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Review Article

## An overview of green synthesis mediated metal nanoparticles preparation and its scale up opportunities

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### Abstract

Nanoparticles in different field of science have a wide range of utility. They come in different forms. Among these, metal nanoparticles (MNP) have become an emerging tool for diagnostic as well as for therapeutic purposes. Metal nanoparticles are nano-sized particles made up of inorganic metals or their metal oxides. Various methods are available for the preparation/production of metal nanoparticles. In addition to the existing physical and chemical methods, green synthesis is an area that has drawn the attention of researchers in the decade and continues to be a potential area of research. The following review introduces about metal nanoparticles and discusses in details about the plant extract mediated metal nanoparticles synthesis, the principle of metal nanoparticle formation, various process parameters that are important for its synthesis, characterization of metal nanoparticles and the scope for commercialization are elaborated. Metal nanoparticles at research, employing plant extract mediated green synthesis have been extensively reviewed. This review tries to bring into light the feasibility of commercializing the green synthesis by using plant extracts.

**Keywords:** Green synthesis; Plant extract; One-step synthesis; Characterization; Process parameters; Scale-up

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## 1. Introduction

Nano-medication is the field of science which combines nanotechnology and the delivery of drugs or medicines <sup>1</sup>. Nanotechnology is the science and engineering involved in the design, synthesis, characterization, and application of materials of small functional organized entities, with at least one dimension being in a nanometer scale or one billionth of a meter <sup>2</sup>. The nanoparticles serve as an important tool for better delivery of cutting edge treatment like genes, proteins, and other therapeutic advancements. They not only benefit therapeutically but also serve in diagnosis <sup>3,4</sup>. There are various types of nano-medicines available for therapy like liposomes, phytosomes, microparticles, nanoparticles, quantumdots, carbon nanotubes, metal nanoparticle, transfereosomes, ethosomes, colloidomes, coated liposomes, etc. Currently, metal nanoparticles are gaining much more importance <sup>5</sup>.

Metals are the most widely recognized materials utilized in the everyday engineering field <sup>6</sup>. They have their own characteristics of ductability, malleability and are good conductors of heat and electricity. They are strong due to their high inter-atomic bonds <sup>7</sup>. Metals have unique properties for studying their microstructure by various techniques like scanning electron microscopy (SEM),

secondary ion mass spectroscopy (SIMS), X-ray Photoelectron Spectroscopy (XPS) <sup>6</sup>. In the health scenario, metals are essential for our body as trace elements and micronutrients viz. iron a significant factor for hemoglobin; copper as a neurotransmitter, magnesium and zinc as enzyme co factors and so forth <sup>8</sup>. As a result of their physicochemical characteristics and physiological essentiality, metals are now being employed and explored as an avenue for therapy and drug delivery <sup>9</sup>.

Metal nanoparticles (MNP) are colloidal particles of metals like titanium, zinc, silver, gold, copper, platinum, etc., in the size range of 1-100 nm <sup>10</sup>. The MNP have a high surface area to volume ratio <sup>10</sup> which helps in the addition of several functional groups like ligands, antibodies, and genes providing better targeting ability to those molecules. The surface properties of metals such as plasmon excitation, dielectric constant, optical properties, and others show a tremendous difference due to their conversion from a macro to a nano-size which makes them ideal for targeting therapeutic agents. These are having greater capability to carry a high dose of drug and increase its circulatory half-life <sup>10, 11</sup>.

MNP have a huge demand owing to their immense utility ranging from catalysts <sup>12</sup>, chemical sensors <sup>13</sup>, electronic

components<sup>14</sup>, medical diagnostic imaging, pharmaceutical products, and medical treatment protocols<sup>15</sup>. For e.g.: Gold nanoparticles (NP) are utilized in biomedical application, disease diagnosis, and pharmaceutical applications like targeting anticancer drugs<sup>16</sup>. Silver NP exhibit the property of anti-inflammatory and anti-bacterial action and are frequently utilized for wound healing purposes<sup>17,18</sup>. Other MNP include copper, zinc, selenium which is employed for functions such as anti-microbial activity<sup>19</sup>, applications in cosmetic formulations, etc.<sup>20</sup>.

