Review Paper:

Green Horizons: Unveiling the Green Alchemy of Biogenic Synthesis, Structural Insights and Applications of Copper Oxide Nanoparticles

Ashok Chithra[1], Suresh Ashwin Raj[2]*, Govindaraj Swathi[2] and Kizhakedathil Moni Philip Jacob[2]*

1. Center for Nanoscience and Technology, Alagappa College of Technology, Anna University, Guindy, Chennai, Tamil Nadu, 600025, INDIA

2. Department of Biotechnology, Bannari Amman Institute of Technology, Sathyamangalam, Erode, Tamil Nadu, 638401, INDIA

*sashwinraj@gmail.com; monipj.95@gmail.com

Abstract

Nanotechnology has attracted considerable attention from researchers over the years, driven by the distinctive physicochemical properties and versatile applications it offers. Green synthesis, an evolving multidisciplinary field, has gained prominence due to its unique attributes including non-toxicity, cleanliness and environmental friendliness qualities that differentiate it from conventional physical and chemical nanoparticle synthesis methods. Among metal nanoparticles, copper oxide has become a focal point, presenting intriguing opportunities in various applications.

This review examines the biogenic synthesis of copper oxide nanoparticles using plants and microorganisms, delving into the associated procedures for synthesizing the nanoparticles and the various characterization techniques employed. The review also discusses key applications. It outlines potential avenues for future research to advance the synthesis process.

Keywords: Copper oxide nanoparticles, Biological synthesis, Biomedical application, Toxicity.

Introduction

Nanotechnology has been extensively researched in recent years and has emerged as an important field in physics, chemistry, engineering, biotechnology, food technology and medical sciences. Its innumerable applications have had a significant impact on all forms of life[116]. The size of these nanomaterials ranges from 1–100nm. Due to its specific properties, such as reactivity, surface area, conductivity and hardness, it is different from bulk materials[12]. As the nanomaterials have a high surface area (surface-to-volume ratio), it has properties like surface plasmon resonance and quantum effects[54]. The synthesis method will play a significant role in the size and characteristics of the nanoparticles.

The top-down and bottom-up approaches are the two major synthesis methods[66]. Laser ablation, sonication, physical vapor deposition and mechanical milling are some of the physical techniques used for the top-down approach. The bulk materials are converted into nanoparticles by using the above physical methods[65]. However, these methods took a lot of time to synthesize the nanoparticles and there is no even distribution[23]. Another method of producing nanoparticles is bottom-up synthesis, which involves using chemical processes like the sol-gel technique, chemical co-precipitation and chemical vapor deposition to build them at the molecular level.

In this process, hydrazine, sodium dodecyl sulfate and sodium borohydride are used as reducing agents. But the reducing agent usage will lead to harmful byproduct production. This restricts them from the usage[40,113]. The difficulties in the synthesis process create a demand for the synthesis of an environmentally friendly bottom-up approach. The green synthesis method is the one that fulfills the demand of a bottom-up approach[96]. This green synthesis uses the plant extract, a culture of microorganisms such as algae, bacteria and fungi. This method has advantages like being safe, eco-friendly and less expensive, as it does not lead to the formation of undesirable side products[45]. The metabolites derived from microorganisms and plants were used as capping and reducing agents in the green synthesis method[125].

Recently, researchers have evaluated various techniques to synthesize both organic and inorganic nanoparticles (NPs). Nanoparticles of Copper, silver, gold and zinc, due to their combination of unique characteristics and low toxic effects, present excellent potential for a wide range of applications. Copper oxide nanoparticles (CuO NPs) find widespread use in biotechnology, textiles and cosmetics, owing to their distinctive structure, large surface area, robust mechanical and thermal strength, as well as their optimal optical, magnetic and catalytic capabilities[12]. As indicated by literature findings, copper oxide nanoparticles have the potential to serve as alternatives to metals in various processes, encompassing inkjet printing, thermal transfer, gas-phase catalysis, electrocatalysis and photo-catalysis[101].

