 2015.
<i>C. gigantean</i> flower	AgNPs	LT	10-50nm/Environmental decontamination.	Pavani & Gayathramma, 2015.
<i>C. gigantean</i> leaf	AgNPs	LT	antibacterial activity.	Baskaralingham <i>et al.</i> , 2012; Priyanka <i>et al.</i> , 2015.
<i>C. gigantean</i> leaf	AgNPs	LT	antilavical activity	Chandrasekar <i>et al.</i> , 2014.
<i>C. gigantean</i> latex	AgNPs	LT	antibacterial activity	Chandrasekar, 2015.
<i>C. gigantean</i> leaf	AgNPs	LT		Sivakumar <i>et al.</i> , 2011.
<i>C. procera</i> leaf	AuNPs	LT	45nm/Inhibitory effect on cancer cells.	Tamar & Gary, 2013.
<i>C. procera</i> latex	AuNPs	MW	5-13nm	Patil Kumar das <i>et al.</i> , 2012.
<i>C. procera</i> leaf	ZnONPs	LT	15-25nm/Environmental decontamination.	Gawade <i>et al.</i> , 2017.
<i>C. procera</i> leaf	ZnONPs	LT	30-35nm/antibacterial activity.	Vidya <i>et al.</i> , 2013; Poovizhi & Krishnaveni, 2015.
<i>C. gigantean</i> leaf	ZnONPs	LT	Growth enhancement.	Sadhankumar & Lalit, 2017.
<i>C. gigantean</i> latex	ZnONPs	LT	Cytotoxic effect.	Panda <i>et al.</i> , 2017.
<i>C. procera</i> leaf, root, Flower & latex	ZnONPs	LT	antibacterial effect.	Salem & Schild, 2015.
<i>C. gigantean</i> leaf	TiONPs	LT	antiparasitic activity.	Marimathu <i>et al.</i> , 2013.
<i>C. procera</i> leaf	CuONPs	LT	environmental decontamination	Dubey & Sherma, 2017.

<i>C. gigantean</i> leaf	CuONPs	LT	Counter electrode in DSSCs.	Sherma <i>et al.</i> , 2015.
<i>C. gigantean</i> flower	CuONPs	LT	Cytotoxic effect.	Kumari <i>et al.</i> , 2017.
<i>C. gigantean</i> flower	ZVIN	LT	Environmental decontamination.	Srivanthi <i>et al.</i> , 2018.
<i>C. gigantean</i> leaf	FeONPs	LT	3-6nm	Davendra <i>et al.</i> , 2013.

N.B: LT = Low temperature; MW = Microwave.

In a study by Panda *et al* (2017), ZnONPs synthesized from latex extract of *C. gigantean* showed cytotoxic effect by inducing oxidative stress and DNA damage in the root assay system of *L. sativus*. Biosynthesized AgNPs and ZnONPs from extract of *C. procera* showed potential inhibitory effect on two bacterial strains (*V. cholera* and *E. coli*) irrespective of the type of extract (leaf, flower, or fruit) used (Salem and Schild, 2015).

The first reported TiO nanoparticles synthesis with excellent antiparasitic activity was by Marimuthu *et al.* (2013), who tested the TiONPs against the larvae of *R. micropulus* and *H. bispinosa*.

CuO nanoparticles (CuONPs) have been synthesized, using leaf extract of *C. procera*, and showed high absorptive capacity for Cr(IV) and hence could serve as good alternative for Cr (IV) removal from aqueous solutions (Dubey and Sherma, 2017). In a similar synthesis using leaf extract of *C. gigantean*, Sherma *et al.* (2015) used the produced CuONPs as counter electrode in dye-sensitized solar cells (DSSCs) and found moderately high solar to electrical energy conversion efficiency of 3.4% with high current density of 8.13mA/cm², open circuit voltage of 0.67V and fill factor (FF) of 0.62. Flower extract of *C. gigantean* was used to synthesize CuONPs in an in-vivo cytotoxic comparative study of the impact of synthesized nanoparticles in comparison to commercially available ones on fish embryo (Kumari *et al.*, 2017). They inferred that the biosynthesized nanoparticles showed less toxicity than the commercial ones at optimum usage. Zero-valent iron nanoparticles (ZVFeNPs or ZVIN) were synthesized from flower extract of *C. gigantean* and showed high adsorptive capacity for aniline and methylene blue, hence have potential for use in treatment of contaminated water (Sravanthi

et al., 2018). Iron oxide nanoparticles (FeONPs) of sizes 3-6nm were synthesized using aqueous leaf extract of *C. gigantean* as reported by Devendra *et al* (2013).

5.0 Applications of nanoparticles

Nanoparticles synthesized from the two species of *Calotropis* have been widely applied for various uses. They have found use in water treatment (Sravanthi *et al.*, 2018), in dye-sensitized solar cells (Sherma *et al.*, 2015). TiO nanoparticles have shown excellent antiparasitic activity (Marimuthu *et al.*, 2013).

Nanoparticles of silver, gold and ZnO have exhibited wide spectrum antibacterial activities (Salem and Schild, 2015; Priyanka *et al.*, 2015; Poovizhi and Krishnaveni, 2015; Chandrasekaran *et al.*, 2015; Baskaralingham *et al.*, 2012) against some bacterial strains (*E. coli*, *P.aeruginosa*, *K. pneumonia*, *S. aureus*, *S. subtilis*, *Streptococcus sp.* and *V. cholera*)

Antiparasitic (Sivakumar *et al.*, 2011) and antifungal (Nadia Hussein Mohamed *et al.*, 2014) activities against *T. rubrum*, *C. albicans* and *A. terreus* was shown by AgNPs.

ZnONPs have shown growth enhancement of seedlings (Sadhankumar and Lalit, 2017) and cytotoxic effect in the root system of some plants (Panda *et al.*, 2017).

CuO have shown potential for use as heavy metals environmental decontaminant (Dubey and Sherma). ZVIN have potential use in treatment of contaminated water because of their high adsorptive capacity for some organics (Sravanthi *et al.*, 2018).

CONCLUSION

Plant extracts are used for synthesis of metallic nanoparticles. The synthesis is simple, rapid easily scaled up and the nanoparticles are environmental friendly. Metallic nanoparticles are used widely for various applications ranging from antimicrobial agents in water treatment; in targeted drug delivery; in clinical diagnostics; in solar cells; in environmental decontamination etc.

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