These are having potential therapeutic applicability; various literatures have been reported on green synthesis and its vast applications. But there is a lack of data on the scale-up feasibility for plant-mediated green synthesis. So this review tries to bring upon some of the possible equipment's that can help in widening the opportunities.

## 2. Production of MNP

MNP are employed in many industries like electronics, biomedical engineering, magnetic imaging, and paints<sup>14,15,21</sup>. They are thus being produced on a commercial scale and the production methods may be classified into

### 2.1. Top-down method<sup>22</sup> and

### 2.2. Bottom-up method<sup>22</sup>.

These methods may further be segregated based on the process involved into physical or chemical processes<sup>23</sup>.

The top down method is based upon breaking big materials into small nano-sized materials<sup>24</sup>. It mainly includes mechanical attrition, nano-lithography<sup>25</sup>, chemical etching, sputtering, thermal and laser ablation while the bottom up increases the size by self-assembling the atoms into nanoscale particles<sup>24</sup>. Bottom up methods include sol-gel process, electrochemical precipitation, laser pyrolysis, spray pyrolysis, vapor phase technique and liquid phase techniques<sup>25</sup>. For most of the metals like iron, gold, zinc oxide, silver and titanium oxide are produced preferably by employing liquid phase synthesis or vapor phase synthesis instead of milling or mechanical grinding. Whereas in the case of, silver and gold, liquid phase precipitation is preferred over vapor phase synthesis due to the ease of control over particle size.<sup>26</sup>

When commercialization is concerned, not only production capacity but other factors need to be considered. Those factors include consistency in product quality and costs related to raw materials, operation, yield, capital equipment, safety, waste disposal and environmental issues such as carbon emission. The reason why only a few types of nanoparticulate materials are used in the current consumer products is due to the technical and commercial restrictions on large scale production<sup>27</sup>. Secondly, chemical processes like electrodeposition, laser ablation, chemical vapor deposition etc., are associated with certain demerits like toxicity due to the use of chemical agents like sodium borohydride, hydrazine hydrate even the use of toxic chemical gas as a precursor in the chemical vapor disposition method; high energy demand which is mostly seen in case of ball milling; lengthy reaction time, and non-eco-friendly by-products. This hauls the enthusiasm of researchers to explore new methods for the manufacture of MNP. One of the upcoming avenues is the green synthesis<sup>28</sup>.

## 3. Green synthesis

MNP preparation by the green synthesis approach uses biological resources i.e. microorganisms<sup>29</sup>, and plants<sup>30</sup>. Green synthesis is promising on an account of a less labor-

intensive and easy method of MNP formation. This synthesis does not involve any use of harmful or toxic chemicals and yields no hazardous by-products<sup>31</sup>. The methods of production may be segregated based on the biological source employed as given below<sup>32</sup>

### 3.1. Green synthesis via micro-organisms

Microbes are used in the production of MNP<sup>33</sup>. Bacteria<sup>34</sup>, fungi<sup>35</sup>, yeast<sup>36</sup>, actinomycetes<sup>37</sup>, and algae<sup>38</sup> have been studied for the same. The development of MNP by means of microorganisms is challenging because of certain factors like a long processing time, availability of specific strains microorganisms, contamination issues requiring extra care during media preparation and culturing, isolation, and culture maintenance<sup>39</sup>.

### 3.2. Green synthesis via Plants

Plants are the best gift from nature<sup>39</sup>. Plants absorb substances from the soil and this include uptake of minerals. Plants are reported to take up heavy metals. This phytoremediation employs to detoxify the environment<sup>40,41</sup>. As plants possess hyper-accumulation and can even reduce inorganic metal ions to MNP in a single-step synthesis<sup>39,41</sup>. Plants have bountiful phytochemicals like alkaloids, alcohols, flavonoids, and so on, which are obtained from different parts like roots, stems, leaves, fruits, flowers, and seeds. These phytochemicals aid in nanoparticle formation<sup>42</sup>. The nanoparticles acquired from the plant can be altered into various shapes and sizes with alluring morphological needs<sup>43</sup>.