Studies have shown that the synergistic action of bioactive compounds derived from medicinal plants with copper oxide nanoparticles (CuO NPs) is advantageous in combating infections and exhibits cytotoxicity against cancer cells[73,101]. A comprehensive outline on the environmentally friendly production of CuO NPs from different sources such as phytosynthesis and microbial synthesis, provided elaborated view on parameters that affect the physicochemical characteristics of synthesized CuO NPs, with its potential applications in the biomedical field. Though the CuO NPs show advantages in different ways, it is necessary to point out their toxicity. This study also shows the toxicity of CuO NPs towards the environment and living organisms.

Biological synthesis of CuO NPs

Synthesis of nanoparticles consists of two different methods such as conventional method (physical and chemical methods of preparation of nanoparticles) which is a top down approach where the large particles are convert into fine particles using physical method and biological synthesis methods (plants and microbes are used for the production of nanoparticles) which is mostly bottom up approach, here the atoms or molecules self-assembled together to produce nanoparticles[52]. In conventional chemical methods, the ratio between precursor, solvent and reducing agent is maintained to get optimized morphology for the synthesized nanomaterials. This technique is very sensitive to water and air media because of the highly oxidizing nature of the nanoparticle.

Employing either an acidic substance or energy sources, the physical method involves reducing large particles into smaller pieces in extremely fine particles through milling. The most illustrative example of a physical approach is the grinding process, which uses extremely effective mills to separate particles with nanometric sizes[17]. In the biological synthesis method as in fig. 1, the green sources of nanoparticle synthesis used in the biological synthesis of nanoparticles are plant extracts, bacteria, algae and fungi. Comparing these conventional and biological methods, the biological method is biocompatible, less toxic and environmentally friendly method for the production of nanoparticles[52].

Phytosynthesis of CuO NPs: The process of synthesizing nanoparticles using the extracts of plants, plant parts, or algae is known as "green synthesis." Because it is non-toxic to humans, animals and the environment, it is a highly significant process[92]. The majority of a plant's parts, including the foliage, seeds, berries and peel, consist of chemicals that scavenge free radicals, nitrogen compounds, terpenoids and molecules filled with antioxidants that function as reducing agents[124]. In this process, plant matter is utilized either in its air-dried or freeze-dried form, before undergoing processing to produce extract[69,127]. In a few instances, extracts are also made of fresh leaves and used for biosynthesis. Visual confirmation of the production of this metal oxide was obtained by watching a shift in solution color[104].

The copper oxide nanoparticles were prepared from various plant parts. The leaf extract was prepared from oven-dried leaves[56]. The fruit extract was obtained just by squeezing the pulp and filtered with muslin cloths, followed by Whatmann no. 1 filter paper[89]. The fresh leaves extract was obtained by boiling it in deionized water at the appropriate temperature, which is further used for nanoparticle preparation[18]. For the synthesis of rind, seed and peel extract, these portions were dried in sunlight or in an oven, then crushed and added to boiling distilled water.

The prepared extracts were then added to the precursor solution at high temperatures[15,39]. In the case of fruits, the extract can also be prepared by both soaking the fresh fruit pulp in deionized water and homogenizing using an electric blender, as well as adding the dried and crushed fruit pulp to the boiling water[72]. The roots were collected, cleaned and shredded. These were shade-dried for one week to remove the moisture content present in them. This dried powder is added to fresh water and can also be added to boiling water to get the extract[27].

Microbial synthesis: Microbes like bacteria, fungi and yeast are frequently used in the extracellular or intracellular procedures for the manufacture of nanoparticles. In case of microbial synthesis, secondary metabolites, reductase enzymes, peptides, amino acids and biomolecules produced by the microorganisms serve as reducing agents for the production of CuO NPs[112]. The cells are cultivated in the right medium under suitable conditions and then extracted by centrifugation or filtering to eliminate the microorganisms[110]. The enzymes produced by the microorganisms also help in synthesizing the nanoparticles with enhanced stability and minimized aggregation by functioning as a capping agent. The enzymes in the medium take up the metal ions and use them as reducing agents during intracellular microbial production.

