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Plant Extracts: A Promising Source for the Green Synthesis of Copper Nanoparticles Towards Agriculture and Environmental Applications

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Copper nanoparticles have received an immense interest from the scientific community due to their remarkable properties, thus offering various uses in a multitude of applications. Many works have been reported on nanoparticle production using numerous approaches. Despite various methods that can be used for copper nanoparticle preparation, green synthesis outweighs other techniques, as it is a simple, environmentally friendly yet adaptable approach. While some techniques suffer from hazardous environments, complicated procedures and equipment, and time-consuming, the usage of plant extracts is an alternative avenue to produce copper nanoparticles by adopting the green synthesis approach. The synthesis mechanisms and insights into various plant extracts are briefly discussed. Although there is a myriad range of copper nanoparticle applications, this review focuses on the potential of copper nanoparticles in agricultural and environmental applications.

Key words: Plant extracts; copper nanoparticles; green synthesis; agriculture; environmental

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Over the last few years, nanotechnology involving metal nanoparticles has emerged and actively explored. Any particulate substance that comes from various types of materials and has size ranging between 1-100 nm is called nanoparticle [1], which possesses remarkable physical and chemical properties. Due to their unique characteristics which render them suitable for many applications [2], many industries and agencies are investing in nanoparticle research to produce and develop a wide range of advanced products. One of the characteristics that contributes to the uniqueness of nanoparticles is high surface area. Due to their nano size, they have a much more prominent surface area to volume ratio compared to average sized particles [3].

Nanoparticles can be divided into two types, which are organic and inorganic. Organic nanoparticles include fullerenes and carbon-based nanoparticles, while inorganic nanoparticles compose of metals, ceramics, or polymer materials [4]. There are various types of metals that can be used to form nanoparticles, such as silver [5], iron [6], zinc [7], cobalt [8], aluminium [9], copper [10], and gold [11], with each having significant characteristics and applications.

In recent years, copper nanoparticles have gained massive interest from researchers and academics, and many industries have focused on copper nanoparticles due to their availability and cheaper as compared to other metals [12]. Albeit cheaper, copper nanoparticles remain valuable, possess interesting qualities, and offer various potential applications. Copper nanoparticles have high electrical conductivity and high melting point, as well as low electrochemical migration behavior [13], thus making them suitable and useful in the electronics sector. Copper nanoparticles have also been used for medical application due to their antibacterial properties [14]. Other potential applications of copper nanoparticles include water pollutant removal [15], gas sensor [16], printed electronics [17], lubricant additives [18], and electromagnetic interference (EMI) shielding [19].

1. Synthesis of Copper Nanoparticles

Metal nanoparticles can be synthesized by a wide variety of methods, either physical, chemical or biological methods [20]. However, physical and chemical methods possess several drawbacks. Physical method, for example, requires the use of complicated techniques that can be very time consuming and the use of expensive instruments. This includes the utilization of a tube furnace that not only takes up a lot of space, but generates an enormous amount of heat as well, raising the environmental temperature [21, 22].

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Equally, chemical method might be harmful to the environment as this method uses harsh chemicals as reducing agents, organic solvents, and non-biodegradable stabilizing agents. Among the chemicals used as reducing agents include sodium borohydride, sodium citrate, and hydrazine. It is possible to use hydrazine as a reducing agent in synthesizing copper nanoparticles, however hydrazine is highly toxic. In addition to these, chemical method utilizes high energy, pressure and temperature, making it quite unfavorable due to the high cost [21, 22]. Apart from the undesirable conditions mentioned above, the synthesis of copper nanoparticles is not suitable to be carried out by physical and chemical methods for other reasons. Firstly, the difficulty that has to be faced in its production process. Secondly, even after going through much hassle to produce, the synthesized copper nanoparticles are unstable as they are readily oxidized in air and aqueous solution, which is not the end result that we want in the first place [22].

When physical or any chemical methods are employed towards producing copper nanoparticles, some excess by-products which can be toxic may also be produced, thus affecting human health and cause pollution to the environment. Due to the toxic by-products, these methods might not be suitable to be used for medical or any pharmaceutical applications. In the case of biological method using microorganisms, the synthesis of copper nanoparticles would be too long and slow as it is a multi-step process. The process is associated with the isolation of microorganisms that have the potential to reduce copper ions, preparation of specific cultures, and maintenance of the cultures. Furthermore, there is a high possibility of contamination by pathogens along the long production process. This method is also unsuitable to synthesize copper nanoparticles for large-scale production as it is hard to maintain large-scale cultures [22]. Various studies have shown that producing nanoparticles using plants is safer and good for the environment, whereby less chemicals are used and the by-products produced are non-toxic. Harmful and toxic chemicals are not required for this method. Owing to this, the synthesis of copper nanoparticles using plant extracts can be a promising green approach to tackle the aforementioned issues.

1.1. Green synthesis of copper nanoparticles

Synthesis of metal nanoparticles using plant extracts outweighs physical, chemical, and biological methods in the aspects that this method is simple, eco-friendly, and can easily be scaled up. By using this green approach, synthesis does not have to deal with the need for continuous changing of liquid media for bacteria growth and involves only a single step process in reducing metal ions to nanoparticles. Green synthesis is eco-friendly in the sense that it does not use harmful toxic chemicals. Besides, it can be readily conducted at room temperature and pressure, thus eliminating the use of high temperature and pressure, in which these issues contribute to huge environmental concerns. Also, not only scale up for large production can be easily done, the synthesized nanoparticles can provide well-defined size and morphology than via other methods of production [23].