Plant based synthesis can be performed via intra-cellular, extracellular and through phytochemical mediation. In the case of intracellular MNP synthesis, living plant cell broth is incubated with metal salt solution leading to its reducing to MNP. In extracellular synthesis and phytochemical mediated synthesis, aqueous metal salt solution is mixed with a plant extract or a specific phytochemical respectively<sup>42,44</sup>.

Plant extracts are non-toxic, biocompatible to human cells<sup>45</sup>, and they are also good in drug delivery, even in diagnostic fields, etc. Moreover, more stable MNP are formed by using plant extracts than the microbial method<sup>39</sup>.

A simple pictorial representation of plant extract mediated MNP synthesis is shown in Figure 1. Plant extract mediated green synthesis is a one step process for synthesis of MNP because the phytochemicals themselves act as reducing as well as stabilizing agents.

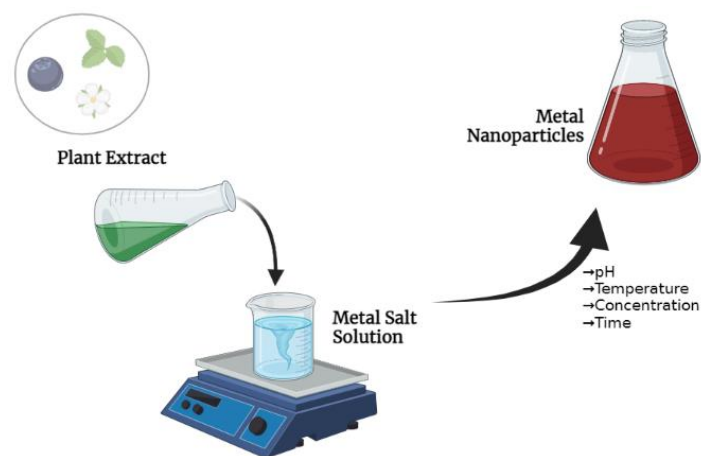


Figure 1: One step process for plant extract mediated green synthesis of MNP.

#### 4. Lab scale synthesis

The lab scale synthesis is mainly opted by researchers due to certain advantages. Synthesis in the lab has a very simple procedure requiring the use of minimal equipment and process parameters<sup>46</sup>. The lab process can be explained by three major steps<sup>47</sup>:

##### 4.1. Preparation of plant extract

##### 4.2. Preparation of Metal salt solution

##### 4.3. Formulation of MNP

4.1. Preparation of plant extract: The extract is prepared by choosing the desired plant part (leaves<sup>48</sup>, seed<sup>49</sup>, flower<sup>50</sup>, root<sup>51</sup>, stem<sup>52</sup> and fruits<sup>53</sup>) or phytochemicals<sup>54, 55</sup> that are required for reduction of the metal ion. The collected material is washed properly and air-dried. After drying, the plant material is milled into finer pieces<sup>56</sup>, the phytochemicals for reduction are extracted either in organic<sup>57, 58</sup>/aqueous media<sup>59, 60, 61</sup>. The most common extraction method employed is decoction<sup>62</sup>. Other methods like maceration<sup>63</sup>, soxhlation<sup>57</sup>, etc. have also been reported. The extract is filtered or centrifuged to remove unwanted debris and stored at 4°C for future use<sup>59-61, 64</sup>.

4.2. Preparation of metal salt solution: The metal precursor is a metal salt. A solution is made by taking a required quantity of metal salt and dissolving it in water. This serves as the source of the metal ion. One of the important factors for MNP synthesis is the concentration of the metal salt solution, which mainly varies from 1mM to 5mM<sup>65</sup>. As mentioned in Fig 1. some metal salts include silver nitrate, zinc oxide, copper sulfate, etc.

4.3. Green synthesis of MNP: In this step the metal salt solution is mixed with plant extract to yield metal nanoparticles<sup>48-65</sup>. The formation of MNP is indicated by visual perception. Change of color in the reaction mixture indicates formation of MNP<sup>66</sup>. The color varies for different metals. For silver the color change occurs from colorless to brown or reddish-brown<sup>67</sup>; for gold the color changes from yellow to reddish shade<sup>68</sup> or sometimes in violet color<sup>69</sup>; Likewise for copper (precursor copper sulfate) the color changes from blue to dark brown<sup>70</sup>.