The necessary concentration of copper precursor was next added to the supernatant of the cell-free solution, which was subsequently incubated under ideal circumstances in the dark. The visible color change confirms the development of copper oxide nanoparticles[108,115]. Microorganisms accumulate reduced metal precursors as nanoparticles in their cytoplasmic membrane, cell wall and cytoplasm[26]. According to recent studies, the cofactor known as Nicotinamide Adenine Dinucleotide Hydrogen (NADH) and its associated enzymes may have a role in the creation of nanoparticles. When copper precursors are reduced to generate copper oxide nanoparticles, the NADH reductase enzyme helps with the electron transfer from NADH[14].

Characterization methods of synthesized nanoparticles

Perceptible observation: After production, there are numerous approaches to examine whether nanoparticles are present. Before endeavoring to characterize something with a different analytical approach, this provides a simpler road[59]. The precursor solution's obvious color change is the earliest sign that copper oxide nanoparticles have been created[59]. The salt and concentration have an impact on the basic precursor hue. The precursor solution's color changes, followed by precipitation, signify the creation of particles[7]. The particle's color changes visibly as it accumulates, mostly it could be a brownish color[37].

Table 1
Phytosynthesis of copper oxide nanoparticles

Name of the Plant	**Precursor Salt used**	**Size and Shape of the Nanoparticle**	**Reaction Time**
Parts of the plant: Leaves			
Hagenia abyssinica (Brace) JF. Gmel.[73]	Copper (II) nitrate trihydrate	Hexagonal, cylindrical, triangular and prismatic shapes	24 h
Catha edulis[8]	Copper (II) nitrate trihydrate	Spherical	Not mentioned
Enicostemma axillare (Lam.)[18]	Copper sulfate	Average size of 6.44nm	24 h
Ziziphus Mauritiana[85]	Copper acetate monohydrate	Spherical shape and 20-45nm	30 min
Punica granatum[86]	Copper sulfate	Mostly Spherical and some Porous (40 and 78 nm)	12, 24 and 36 h
Cissus quadrangularis[30]	Copper acetate	Spherically sphere	2 h
Convolvulus percicus L[43]	Copper (II) sulphate pentahydrate	Crystal structure with spherical shape	10 min
Tinospora cordifolia[119]	Copper nitrate trihydrate	Crystalline, 6–8 nm.	5min.
Eichhornia crassipes[121]	Copper sulphate	Spherical	7-8 h
Tinospora cordifolia[90]	Copper (II) sulphate pentahydrate	Spherical, with an average particle size of 15 to 70 nm	2 h
Simarouba glauca[51]	Copper (II) nitrate trihydrate	Spherical and rod-like nanostructures	1h
Cedrus deodara[95]	Copper (II) sulphate pentahydrate	Agglomerated and formed larger grains / Spherical	5 days in the dark
Cissus quadrangularis and *Piper betle*[53]	Copper (II) sulphate pentahydrate	Spherical and size increases as the concentration of the plant extract increases	1 Day
Morinda citrifolia[28]	Copper (II) sulphate pentahydrate	Crystalline	Not specified
Ginkgo biloba L[44]	Copper sulfate	Short rod	Not specified
Mussaenda frondosa L.[70]	Copper (II) nitrate trihydrate	Spherical crystalline/rod-shaped	Not specified
Catharanthus Roseus[27]	Copper (II) sulphate pentahydrate	Orthorhombic in structure, with crystalline sizes of 43.7 nm	Not specified
Cinnamomum malabatrum[62]	Copper(II) nitrate trihydrate	The average grain size was estimated to be about 17nm.	1 h at 85°C using a magnetic stirrer
Azadirachta indica[76]	Copper chloride solution	Cubical in shape, with an average size of 48 nm	15min
Parts of the plant: Peel			
Punica granatum fruit[39]	Copper(II) Acetate Monohydrate	Crystalline & 40nm average size	5 min
Musa paradisiaca[6]	Copper nitrate trihydrate	Spherical 50-85nm	2h
Citrus limetta[83]	$CuSO_4$ solution	Particle sizes measured from SEM ranged from 90-175 nm	20 min
Punica granatum[35]	Copper chloride	Cube-like, rod-like and spherical-like structures	30 min
Citrus sinensis, *Citrus limon* and *Citrus tangerina*[118]	Copper nitrate trihydrate	Rod and spherical	30 min
Parts of the plant: Fruits			
Citrus limon[89]	$CuSO_4$	Spherical and rod-shaped	1 h
Freshly excised seedless *Phoenix dactylifera*[72]	Copper sulfate pentahydrate	Spherical shape	5 min