Plant extracts to synthesize metal nanoparticles can be extracted from various parts of plants, such as leaves, fruits, stem, roots, bark powder, latex, fruit peel, and seeds. Plant extracts consist of metabolites that are capable to act as both reducing and stabilizing agents. Among the metabolites with such properties include alkaloids, phenolic acids, polyphenols, terpenoids, flavonoids, tannins, saponins, steroids, proteins, and sugars [23]. Plant extracts which consist of these metabolites produce electrons that can cause the reduction of copper ions, leading to nanoparticle formation. It is reported that the metabolites present in plant extracts can reduce metal ions way much faster than by using microorganisms and often lead to stable formation of metal nanoparticles [23]. Besides, the application of green technology for the synthesis of nanoparticles have also been employed using other natural resources such as algae and fungi as the reducing agents in order to eliminate the dependency on toxic chemicals [24]. By utilizing plants or biological materials, an ideal synthesis of nanoparticles can be achieved with a simple, sustainable, and environmentally friendly approach as compared to conventional chemical processes [25].

Essentially, the formation of copper nanoparticles requires two main components: a precursor that provides copper ions and a reducing agent to reduce the copper ions to copper atoms, which then aggregate into copper nanoparticles [26]. The first step in the synthesis process is the preparation of plant extracts and metal salt solutions. Once a plant extract mixes with a metal salt solution at room temperature, the reduction process starts immediately and the formation of copper nanoparticles is indicated by the change in the color of the reaction mixture. The ability of plant extracts to stabilize copper nanoparticles will determine the most energetically favorable and stable morphology [27].

Several factors such as concentration of metabolites in plant extracts, concentration of metal salt solutions, temperature, pH, and reaction time may affect the quality, size, shape, morphology, and yield of the product. Different plant extracts contain different compositions and concentrations of reducing agents, which will affect the capability to reduce metal ions and subsequently varying the size and shape of nanoparticles produced. The size and shape of nanoparticles might also be affected by variation in the temperature of the reaction. At higher temperature than room temperature, occurrence of defects happens at a faster rate along with the growth of nanoparticles, hence affecting the crystal quality [28].

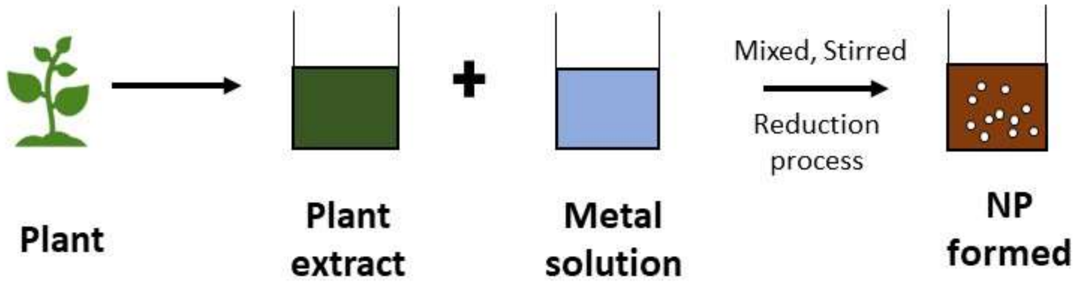

Figure 1. Green synthesis of nanoparticles using plant extract.

On the other hand, pH is used to achieve better stability in the mixture of extract-precursor in terms of electrical charges [28]. The change of electrical charges may affect the stabilizing capability of the metabolites and thereby affect the growth of nanoparticles [28]. Under acidic conditions, the growth of nanoparticles does occur, but it will be in the unstable form, where the nanoparticles form clusters that agglomerate. Meanwhile, in the case of alkaline conditions, the growth of nanoparticles occurs faster with pearl-like formation along with some large diameter nanoparticles. As for reaction time, better control of nanoparticles size can be achieved with smaller nucleation time and nanoparticles might aggregate due to long time storage of incubation [28].

Many researchers have already adopted green method in producing copper nanoparticles. Green method or approach is applicable by eliminating or reducing hazardous substances and reducing wastes that are possibly generated from the process. Using plant extracts is considered as green method since the usage of toxic chemicals can be avoided in the process [4]. Active compounds such as terpenoids, phenols, and flavonoids that exist in most plant extracts play an important role in the synthesis of copper nanoparticles [29]. A simple process involves the reaction between a plant extract with a metal solution and allowing a reduction process to occur in order to produce copper nanoparticles [29]. The reaction scheme is illustrated in Figure 1.

Copper chloride dihydrate ($CuCl_2.2H_2O$), copper sulphate pentahydrate ($CuSO_4.5H_2O$), and cupric acetate monohydrate ($(CH_3COO)_2Cu{\cdot}H_2O$) are some examples and the most common metal solutions or metal precursors used to produce copper nanoparticles [29]. There are many works reported in synthesizing copper nanoparticles using various plants and precursors. For example, in a study conducted by Nasrollahzadeh, Sajadi, & Khalaj [30], the leaves of *Euphorbia esula* L were used. The leaf extract was used as both reducing and stabilizing agents, while $CuCl_2.2H_2O$ was used as the metal precursor [30]. The presence of flavonoids and phenolic acids in the *Euphorbia esula* L extract was responsible for the reduction of copper ions, allowing nanoparticle formation. The reaction was carried out at 80°C and pH 9 for 30 minutes, producing nanoparticles with size range between 20 to 110 nm.

In another study by Demirci *et al.* [31], the synthesis was made using peroxidase enzymes that were purified from the leaves of *Ficus carica,* and $CuCl_2$ at various concentrations was used as the precursor. The optimum conditions for the synthesis of copper nanoparticles using the peroxidase enzymes were also determined based on various temperatures, pH and contact times, which were found to be 25°C, pH 8 and 30 min, respectively [31]. The copper nano-particles obtained had size ranging from 50 to 120 nm with spherical shape. Although the plant used may consists various phytochemicals, including poly-phenols which can contribute towards the nanoparticle formation, the group selectively focused on the use of peroxidase enzymes that are commonly responsible in catalyzing redox reactions. In addition, antimicrobial activity of the copper nanoparticles produced in their study was also observed against *Pediococcusadilactici* bacteria. The green synthesis of copper nanoparticles using *Nerium oleander* leaves has been reported by Gopinath *et al.* [32]. They also focused on anti-microbial properties of the copper nanoparticles against five different bacteria namely *Escherichia coli, Staphylococcus aureus, Klebsiella pneumoniae, Salmonella typhi*, and *Bacillus subtilis,* whereas the optimum conditions and the mechanism for the production of the nanoparticles using the said leaf extract has not been reported. However, it is expected that the presence of various phytochemicals in the aqueous leaf extract of *Nerium oleander* such as flavonoids and alkaloids directly influenced the trans-formation of copper ions into copper nanoparticles.