#### 5. Mechanism of MNP formation by plant extract mediated green synthesis

The proper mechanism for MNP formation is unclear yet but several hypotheses have been postulated<sup>71</sup>. Plant extracts, due to the presence of various phytochemicals serve as a good reducing agents as well as a stabilizing agents for NP preparation. Bioactive molecules like flavonoids, alkaloids, saponins, steroids, terpenoids, and tannins, etc. reduce metal ions into metals and then stabilize them in the colloidal size range<sup>72</sup>.

The mechanism of MNP formation may be complex to understand due to the presence of a large number of phytochemicals in the extract having various reactive moieties like aldehyde, ketones, carboxyl, hydroxyl, etc.<sup>73</sup>. MNP formation by plant extract mediated green synthesis is a bottom up approach and can be divided into three phases<sup>74</sup>:

##### 5.1. Activation phase

##### 5.2. Growth phase

##### 5.3. Termination phase.

In the activation phase, the metal salt solution is reduced into metal ions via phytochemical constituents. The MNP formation rate at this phase is slow as it primarily involves the reduction of aqueous metal ion in mono or divalent oxidation state to neutral metal atoms<sup>39, 74, 75</sup>. Next, nucleation of metal atoms occur leading to the formation of particles increased size range than the atomic level. The metal atoms coalesce to give different morphological shapes like spheres, triangles, hexagons, pentagons, etc<sup>39, 74</sup>. The bioactive molecules like flavonoids, terpenoids, proteins, polyphenols, etc interact with the aggregated metal atoms and get adsorbed onto the surface due to the  $\pi$  electrons interactions<sup>74</sup>. The continuous growth phase emerges to be with improved thermodynamic stability of nanoparticles but an increase in the nucleation phase causes aggregation of nanoparticles that distorts their morphology. The last step in the synthesis is the termination phase, where capping of active molecules onto the surface of the metals provides a steric hindrance that limits particle aggregation thereby providing a stable morphology and size in the nano-range thus leading to formation of stable MNP<sup>74</sup>.

The reaction mixture is centrifuged to yield the MNP which sediments. The supernatant is decanted and the sediment is re-dispersed in deionized/distilled water to remove impurities<sup>76</sup>. Figure.2 represents the mechanism of formation of MNP via green synthesis from plant extract.

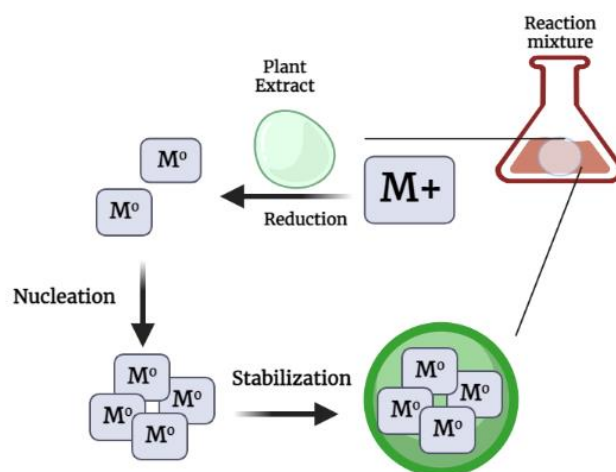


Figure 2: Mechanism of MNP formation by plant extract mediated green synthesis.

#### 6. Analytical methods employed

Analytical methods are employed in the plant extract mediated green synthesis are: phytochemical screening of the plant extract and for the characterization of MNP<sup>77</sup>.