https://doi.org/10.25303/211rjbt3840395

Crataegus monogyna Jacq.[31]		Copper sulfate or Copper(II) Acetate Monohydrate	Spherical morphology	3 h
Quercus pinus[109]		Copper (II) acetate monohydrate	Quasi-spherical 40nm	4 h
Citrus limon[5]		Copper sulfate pentahydrate	Spherical shape with an average diameter of 28 nm.	4 h
Tamarindus indica L[129]		Copper chloride solution	Smaller in size (5−10 nm)	12 h
Capparis spinosa[68]		Copper sulfate solution	Spherical morphology and the size of the particles were measured between 17 and 41 nm	24 h
Piper retrofractum[3]		Copper sulfate	Spherical with a particle size of 2–10 nm,	60 min
Carica papaya[87]		Copper (II) nitrate trihydrate	Spherical in shape	2 h
Opuntia ficus[74]		Copper sulfate	Spherical	24 h
Parts of the plant: Flowers				
Euphorbia pulcherrima[99]		Cupric acetate	Average particle size of 19.2 nm	2 h
Bougainvillea glabra[106]		Copper acetate monohydrate	Crystalline size 18 nm	2 min
Stachys lavandulifolia[58]		Copper chloride solution	Spherical 80nm	Not specified
Magnolia Champaca[102]		Copper acetate aqueous	Spherical shape and agglomerated	24 h
Lantana camara[21]		Copper (II) acetate	Spherical shape	2 h
Caesalpinia pulcherrima[64]		Copper (II) nitrate hydrate	Spherical 18-20nm	20 min
Parts of the plant: Seeds and Root				
Triticum aestivum[15]	Root	Copper (II) sulfate pentahydrate	Spherical shape	30 min
Rheum palmatum L.[13]	Seed	Copper chloride solution	Spherical	2 h
Krameria sp. (Rhatay)[2]	Seed	Copper (II) sulfate pentahydrate	Spherical to oval with 5.2 to 7.7 nm in size	3hrs
Caesalpinia bonducella[114]	Root	Cupric nitrate trihydrate	Rice-grain-shaped	7 h
Parts of the plant: Others				
Channa striatus[20]	Mucus	Copper acetate	Spherical	3 h
Parthenium hysterophorus[84]	Whole plant aqueous extract	Copper (II) sulphate	59.99 nm with spherical	15 min
Bergenia ciliata[32]	Rhizomes	Copper (II) sulfate pentahydrate	The average size of cuo nps was measured to be about 20 nm.	Not specified
Euphorbia maculata[1]	Fresh aerial parts	Copper (II) sulfate pentahydrate	Not conducted	2 h
Syzygium alternifolium[128]	Stem bark	Copper (II) sulfate pentahydrate	Spherical in shape & 5 to 13 nm	2 h
Brassica oleracea var.[98]	Brocolli	Copper(II) Acetate Monohydrate	26 nm more or less uniform shape, but varying in size and also no aggregation is seen.	1h
Corallocarbus epigaeus[105]	Rhizome	Copper sulfate	Spherical	12 h
Moringa oleifera[94]	Raw gum	Copper chloride solution	Small needle-like structures	1h
Allium sativum[123]	Garlic	Copper nitrate	Spherical, circular, rectangular and oval-shaped surface morphologies are defined	2−3 h.