Hassanien, Husein, & Al-Hakkani [33] reported the synthesis of copper nanoparticles using the leaves of *Tilia* as a reducing material and copper(II) sulfate pentahydrate salt ($CuSO_4{\cdot}5H_2O$) as a precursor. The reaction was conducted at 80℃ and stirred continuously for 25 minutes before being left in the dark for 24 hours. The copper nanoparticles obtained had spherical shape with size between 4.7 - 17.4 nm. The nanoparticles were significantly smaller in size as compared to the nanoparticles produced by Nasrollahzadeh *et al*. [30] under similar reaction conditions, which revealed the effectiveness of the functional molecules in the *Tilia* leaf extract. The presence of active phenolic compounds including flavonoids and phenolic acids, as identified in the study, contributed to the reduction mechanism of copper ions into copper nanoparticles. Copper nanoparticles had also been synthesized using leaf parts of *Eclipta prostrata*, as reported by Chung *et al.* [34]. $Cu(OAc)_2$ was used as a precursor and was stirred with the plant extract for 24 hours at room temperature. The size of the copper nanoparticles obtained ranged from 28 to 105 nm. Their work revealed that the formation of copper nanoparticles can also be achieved under ambient temperature reaction, as similarly reported by Demirci *et al.* [31]. Various shapes of copper nanoparticles were produced including spherical, hexagonal, and cubical. The authors did not state any specific phytochemicals which may be responsible for the reduction of the copper ions, but the reported FTIR analysis may suggest possible bands attributed to the presence of flavonoids. Kulkarni & Kulkarni [35] also attempted to produce copper nanoparticles via reduction process of $CuSO_4.5H_2O$ with *Ocimum Sanctum* leaf extract at room temperature, but the shape and size of the copper nanoparticles produced were not reported. The authors mentioned several constituents of the *Ocimum sanctum* extract including alkaloids, glycosides, tannins, saponins, and aromatic compounds. These electron rich compounds are expected to be responsible for the synthesis of the copper nanoparticles.

Tahvilian *et al.* [36] reported in their study that *Allium saralicum* leaf extract could also be used to synthesize copper nanoparticles. However, compared to other extracts, the leaf extract acted only as a stabilizer and hydrazine hydrate was used instead as the reducing agent. NaOH was used as the catalyst while L-ascorbic acid was used as an antioxidant agent. All the reagents and solutions were mixed and stirred for 1 hour at room temperature. Spherically shaped 45 - 50 nm copper nanoparticles were formed. The presence of linolenic acid and methyl ester as the major components of *Allium saralicum*, both of which are fatty acids, render them suitable as stabilizers. Although the production of the nanoparticles was achieved in a short reaction time (1 hour) as compared to 24 hours when conducted under room temperature conditions as reported by Chung *et al*. [34], the use of other chemicals, such as hydrazine hydrate, is not sustainable with environmentally benign approaches. The usage of the leaf extract containing fatty acids, however, was significant as a stabilizer to produce a narrow range of diameter and size of copper nanoparticles. In addition, the copper nanoparticles produced were tested against cell toxicity by MTT assay and for antioxidant, antimicrobial, and wound healing properties. Elisma *et al.* [37] used the leaf extract of their local plant, *Uncaria gambir* Roxb. as a reducing agent to synthesize copper nanoparticles. 40 mL of copper sulphate was mixed with 20 mL of plant extract and the mixture was stirred at room temperature for 24 hours at 1000 rpm. The size of copper nanoparticles produced ranged from 2.1 to 6.9 nm and spherically shaped. Although a lower ratio of plant extract to metal precursor was used, the production of the nanoparticles was successful with small particle sizes. The authors clearly indicated that the high level of tannin in the *Uncaria gambir* Roxb. leaf extract played a critical role as a reducing agent in the synthesis of copper nanoparticles. The work also revealed that the *Uncaria gambir* Roxb. extract can serve as a highly potential and efficient plant source for the green synthesis of copper nanoparticles.

Other studies that used leaf extracts such as from *Cinnamomum* [38], *Bacopa monnieri*, *Asparagus adscendens* [39], and *Smithia sensitiva* [40] had also successfully synthesized copper or other metallic nanoparticles via the green synthesis method [41]. Besides leaf extracts, other parts of plants can also be used to synthesize copper nanoparticles. For example, Rajesh *et al*. [42] reported the production of copper nanoparticles using the seed extract of *Cuminum cyminum*. The synthesis was conducted using $Cu(CH_3COO)_2H_2O$ as a precursor and spherically shaped copper nanoparticles were obtained. The use of the seed extract was fast and efficient since the copper nanoparticles were obtained within 5 – 15 min of reaction. The presence of the biological components of the seed extract, as evidenced by the FTIR analysis, was responsible for the interaction and reduction of the metal ions. The authors also indicated the capping activity exhibited by the seed extract towards the formation of the nanoparticles.