##### 6.1. Screening of Plant Extract:

As discussed in the principle of MNP formation by plant extract mediated green synthesis that many phytochemicals are involved<sup>72</sup>. Screening of the extract has to be done to identify the presence of the desirable phytochemicals in the extract. Wet lab methods are used for qualitative study of the extract. Some chemical tests include ferric chloride test for phenolic compounds, Mayer's test for alkaloids, Fehling's test for glycoside, Liebermann-Burchard test for terpenoids, Lead-acetate test for tannins, Sulphuric acid test for flavonoids, etc<sup>78,79, 80</sup>. Instrumental methods of analysis include chromatography techniques like Gas Chromatography (GC), High Performance Liquid Chromatography (HPLC), Thin Layer Chromatography (TLC) etc and Fourier Transform Infrared (FTIR) spectroscopic techniques<sup>78, 79, 81</sup>.

## 6.2. Characterization of MNP

Upon completion of green synthesis process, the MNP are characterized for size, shape, yield, and dispersity of the particles. The various characterization techniques include UV-visible spectroscopy (UV-vis) for identification, characterization, and analysis; Dynamic Light Scattering (DLS) for the surface charge, size distribution, and quality; Atomic Force Microscopy (AFM) for surface characterization at the atomic scale; Scanning Electron Microscope (SEM) & Transmission Electron Microscopy (TEM) are for surface and morphology characteristics; X-Ray Diffraction (XRD) for crystal structure; FTIR for identification of functional groups present and groups which stabilized the compound; zeta sizer for determination of indirect surface charge of the nanoparticles; Auger Electron Microscopy (AEM) for primary surface analysis; Inductively Coupled Plasma-optical Emission Spectroscopy (ICP-OES) for optical properties; Raman Spectroscopy and Energy Dispersive Spectroscopy

(EDS) for elemental composition [82,83,84]. Among them, microscopic techniques are known to be direct techniques for characterizing the nanoparticles from their image while the spectroscopy techniques include the indirect method of collecting data about the composition, crystal phase, structure, and properties of nanoparticles. Most reported work on MNP green synthesis includes commonly used techniques which are UV, FTIR, ZETASIZER, SEM & TEM [82,84].

## 7. Process parameters for plant extract mediated green synthesis

The synthesis involves the use of metallic salts of metals like copper, zinc, iron, silver, gold, etc combining with the plant extract giving rise to MNP. The formation and morphology of nanoparticles differs according to the process parameters. Figure 3 indicates an overview of the process and parameters involved.

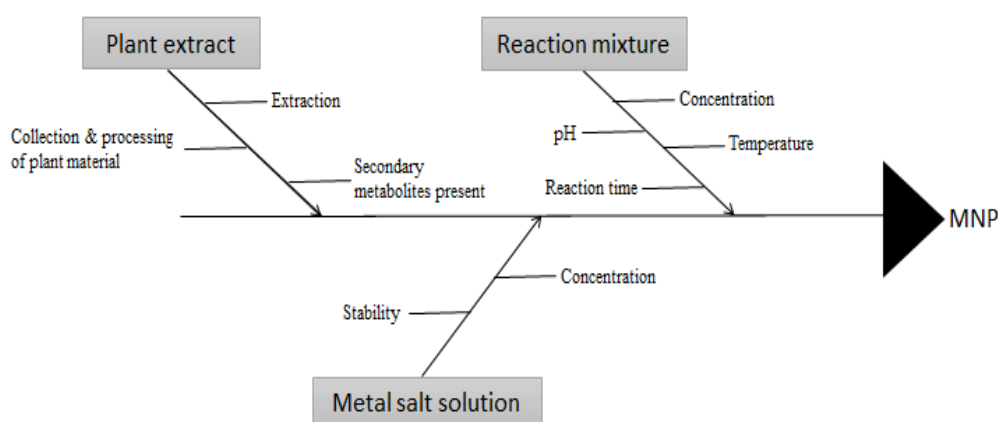


Figure 3: Process parameters in the synthesis of plant extract mediated green synthesis.

Some process parameters include:

### 7.1. Collection & processing of plant material:

Presence of desirable phytochemicals is the pre-requisite for the MNP formation. The phytochemical constituents are dependent on the source of plant (wild/cultivated, geographical location), collection (season, method), processing (washing, drying, milling, etc.). The collection and processing of plant material if not done in standardized manner, may lead to low yield of phytochemicals which effects MNP formation [78].