Agaricus bisporus[111]	Mushroom	Copper nitrate	Spherical-shaped particles with a minor agglomeration size of 10 nm	24 h
Curcuma longa[50]	Tubers	Copper acetate dihydrate	Spherical in shape and crystalline in nature, with average sizes between 5 - 25 nm	4 h
Camellia sinensis assamica[34]	Powder	Copper nitrate trihydrate	Spherical (35-65nm)	12 h
Saccharum officinarum[9]	Stem (juice)	Copper nitrate	Spherical, square, cube, plate, rectangular - 84.40 nm	8 h
Pterocarpus marsupium[38]	Wood	Copper (II) sulfate pentahydrate	Spherical 20nm-50nm	10min

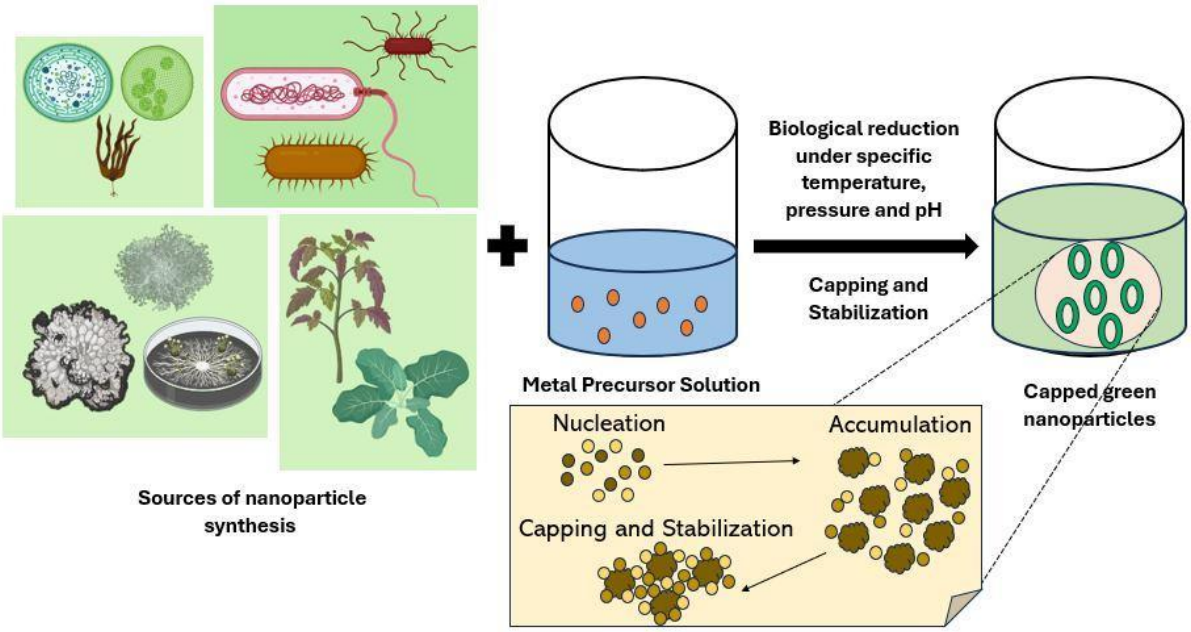

Figure 1: Biological synthesis of nanoparticles using plant extract, algae, fungi and bacteria.

UV-Visible spectroscopy: Copper oxide nanoparticles may be quickly and easily characterized using UV-visible spectroscopy[126]. Through the action of surface plasmon resonance, the nanoparticles exhibit a high absorption peak in the UV-visible spectral range[33]. The free electrons found on the outermost layer of metal resonate with the surface plasmon oscillation at a particular wavelength, giving rise to the distinct peak for each distinct metal nanoparticle[117]. In green synthesis, the reduction of copper precursors by plant extract with phytochemical substances boosts the development of nanoparticles as well as the absorption value[47]. The maximum peak of copper oxide nanoparticles exhibits UV-visible spectroscopy between 200 to 290 nm[41,61].

X-ray diffraction: The diffraction of X-rays can be used to identify the phase, chemical composition and crystalline form of the nanoparticles. Every particle has a unique diffraction pattern, which is the fundamental tenet of XRD[82]. The broadening of diffraction lines is influenced by the size of particles and it was shown as peaks in XRD[88]. Copper oxide nanoparticles that have formed common peaks with 2ϴ values in their XRD pattern at 32.1°, 35.2°, 39.5°, 49.5°, 53.2°, 62.3°, 67.2°, 68.5° and 75.2° correspond to the (110), (002), (111), (202), (020), (113), (311), (220) and (222) planes respectively[130]. The diffraction pattern indicates that all CuO NPs peaks possess a monoclinic crystal arrangement[25].