In addition, Sirisha *et al.* [43] also successfully produced copper nanoparticles using the seeds of *Sesamum indicum* with copper sulphate as a metal source. The seed extract was mixed with copper sulphate and left in a microwave oven at 180 watts for 10 minutes. The phytochemical constituents of the seed extract and the reducing mechanism involved were not adequately described, but the authors focused on the investigation of the adsorption phenomena towards removal of SO_2 and NO_2 in aqueous solution. However, it is well known that the seeds of the *Sesamum indicum* contain phenolic components such as sesamol, which might play a significant role as reducing agents in transforming the metal ions into copper nanoparticles. *Caesalpinia bonducella* seed extract had also been used to synthesize copper nanoparticles [44]. The study was conducted using copper(II) nitrite trihydrate solution as a metal precursor. The seed, also known as fever nut or molucca bean, was reported to possess strong antioxidant properties and consists of various constituents such as citrulline, phytosterinin, flavonoids, aspartic acid, arginine, and furanoditerpenes [44]. These phytochemicals might serve as reducing, stabilizing and capping agents for the formation of the copper nanoparticles. Additionally, the copper nanoparticles obtained were tested against *S. aureus* and *Aeromonas* to observe the antibacterial activity, and the electrocatalytic properties of the nanoparticles were also evaluated.

Karimi & Mohsenzadeh [45] had synthesized copper nanoparticles using the flower part of aloe vera with $Cu(CH_3COO)_2H_2O$ as a precursor. The reduction process was performed at 50°C in a steam bath for 30 minutes until the solution changed its color. The morphology of the synthesized copper nanoparticles was spherical in shape with the size around 40 nm. The study also revealed the significance of FTIR analysis in identifying several important bands ascribed to the presence of metabolites, presumably to be flavonoids, tannins, and alkaloids, which were responsible for the synthesis of copper nanoparticles. Valli & Suganya [46] had produced copper nanoparticles using *Cassia fistula* flower extract, whereby the flower extract was mixed with copper sulphate and kept at room temperature for about one week. The color changed from dark brown to light brown, indicating the formation of copper nanoparticles. *Cassia fistula* is rich with a variety of natural antioxidants such as phenolic acids, flavonoids, saponins, alkaloids, anthraquinones, and tannins, which allow the reduction of copper ions to form copper nanoparticles. Kurkure, Jaybhaye, & Sangle [47] also had successfully synthesized copper nanoparticles using *Caesalpinia pulcherrima* flower extract and the size of the copper nanoparticles produced was between 18 - 20 nm with spherical shape. The authors mentioned that the flower extract of *Caesalpinia pulcherrima* contained tannins, polyphenols, and trace amounts of ascorbic acid, whereby tannins were culpable for the reduction of metal ions and capping action, while ascorbic acid was responsible as a protective agent to prevent the oxidation of nascent copper nanoparticles during synthesis and storage.

Some researchers also utilized fruits as reducing and stabilizing agents to form copper nanoparticles. For example, Ismail [48] used *Rhus coriaria* L., or commonly known as Sicilian sumac, fruit extract with copper sulphate pentahydrate ($CuSO_4.5H_2O$) as a metal precursor. In his work, spherically shaped copper nanoparticles were formed with the size between 22 to 27 nm. The *Rhus coriaria* L. fruit extract was specifically used as a stabilizing agent due to the high capping ability. The fruit extract, however, had low ability to reduce copper ions into Cu^0. The author did not state any phytochemicals contained in the fruit extract which were responsible for the capping activity. Długosz, Chwastowski, & Banach [49] reported the use of hawthorn berries extract to synthesize copper and silver nanoparticles. Reactions using various pH, temperature, and time were carried out in order to obtain optimum size of the nanoparticles, and they concluded that 60°C, pH 11, and reaction time of 60 minutes were the best conditions to synthesize the copper nanoparticles. The quantitative analysis of compounds in hawthorn berries has been rigorously carried out by the authors, which revealed the presence polyphenols, ascorbic acid, and anthocyanins that directly influenced the reduction and stabilization of copper ions in the process of copper nanoparticle synthesis.

In another study conducted by Batoool & Masood [50], tomato fruit extract was used with copper sulphate ($CuSO_4$) as a metal precursor to produce copper nanoparticles. Copper sulphate and tomato fruit extract were mixed and heated continuously at 70°C in a water bath shaker. The color changed from colorless to dark brown- black, indicating the formation of copper nanoparticles. Crystallite size of 40 - 70 nm of the copper nanoparticles was approximately determined from X-ray diffraction analysis using a Scherrer equation. The authors specifically mentioned the ability of ascorbic acid contained in tomato juice acting both as reducing and capping agents for the nanoparticle synthesis. *Psidium guajava*, or commonly known as guava, had also been used to synthesize copper nanoparticles in a study that was conducted by Caroling *et al*. [51]. They successfully synthesized copper nanoparticles with an average size of 15 - 30 nm with spherical shape. The presence of ascorbic acid and polyphenols in the aqueous guava extract was mainly responsible for the bioreduction process.

The green-synthesized copper nanoparticles produced using various plants are summarized in Table 1. Despite the reaction conditions may vary, the size of the copper nanoparticles produced was very much dependent on the plant used. This is mainly due to the nature of reducing components existing in the plant extracts. The presence of various types and quantities of chemical compounds in certain plant extracts may influence the formation degree of nanoparticles. In other words, the phytochemical content of the plant extracts in turn determines the ability to reduce the metal precursor to a certain extent. Most of the copper nanoparticles produced were spherically shaped. The reaction parameters can significantly influence the size and morphology of the nanoparticles. For example, it can be observed that utilization of higher pH condition in nanoparticle synthesis resulted in lower particle size formation. This observation is also supported by Rajesh *et al*. [52], which reported the decrease of particle size from 18 nm to 9 nm when pH was increased from 6 to 10. A similar trend of particle size reduction was also observed by Długosz *et al*. [49], which revealed the significant influence of alkaline environment towards the reduction of particle size. The concentration of reducing agents also influences the size of copper nanoparticles produced as higher concentration leads to smaller sized nanoparticles, potentially due to the increase of effective capping activity. In addition, the concentration of the reducing agents also may influence the nucleation rate during the particle formation. It was reported that the concentration of the reducing agent should be at least five times more concentrated against the precursor [49]. Besides, Jain *et al*. [53] also reported that the increase of reducing agent concentration may decrease the size of copper nanoparticles, while maintaining the concentration of the precursor. On the other hand, although it was reported that reaction temperature affects the size of the nanoparticles in such a way that the size decreased with the increase of temperature [49], many works had shown that it is also possible to produce nanoparticles at room temperature condition. However, longer reaction time (~24 hours) is sometimes required compared to nanoparticles synthesized at higher temperatures, which can be achieved at 30 – 60 minutes of reaction time. This indicates that temperature affects the progress of the reaction. As presented in Table 1, the production of copper nanoparticles can be achieved using ambient atmospheric temperature or moderate temperature between 60 – 80°C, which can influence the reduction rate of copper ions or the synthesis rate. Albeit various plant extracts may require certain optimum conditions, it can be suggested that efficient synthesis of copper nanoparticles can be employed at alkaline pH, high ratio of plant extract to metal ion precursor, and moderate reaction temperature.