### 7.2. Extraction method:

For green synthesis, water is the commonly employed solvent to prepare the plant extract. Sometimes organic solvent like ethanol is also used. Phytochemical extraction may be carried out by decoction, maceration, soxhlation, etc [86]. The extraction method should ensure stability of the desired phytochemicals.

### 7.3. Phytochemical content:

There are many phytochemical constituents like flavonoids, polyphenols, terpenoids, and enzymes, etc. which not only contribute to the formation of nanoparticles but also aid in the stabilization of MNP. Additionally, they also impart pharmacological activity [87]. Some of the possible phytochemicals responsible are listed below:

Flavonoids are polyhydroxy phenolic compounds which undergo tautomeric transformation from enol to keto form,

releasing reactive hydrogen thereby contributing for the reduction of metal [31,44, 88-91].

Terpenoids belongs to hydrocarbon group. It contains alcohols, ketones, aldehydes, and lactones group which are responsible for reduction as well as stabilization of MNP. Terpenoids can easily get adsorbed onto the surface by interaction of  $\pi$  electrons and carbonyl groups [31,44, 88-91].

Sugars are chemically Carbon, Hydrogen and Oxygen. There are different types of sugars – monosaccharides (simple sugar), disaccharides (complex sugar) and polysaccharides. It is seen that monosaccharides contain linear chain with aldehyde group that helps in reducing metal easily while disaccharides and polysaccharides reducing ability depends upon the opening of the chain giving ability to access the aldehyde group [31,44, 88-91].

Proteins consist of amino acid. It is seen that amino acids like tyrosine, arginine, and lysine have ability to reduce metal ions [31,44, 88-91].

### 7.4. Stability of components:

Stability of the reaction components is imperative for MNP synthesis. Metal salt solutions are prone to degradation. It is seen that silver salt solution degrades easily by photolytic degradation and hence precaution is to be taken during processing [92]. Similarly, the plant extracts too should be ensured to be stable and not be contaminated. The extracts are generally kept in cold condition (4°C) to prevent microbial contamination and chemical degradation of phytoactives.

## 7.5. pH:

The pH of the medium plays an essential role in the formation, shape and size of the nanoparticles. Alteration of pH affects the charge alteration in the plant metabolite thereby influencing the reduction and chelating of metal ions in the process. The ranges reported for pH maintenance of the metal solution / extract / reaction mixture include from pH 3-12. It is seen that increase in the pH generally above 7 causes the formation of smaller and spherical nanoparticles as compared to the lower pH<sup>92,93</sup>.

*Gurubasavara et al*<sup>94</sup> reported that the silver NP formed in alkaline pH is more stable than those in acidic medium. The pH also influenced the size of silver NP where size is inversely proportional to the pH of the reaction mixture. They found that the formed size is uniform and well distributed at pH 9.

While in his research *Ashwani Kumar Singh*<sup>95</sup> clearly demonstrated the difference in shape and size of MNP by varying the pH. The gold nanoparticles mediated by black cardamom extract were synthesized employing solutions of different pH. It was observed that at pH 3 the particles had a spherical flower shaped morphology with a particle size of 90-100nm and at pH 7 the particles were almost spherical in shape with an average size 20-40nm.

## 7.6. Temperature:

The reaction temperature for any synthesis is important to give the desired product according to the quality and quantity. Here, the temperature has an impact on the size, shape, and yield of nanoparticles. It is generally seen that high temperature boosts the nucleation rate thereby leading to the production of crystalline nanoparticles. Basically, the temperature and size of nanoparticles are seen to be inversely proportional to each other<sup>92,93</sup>.

*Bo Rao*<sup>96</sup> looked into the green synthesis of silver nanoparticles with *Eriobotrya japonica* and studied the effect of increasing the temperature upon the particles. It showed when the temperature has been increased from 25 °C to 80 °C the particle size decreased from 76.10 nm- 54.47 nm. At higher temperature, the particles were found to have uniformity in their size and were having high yield. Likewise, *Husan*<sup>97</sup> got the outcome of increasing the temperature is an increase in the reaction rate. In this work different temperature condition was maintained i.e. 25 °C, 35 °C and 45 °C, which showed that at 45°C the absorbance, was more, marking the outcome of nanoparticles.