Infrared spectroscopy: In the technique of Fourier transform infrared spectroscopy (FTIR), substances are scanned at ambient temperature in the 4000–400 cm^{-1} range to determine their composition. The numerous functional groups arising from the plant or microbial metabolites linked to the nanoparticles as capping agents are shown by the change in the FT-IR spectra. FTIR analysis was used to look at the surface-attached functional components of biomolecules acting as capping/stabilizing reagents on CuO NPs. Peaks were discernible at 3573 cm^{-1}, 3300 cm^{-1}, 2093 cm^{-1}, 1612 cm^{-1}, 1379 cm^{-1}, 887 cm^{-1}, 693 cm^{-1} in the CuO NPs FTIR spectrum.

Based on the recognized peaks, it can be deduced that the broad CuO NP absorption peaks at 3573 cm^{-1} and 3300 cm^{-1} are signs of O-H stretching and vibration. The peak at 1612 cm^{-1} corresponds to the vibrations caused by the stretching of C=C. The peaks at 1379 cm^{-1} are present in the substances having C=H bending vibration.

Table 2
Microbial synthesis of copper oxide nanoparticles

Name of the Microbe	Bacteria/Fungi /Yeast/Algae	Location (Intracellular/ Extracellular)	Size and Shape of the Nanoparticle	Reaction Time	Precursor Salt used
Streptomyces MHM38[16]	Bacteria	Extracellular	Spherical	90 min	$CuSO_4$
Penicillium aurantiogriseum, Penicillium citrinum[42]	Fungus	Extracellular	Spherical	24 h	$CuSO_4$
Macrocystis pyrifera[10]	Algae	Extracellular	Spherical nanostructures	24 h	$CuSO_4$ (100 mM)
Lactobacillus casei subsp. Casei[60]	Bacteria	Extracellular	Spherical	48h	$CuSO_4$ (1mM)
Aspergillus flavus[11]	Fungus	Extracellular	Spherical, 20nm	24h	$CuSO_4.5H_2O$
Trichoderma asperellum[103]	Fungus	Not mentioned	Spherical 110nm	120 min	$(Cu(NO_3)_2.3H_2O$
Stereum hirsutum[24]	Native white-rot fungus	Extracellular	Spherical and 4-5 nm	7 days	$CuSO_4$, $Cu(NO_3)_2$ and $CuCl_2$
Escherichia coli[108]	Bacteria	Extracellular	Spherical, 10 – 40nm	42 h	$CuSO_4$ (0.001M)
Lactobacillus casei subsp.[60]	Bacteria	Not mentioned	Spherical, 30 - 75 nm	48 h	$CuSO_4$ (1mM)
Actinomycetota[75]	Actinomycetes	Not mentioned	61.7 nm, agglomerated clusters	15 min	10 mM ($CuSO_4.5H_2O$)

The band between 600 cm^{-1} to 400 cm^{-1} exhibits the metal-oxide (CuO) vibration, which is consistent with the existence of CuO NP. The functional groups seem to be crucial in the formation of the copper oxide nanoparticles because they provide reducing compounds that facilitate the development of nanoparticles[11,48,63].

Electron microscopy: The morphological characteristics (dimensions and form) and size dispersion of the copper oxide nanoparticles are defined using the Transmission Electron Microscopy (TEM) and Scanning Electron Microscopy (SEM) techniques[97]. Even though one can determine the size range by electron microscopy, one should still correlate the results to the average size estimated through XRD analysis. The nanoparticle size ranges between 6 nm to 32 nm. To ascertain the elemental compositions and quantify the produced nanoparticles, Energy dispersive X-ray analysis (EDX) or spectroscopy (EDS) can be used in conjunction with electron microscopy examination.