Despite the remarkable advantages of the green synthesis technology using plant extracts, several drawbacks are also worth to be mentioned. For example, the amount of phytochemical contents might vary depending on plants and parts of the plants used. Besides, a rigorous study might still be required to obtain consistent reaction conditions and parameters for a particular plant extract, i.e., different plant extracts may require different optimum conditions for the nanoparticle synthesis. Prior to the synthesis of copper nanoparticles, an optimum procedure for the plant extraction must be employed to allow efficient reduction of copper ions.

Table 1. Summary of green synthesis of copper nanoparticles from different plants and precursors.

Plant	Precursor	Conditions during reduction process	Size	Morphology	Phytochemicals / constituents	References
Euphorbia esula L. (Leaf part)	Copper(II) chloride dihydrate ($CuCl_2.2H_2O$)	Heat at 80°C, pH 9 shake vigorously for 30 minutes	20-110 nm	Spherical	flavonoids, phenolic acids	[30]
Ficus carica (Leaf part)	Copper(II) chloride solution ($CuCl_2$)	Incubated in a closed space for 4 hours -Optimum temperature: 25°C -Optimum pH: 8 -Optimum contact time: 30 minutes	50-120 nm	Spherical	peroxidase enzymes (catalyst)	[31]
Nerium oleander (Leaf part)	Copper sulfate ($CuSO_4$)	Room temperature	n.a	n.a	n.a	[32]
Tilia (Leaf part)	Copper(II) sulfate pentahydrate salt ($CuSO_4 \cdot 5H_2O$)	Heated to 80°C with continuous stirring for 25 minutes	4.7-17.4 nm	Spherical	flavonoids, phenolic acids	[33]
Eclipta prostrata (Leaf part)	Copper acetate ($Cu(OAc)_2$)	Room temperature, subsequently stirred for 24 hours	28-105 nm	Spherical, cubical, hexagonal	n.a	[34]
Ocimum sanctum (Leaf part)	Copper sulfate pentahydrate ($CuSO_4.5H_2O$)	Kept overnight at room temperature	n.a	n.a	alkaloids, glycosides, tannins, saponins, aromatic compounds	[35]
Allium saralicum (Leaf part)	Copper sulphate ($CuSO_4$)	Hydrazine hydrate as reducing agent, NaOH as catalyst	45 - 50 nm	Spherical	linolenic acid, methyl ester	[36]

		and L-ascorbic acid as antioxidant agent Mixed and stirred for 1 hour at room temperature				
Uncaria gambir Roxb. (Leaf extract)	Copper sulphate ($CuSO_4$)	Stirred at room temperature at 1000 rpm for 24 hours	2.1-6.9 nm	Spherical	tannin	[37]
Cinnamomum tamala (Leaf part)	Copper sulphate ($CuSO_4$)	incubated at room temperature	5 - 12 nm	Spherical	caryophyllene, eugenol	[38]
Bacopa monnieri (Leaf part)	Copper sulphate ($CuSO_4$)	Stirred at room temperature	50 - 60 nm	Spherical	triterpenoid, saponins, alkaloids	[39]
Asparagus adscendens (Leaf part)	Copper sulphate ($CuSO_4$)	Stirred at room temperature	10 - 15 nm	Spherical	saponins, glycosides	[39]
Smithia sensitiva (Leaf part)	Copper acetate ($Cu(CH_3COO)_2$)	Stirred at room temperature and kept in dark for 24 hours	50 nm	n.a	flavonoids, terpenoides	[40]
Cuminum cyminum (Seeds)	Copper acetate (monohydrate) ($Cu(CH_3COO)_2$ H_2O)	Stirred magnetically at 1000 rpm for 15 minutes at room temperature	25 nm	Spherical	cuminaldehyde, pinene, limonene, cymene, 1,8-cineole, terpinene, linanool, safranal	[42]
Sesamum indicum (Seeds)	Copper sulfate solution ($CuSO_4$)	Heated in microwave oven at 180 watt for 10 minutes	n.a	n.a	n.a	[43]
Caesalpinia bonducella (Seeds)	Copper(II) nitrite trihydrate ($Cu(NO_3)_2{\cdot}3H_2O$)	Constant stirring at room temperature for 7 hours	n.a	Rice grained shaped	citrulline, phytosterinin, β-carotene, flavonoids, bonducellin, aspartic acid, β-sitosterol, arginine, furanoditerpenes	[44]
Aloe vera (Flower part)	Copper(II) acetate monohydrate ($Cu(CH_3COO)_2$ H_2O)	Heated at 50°C in steam bath for 30 minutes	40 nm	Spherical	tannins, flavonoids, alkaloids, carotenoids	[45]
Cassia fistula (Flower part)	Copper sulphate ($CuSO_4$)	Kept at room temperature for 1 week	20μ m	n.a	phenolic acids, flavonoids, saponins, alkaloids, anthraquinones, tannins	[46]