## 7.7. Reactant concentration:

The reactant concentration of metal salt, as well as the plant extracts, has a great impact on the formation of nanoparticles. A study by *Roya et al.*<sup>98</sup> proclaimed that concentration plays an important role in both the reactant. It is seen that the synthesis of nanoparticles increases with an increasing amount of concentration. The plant extract addition increases the reaction due to an increase in the functional group reacting with the silver ions, while the addition of silver ions increases the reducing group. The reaction increases up to a certain level of concentration and declines when it exceeds the optimal concentration<sup>92,93</sup>.

## 7.8. Reaction time:

Reaction time influences the proper synthesis and stability of nanoparticles. The change in the color of the medium is indicative of the change in the surface resonance. When the color remains constant for a long time, indicates that the MNP are completely synthesized<sup>92,93</sup>. The study by *Sekhar et al*<sup>99</sup> showed that reaction time is an important factor. In this case, the color change occurred in 8 min from yellow to light red in the reaction medium but the actual reaction continued till 60 min with the color change to intense wine red. It was seen that at 5 min there were no Surface Plasma Resonance (SPR) reading but after 10 min the SPR band increased and became constant at 60 min. The UV study showed an increase in absorbance from 5 min till 60 min and then getting it in constant phase after the final reduction and formation of gold nanoparticles with an average particle size of 55.22±42.86 nm.

## 7.9. Product recovery

The unreacted extract components need to be discarded and free flowing powder NP needs to be collected for further characterizations. The MNP formed via plant extract mediated synthesis are more stable therefore they are mainly centrifuged at 10,000 rpm for 15 min so that all particles how much small, it may be collected. The NPs collected are then rinsed off with water thrice to remove any stuck components within them. The free flowing powder is collected by undergoing a lyophilization process.

## 8. Scope for scale up

Plant mediated nanotechnology is novel approach, environmentally as well as pharmacologically. The green synthesis can be easily scaled up<sup>100</sup> as the machinery which may be employed is most commonly found in herbal, ayurvedic and pharmaceutical industry. Table 1 given below summarizes the possible unit operations that may be involved in plant extract mediated green synthesis of MNP and the availability of machinery for the same.

Table 1: Possible unit operations for plant extract mediated green synthesis of MNP.

UNIT OPERATION	MACHINERY EMPLOYED <sup>101</sup>
Plant material and processing	Milling- Hammer mill, roller flake, seed grater etc. Phytochemical screening- LCMS-MS, Super Critical Fluid Chromatography etc.
Plant extraction	Principle equipment- distillation, soxhalation in Hydro distillation unit Buchi Extraction system B-811, Buchi Rota vapors, Phase exchange-liquid liquid extraction facility etc.
Metal salt solution and Green Synthesis	Equipment-stirring tanks , reactors etc.
Product collection	Common equipment- centrifugation, lyophilizing .

## 9. Recent works

The popularity of green synthesis is reflected in the quantum of work being undertaken. Numerous works have been carried out in this field using different standardization

techniques. Few of the latest research works are stated in the table 2 given below.

Table 2: Recent works on the preparation of metal nanoparticles by green synthesis along with the probable reducing groups responsible in the synthesis