Atoms that reside on the surface of the nanomaterial are attacked by the SEM's electron beam[120]. The excited atom releases X-rays and these rays' wavelengths are unique to particular elements. These distinctive X-rays are examined by a particular detector that is able to interpret them. Thus, the purity and quantity of copper, as well as various particle compositions, such as impurities or plant substances, can be examined using EDX in conjunction with SEM[107].

Process parameters effects

The extensive study of the physicochemical characteristics of nanoparticles is crucial for the characterization evaluation of copper. oxide nanoparticles. The key parameters that affect the properties of the nanoparticles are the synthesis circumstances including the amount of the copper precursor, response time, temperature and extract concentration. Gaining awareness of these physicochemical characteristics is vital. The range of temperatures between 20 °C and 100 °C is crucial for the formation of nanoparticles[31,99]. In some instances, the nanoparticles are created at room temperature while being stirred continuously[73].

The development was aided by the foliage, peel and rind extracts being heated to a temperature of 100 °C[86,106]. This difference in both time and temperature has a significant impact on the nanoparticle's size and morphology as well as the antioxidant properties of plant extracts, which subsequently impact the speed of synthesis[2]. The precursors widely used for the production of copper oxide nanoparticles are copper nitrate, copper sulphate, copper acetate, copper chloride[29,30,49,58]. Mostly 0.1 M of precursor concentration is used for the synthesis of spherical-shaped nanoparticles[20,36]. The size of the nanoparticles can be tuned by optimizing the concentration and reaction hours. The improper optimization of precursor concentration will lead to the aggregation of particles, which will increase the size of the nanoparticles. The copper oxide nanoparticles prepared using 1 M of copper sulphate precursor also show spherical-shaped particles with particular sizes of 15 to 40 nm[90].

Applications

Copper oxide nanoparticles are versatile by the environment and play a significant role in a variety of processes such as catalytic breakdown, photocatalytic degradation, cancer-fighting properties[67], antiviral activity, creation of biofilm, nitrate elimination, success against human pathogens, photoluminescent activities and catalytic activity for the decomposition of organic dyes and antibiotics among others[84]. CuO NPs prepared from *Syzygium aromaticum* showed a strong fungicidal impact on *Penicillium spp.* Microorganisms and a strong antibacterial effect on *Bacillus sp*[93]. Even though CuO NPs act against some strains such as *Salmonella typhi*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae* and *Propionibacterium acnes*. Among those, *Escherichia coli* was more inhibited by CuO NPs[116]. Additionally, the cytotoxic and antioxidant functions of CuO NPs were utilized[22]. For the Huisgen [3 + 2] reaction, CuO NPs green generated from *Ginkgo biloba L.* leaf extract were used as a catalyst[78]. CuO NPs created using the fruit extract from *Z. spina-christi* turned out to be an efficient nano-adsorbent for removing crystal violet from a water-based solution[57].

CuO Nps made from oak fruit hull extract successfully catalyzed the breakdown of basic violet-3 dye in aqueous solution[34]. Additionally, the CuO nanoparticles produced from the extract of *Drypetes sepiaria* show greater photocatalyst activity towards the degradation of Congo red[77]. The *Aglaia elaeagnoidea* flower extract was utilized to create CuO nanoparticles, which turned out to be an effective catalyst for the oxidation of Congo red, methylene blue and 4-nitrophenol[71]. The catalytic application that works CuO's function as a catalyst, can be attributed to its great surface-to-volume ratio and numerous sites of activity. The particles were discovered to be arylation reaction nano-catalysts[122] and photocatalysts for Congo red and Coomassie brilliant blue R-250 dye breakdown along the same lines[100].

CuO NPs were found to be catalytically effective for the production of propargyl amines through the aldehyde-amine-alkyne (A3) coupling process and the Ullmann-coupling reaction respectively. These NPs were created by combining water-soluble extracts of *Anthemis nobilis* flowers[79], *Thymus vulgaris L.* leaves[81] and *Euphorbia esula* L.[81]. *Saraca indica* leaves produced CuO particles with photoluminescent application[91]. Copper oxide nanoparticles and nano-biocomposites made from sources such as animals and plants have been shown to have potential uses in electronic devices[19]. CuO NPs made from *Punica granatum* peel extract have shown substantial antibacterial suppression against microorganisms[55]. In general, botanical extracts have been used in the environmentally friendly production of CuO nanoparticles for uses like catalysis, antibacterial action (urinary tract), photocatalysis, antioxidants and the breakdown of chemical dyes.