Caesalpinia pulcherrima (Flower part)	Copper(II) nitrate hydrate ($(Cu(NO)_3)_2.xH_2O$)	Stirred using magnetic stirrer at room temperature	18-20 nm	Spherical	polyphenols, tannins, ascorbic acids	[47]
Rhus coriaria L. (Fruit part)	Copper sulphate pentahydrate ($CuSO_4.5H_2O$)	Hydrazine hydrate as reducing agent, NaOH as catalyst All the solutions were mixed and heated to 60°C	2-27 nm	Semi-spherical	n.a	[48]
Hawthorn berries	Copper sulphate ($CuSO_4$)	Optimum pH: 11, at 60°C for 1 hour	60-200 nm	n.a	polyphenols, ascorbic acid, anthocyanins	[49]
Solanum lycopersicum (tomato) (Fruit extract)	Copper sulphate ($CuSO_4$)	Solutions were heated continuously at 70°C in water bath shaker	40-70 nm	n.a	ascorbic acid	[50]
Psidium guajava (guava) (Fruit extract)	Copper sulphate ($CuSO_4$)	Vigorous stirring in water bath at 80°C temperature	15-30 nm	Spherical	ascorbic acid, flavonoids, ellagic acid, gallic acid	[51]

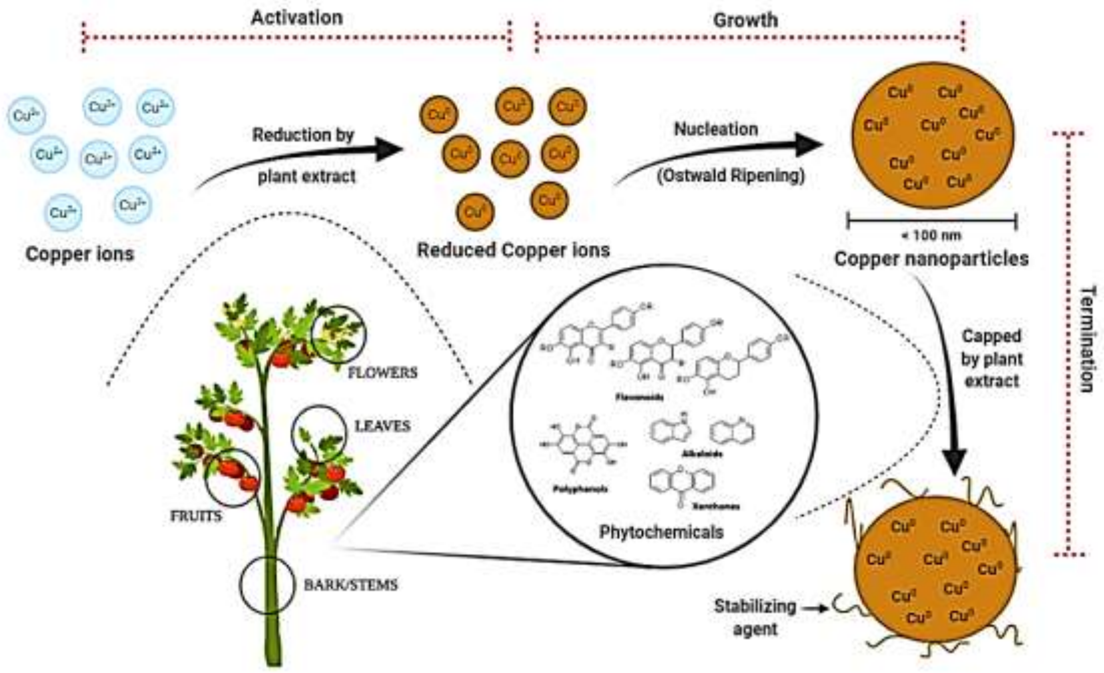

Figure 2. Mechanism of copper nanoparticle formation by plant extracts. Image adapted from Singh *et al.* [56].

2. Mechanism for Formation of Nanoparticles via Plant Leaf Extract

Generally, the formation of nanoparticles using a plant extract involves the interaction between the phytochemicals from the plant with any metal precursor solutions. The nanoparticles formed will vary depending on several factors such as class and composition of phytochemical compounds, concentration of metal precursor solutions, pH, and temperature. These factors will control the yield and stability of the nanoparticles [54]. Chokkareddy & Redhi [55] stated that phytochemicals such as phenols, alkaloids, flavonoids, saponins, tannins, terpenoids, and carbohydrates can influence the phytosynthesis of nanoparticles.

According to Singh *et al*. [56], the mechanism for the formation of nanoparticles via plant extracts consists of three main parts, which are activation, growth, and termination phases. During the activation phase, plants' phytochemicals or metabolites will reduce the metal ions, and the metal ions will transform from mono/divalent oxidation state to zero valent state and nucleation process will occur [56]. Next, the reduced copper ions undergo the growth phase forming nanoparticles with assortments of morphologies. During this stage, the tiny particles will join and form various types of morphologies such as spheres, rods, cubes, and wires [56]. The last stage, which is termination step, is where the nanoparticles reach their maximum activity. At this stage, plant phytochemicals will act as capping agents to stabilize the nanoparticles. The formation process of copper nanoparticles by plant extracts is depicted in Figure 2.

Plant phytochemicals such as flavonoids, polyphenols, alkaloids, and xanthones contain various functional groups such as -C-O, -C-O-C, -C=O, -C=C-, and -OH that will assist the reduction process of metal ions. In a research conducted by Ahmad *et al*. [57], the reduction process of nanoparticles was noticeable by the tautomerization of hydrogen atom that transformed flavonoid molecules from enol to keto. Flavonoid acted as an enhancer for the reduction process. Singh *et al*. [56] also highlighted a phenolic compound, eugenol responsible as a reducing agent to form gold and silver nanoparticles from their respective metal salts. Their FTIR analyses showed that the -OH- component in eugenol disappeared after silver and gold nanoparticles had been formed. The same mechanism can be proposed for copper nanoparticles since copper belongs to the same group as silver and gold. The proton from the hydroxyl group is eliminated to form an intermediate bearing oxygen anion. The negative charge is delocalized around the benzene ring to form a resonance-stabilized intermediate. Copper ions are reduced to Cu^0 due to the loss of two electrons from the anion intermediate, resulting in the formation of cation intermediate species followed by loss of protons to form stable conjugated species. The proposed mechanism is illustrated in Figure 3.