Sl no	Metal	Plant	Part used	Phytoconstituents	Applications	Ref
1.	Gold	<i>Curcuma kwangsiensis</i>	Leaves	Flavonoids, alkaloids, terpenoids.	Cytotoxicity specifically for ovarian cancer.	102
2.	Gold	<i>Cannabis sativa</i>	Leaves	$\delta$ 9-tetrahydrocannabinol	Leukaemia	103
3.	Gold	<i>Allium sativum</i>	Leaves	Methyl methane sulfinat, Dimethyl sulphide, Methyl propyl disulphide	Cytotoxicity	104
4.	Gold	<i>Curcuma pseudomontana</i>	Rhizomes	Flavonoids	Antibacterial, anti-inflammatory	105
5.	Gold	<i>Mentha longifolia</i>	Leaves	Phenolic compounds	Breast cancer	106
6.	Silver	<i>Nigella sativa</i>	Seeds	Fatty acids and volatile oils	Anti-diabetic	107
7.	Silver	<i>Phyllanthus emblica</i>	Fruits	Polyphenols	Reducing agent	108
8.	Silver	<i>Terminalia bellirica</i>	Fruits	Ellagitannins	Purification of water	109
9.	Silver	<i>Sambucus nigra</i>	Fruits	Polyphenols	Treat oral dysplasia	110
10.	Silver	<i>Zingiber officinale</i>	Leaves	Gingerol	Anti-oxidant	111
11.	Copper	<i>Citrus sinensis</i>	Fruits	Terpenes	Antibacterial property	112
12.	Copper	<i>Psidium guajava</i>	Leaves	Terpenoids	Antibacterial property	113
13.	Copper	<i>Camellia sinensis</i>	Leaves	Alkaloids and flavonoids	Cytotoxicity and antioxidant	114
14.	Copper	<i>Syzygium cumini</i>	Flower and seeds	Anthocyanins and alkaloids	Antimicrobial property	115
15.	Copper	<i>Eucalyptus globulus</i>	Leaves	Phenols	Antimicrobial activity	116
16.	Zinc	<i>Alchornea laxiflora</i>	Leaves	Quercetin	Catalytic activity	117
17.	Zinc	<i>Alhagi maurorum</i>	Leaves	Nonacosane	Antioxidant	118
18.	Zinc	<i>Gynostemma pentaphyllum</i>	Leaves	Saponins and flavonoids	Antitoxicity agent	119
19.	Zinc	<i>Salvia officinalis</i>	Leaves	Flavonoids and phenols	Antifungal activity	120
20.	Zinc	<i>Raphanus sativus</i>	Leaves	Flavonoids and alkaloids	Antioxidant and antitumor	121
21.	Selenium	<i>Zingiber officinale</i>	Rhizomes	Gingerol	Antimicrobial	122
22.	Selenium	<i>Azadirachta indica</i>	Leaves	Azadirachtin and quercetin	Antimicrobial activity	123
23.	Iron	<i>Zingiber officinale</i>	Rhizomes	Gingerol	Antibacterial activity	124
24.	Iron	<i>Chlorophytum comosum</i>	Leaves	Saponins	Antibacterial activity	125
25.	Iron	<i>Mikania mikrantha</i>	Leaves	Steroids, flavonoids and terpenoids	Antibacterial activity	126

## 10. Clinically approved MNP

There are a few approved MNP which are shown in the table 3 below

Table 3: List of clinically approved MNP.

Sl no.	Brand name	MNP	Clinical application	Refs
1	Feraheme®	Superparamagnetic iron oxide nanoparticle (SPION)	Anemia in chronic kidney disease	127
2	Ferinject®	Nanoparticles of ferric oxide	Iron deficiency anemia in chronic kidney disease	127
3	NanoTherm®	Nanoparticles of superparamagnetic iron oxide	Glioblastoma, prostate, pancreatic cancer	127
4	Acticoat®	Nanocrystalline silver	Dressings for a range of wounds including burns, bacterial infection	128
5	SilvaSorb®	Nanosilver	Wound dressings and cavity filler prevent bacterial infection	128

## Conclusions

Plant extract mediated green synthesis, as in understood from the review literature has gained importance and has also shown to be promising in terms of the pharmacological activity. The various process parameters determine MNP formation and clearly indicate that plant extract mediated green synthesis has tremendous potential for researcher in the role to streamline and validate the process. The yield of MNP from plant extract mediated green synthesis has not been highlighted much, which calls for attention. Literature also reveals that commercialization of plant extract mediated green synthesis of MNP is quite feasible.

Thus, conclusively this review shows that there is a scope for research and startups in the area of plant extract mediated green synthesis of MNP.

## Abbreviations

MNP: Metal nanoparticles, NP: Nanoparticles, nm: nanometer, rpm: Revolution per minute, min: Minute.

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