3. Environmental and Agricultural Applications of Copper Nanoparticles

Although copper nanoparticles are widely utilized in various fields including the medical field, the role of copper nanoparticles in the agricultural field is sparsely discussed. Copper nanoparticles can serve as an excellent bifunctional ingredient for the formulation of nanofertilizers, nanopesticides, and nano-fungicides. Formulations containing copper nanoparticles have one of the key micronutrients for growth and development of plants and it shows broad spectrum antimicrobial activity that can be utilized for management of pests and pathogenic microbes. It can also minimize the toxicity problem due to excessive use of chemical pesticides. Proper management of pests, pathogens, and parasites eventually will be able to reduce food crop wastage issues starting from initial agriculture production to final household consumption [58].

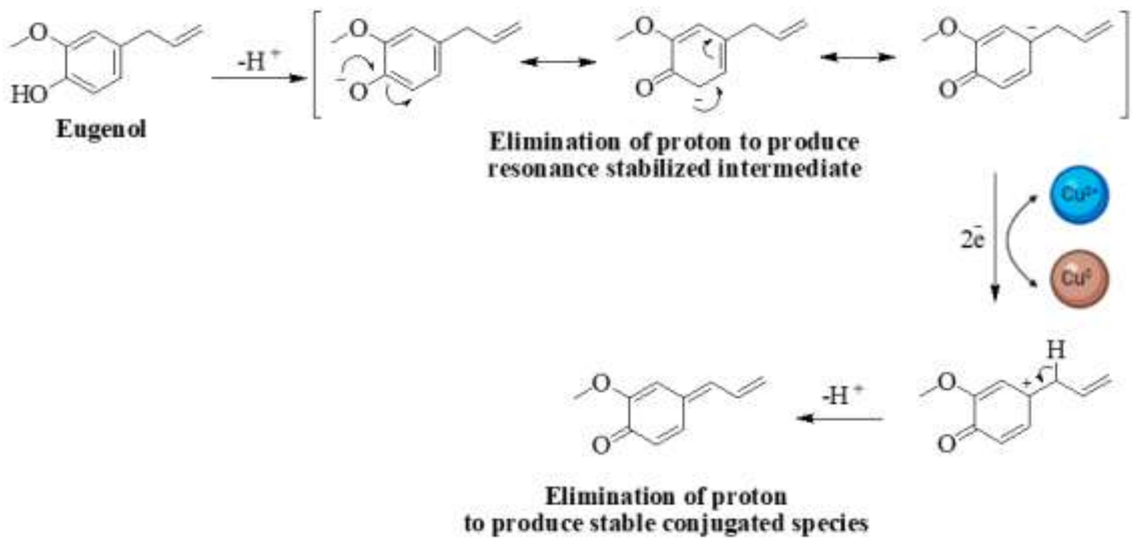

Figure 3. Proposed mechanism for reduction of Cu ions. Image adapted from Singh *et al*. [56].

The formulation of fungicides containing green-synthesized copper nanoparticles is an eco-friendly and cost-effective way for the agricultural field. Pariona *et al*. [59] had reported the antifungal activity of copper-based fungicides against *Fusarium solani*, *Neofusicoccum* sp., and F. *oxysporum* through the mechanism of cell membrane destruction and induced strong morphological changes on the mycelium. Copper nanoparticles synthesized using *Citrus medica* demonstrated antifungal activities against plant pathogenic fungi *F. culmorum*, F. *oxysporum,* and *F. graminearum* [60]. In another study, copper nanoparticles also showed antifungal activities against *F. equiseti*, along with *F. oxysporum* and *F. culmorum* [61]. Utilization of three different copper nanoparticles, i.e., Cu_2O, CuO, and Cu/Cu_2O, was more effective compared to copper-based agrochemicals against *Phytophthora infestans* on *Lycopersicon esculentum* [62]. The summary of the copper nanoparticles' efficiency as fungicides is tabulated in Table 2.

According to Shende *et al*. [60], the mechanism of action for copper nanoparticles against microbes is not yet completely understood. It can be hypothetically proposed copper nanoparticles act through five different mechanisms as shown in Figure 4. The first mechanism is the formation of pits on the cell membrane causing cell leakage due to accumulation of copper nanoparticles on the cell surface. The second mechanism is the entry of copper nanoparticles and copper(II) ions into the cell and development of oxidative stress, which leads to cell death. The third mechanism involves protein inactivation due to interaction of copper(II) ions with sulphydryl group of proteins, while the fourth mechanism is DNA damage due to interaction with copper nanoparticles. The decrease of transmembrane electrochemical potential due to the interaction of cell membrane and copper nanoparticles is postulated as the fifth mechanism.

Table 2. Summary of copper nanoparticle efficiency against plant pathogenic fungi.

Nanoparticles	Fungi	Efficiency	Ref
Cu	*F. solani*	> 70% [a]	[59]
	Neofusicoccum sp.	> 95% [a]	
	F. oxysporum	> 95% [a]	
Cu	*F. oxysporum*	28 mm [b]	[60]
	F. culmorum	33 mm [b]	
	F. graminearum	21 mm [b]	
Cu	*F. equiseti*	25 mm	[61]
	F. oxysporum	20 mm	
	F. culmorum	19 mm	
CuO	*P. infestans*	61.43% [c]	[62]
Cu_2O		73.53% [c]	
Cu/Cu_2O		69.61% [c]	

[a] Percentage of Inhibition Radial Growth at 0.5 mg/mL CuNP; [b] Zone of inhibition at 20 µL of CuNP solution; [c] percentage of infection on 50 leaves

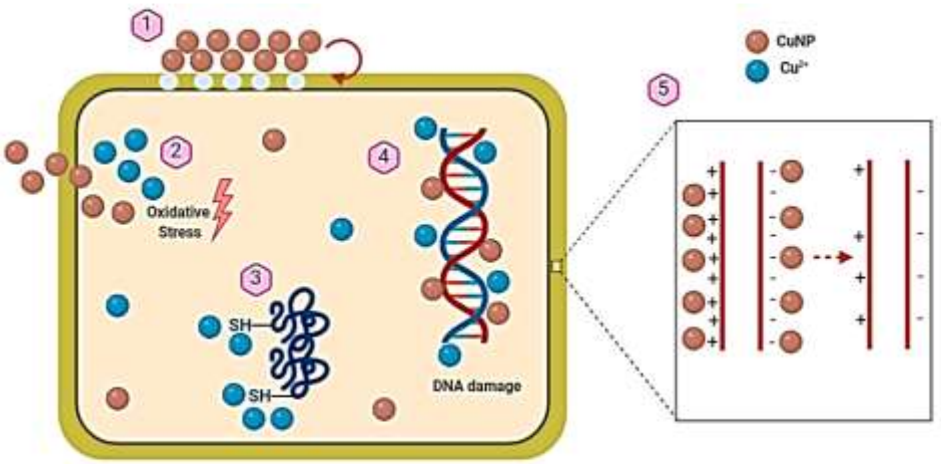

Figure 4. Schematic hypothetical mechanisms of action for CuNP in bacteria. Image adapted from Shende *et al*. [60].

Improper balance between plant growth and stress responses could detrimentally affect the productivity of many economically important crop plants. Copper nanoparticles have been reported to improve plant responses towards abiotic stresses, including drought response by regulating plant protective mechanisms associated with drought tolerance. Nguyen *et al.* [63] discovered maize treated with copper nanoparticles displayed enhanced drought tolerance stress indicated by higher leaf water content and plant biomass, higher anthocyanin, chlorophyll and carotenoid contents, and higher total seed number and grain yield compared to water-treated maize.

In addition, the characteristics of nanoparticles including high surface area and nanoscale dimension render them suitable to be used as adsorbent [64]. Taghipour, & Jalali [65] stated that using metal nanoparticles as adsorbent to remove hazardous metal ion in the environment is rather effective. Hosseini, Sayadi, & Shekari [66] reported that copper nanoparticles can be used as efficient and environmentally compatible adsorbent to remove nickel and chromium from aqueous solution. The study revealed that increase of adsorbent dosage and contact time increased the removal efficiency of nickel and chromium. This is because the higher the dosage, the more active sites available on the adsorbent to remove the metal ions. Sreekala, Fathima, & Beena [67] also reported the application of copper nanoparticles as adsorbent and revealed that copper nanoparticles showed efficient removal of lead from wastewater. There was also a study that had been carried out by Chandra & Khan [68] using copper nanoparticles as adsorbent to remove uranium. Uranium waste can be found mostly from nuclear power plants and can cause harmful effects when it accumulates in wastewater [69]. Based on the result, it could be seen that the percentage of uranium decreased as the concentration of copper nanoparticles increased [68].

Other than that, copper nanoparticles can also be used as adsorbent to adsorb hazardous gas such as SO_2 and NO_2. In an experiment conducted by Sirisha *et al*. [43], copper nanoparticles synthesized from plants managed to adsorb SO_2 and NO_2 since they have large surface area due to their nano size. In another research conducted by Ruparelia *et al*. [70], copper nanoparticles were used as disinfectant for wastewater. This is possible due to the antibacterial properties that copper nanoparticles possess.

Many hazardous wastes produced from the pharmaceutical industry such as diclofenac, naproxen, and ibuprofen can cause damage to human health [71]. Thus, it is vital to remove all the pollutants from the environment. Although there are many methods that can be used for the removal of pharmaceutical pollutants such as photocatalytic degradation, micro extraction, oxidation, chlorination, electro-coagulation-flotation and electrochemical oxidation, these methods are associated with certain drawbacks including time and money-consuming and limited scope [72]. In a study by Husein, Hassanien, & Al-Hakkani [72], synthesized copper nanoparticles were used as adsorbent to remove pharmaceutical pollutants from wastewater. Therefore, the application of green-synthesized copper nanoparticles towards the removal of pharmaceutical pollutants via the adsorption technique can be an alternative and low-cost effective treatment [72].

CONCLUSION

Diverse applications of copper nanoparticles in many fields make it one of the important nanomaterials among other metals. In recent times, the use of plant extracts as biocatalysts to synthesize copper nanoparticles has received wide attention due to the ease in production, more economical, and green approach rather than chemical catalysts. Utilization of various types of plant extracts also leads to the diversity of the structures, properties, and morphologies of copper nanoparticles. Despite these advantages, the standardization of the plant extract active compound composition is crucial to ensure reproducibility and uniformity of the synthesized copper nanoparticles. Factors including maturity, locality, and preparation and extraction processes of plants need to be further investigated. The application of the green synthesis should be implemented by considering the following: 1) ideal plant extraction conditions towards production of high yield phytochemical contents responsible for efficient copper ion reduction; 2) optimum reaction conditions suitable for high quality copper nanoparticle production; and 3) avoiding usage of any excessive or toxic chemicals other than plant extract media. Exploitation of copper nanoparticles in the agricultural field has shown some encouraging results against plant pathogens, but its application in the field is still in a preliminary stage and requires further thorough studies including the required doses for plant growth and disease control to fully maximize its bifunctional properties. The large surface area and excess of available adsorption sites of copper nanoparticles open a gateway for the development of efficient and green adsorbents for a variety of pollutant decontamination either in water or air, so as to ensure a sustainable alternative to handle environmental issues. We believe this review will unlock windows of opportunities in employing plant extracts for the green synthesis of nanoparticles, and also might pave the way towards substantial agricultural application and environmental remediation

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