Potential Toxicities and Future Scope

CuO nanoparticles primarily cause oxidative stress induction and ROS production as their toxicological mechanisms. CuO NPs produce direct toxicity by initiating the generation of ROS and indirect toxicity by inducing a redox system in the cell that triggers the formation of ROS. CuO NPs associate with the acidic lysosome environment or with mitochondria, which are oxidative organelles, upon penetration through any route of exposure (respiration, consumption, or skin). This leads to ROS generation, which is a compelling reason for the toxicity associated with CuO NPs. Copper oxide nanoparticles, after being discharged into nature, find their way into surface and ground waterways. When soil particles adsorb onto the surface of organic matter and other soil constituents, a fraction of the liberated copper oxide nanoparticles settle in the soil.

CuO NPs undergo ecological change as they move through the environment, which drastically alters their intrinsic physicochemical characteristics. It is probable that the produced toxicities will change if the physicochemical characteristics of copper oxide nanoparticles alter. Developing risk assessment techniques is crucial in order to figure out how to lessen exposure to copper oxide nanoparticles in order to lessen the risks related to the release into the environment. Knowing the precise harmful modes of activity of copper oxide nanoparticles will enhance their utility as drug delivery systems for cancer therapy and as antimicrobial substances in the future.

Conclusion

Biological approaches for the synthesis of copper oxide nanoparticles are meticulously crafted to yield products that are not only non-toxic and environmentally friendly but also economically viable. Consequently, these nanoparticles have gained substantial attention in diverse sectors including biomedical, environmental and agricultural fields. This review provides insights into the biogenic technology-mediated techniques employed in copper oxide nanoparticle production. The manipulation of various factors allows for the adjustment of the size and shape of the nanoparticles, addressing concerns related to stability.

Ongoing research focuses on identifying specific biomolecules within plant extracts that act as both reducing and capping agents, aiming to enhance the efficiency of copper oxide nanoparticle synthesis. Additionally, in-depth investigations into optimal concentrations of plant extracts contribute to refining synthesis methods. A comprehensive understanding of the copper oxide nanoparticle production process is pivotal for optimizing their applications in vital fields such as biomedicine and agriculture.

Acknowledgement

The authors would like to thank Bannari Amman Institute of Technology for providing the necessary facilities to carry out this work.

References

1. Alinezhad H. and Pakzad K., Green Synthesis of Copper Oxide Nanoparticles with an Extract of Euphorbia Maculata and Their Use in the Biginelli Reaction, *Org. Prep. Proced. Int.*, **52(4)**, 319–327 **(2020)**

2. Alshammari S.O., Mahmoud S.Y. and Farrag E.S., Synthesis of Green Copper Nanoparticles Using Medicinal Plant *Krameria sp*. Root Extract and Its Applications, *Molecules*, **28(12)**, 1–13 **(2023)**

3. Amaliyah S., Pangesti D.P., Masruri M., Sabarudin A. and Sumitro S.B., Green Synthesis and Characterization of Copper Nanoparticles Using *Piper retrofractum Vahl* Extract as Bioreductor and Capping Agent, *Heliyon*., **6(8)**, e04636 **(2020)**

4. Ameh T. and Sayes C.M., The Potential Exposure and Hazards of Copper Nanoparticles: A Review, *Environ. Toxicol. Pharmacol.*, **71**, 103220 **(2019)**

5. Amer M.W. and Awwad A.M., Green Synthesis of Copper Nanoparticles by Citrus Limon Fruits Extract, Characterization and Antibacterial Activity, *Int. Sci. Organ*., **7(1)**, 1–8 **(2021)**

6. Aminuzzaman M., Kei L.M. and Liang W.H., Green Synthesis of Copper Oxide (CuO) Nanoparticles using Banana Peel Extract and Their Photocatalytic Activities, AIP Conf. Proc., 1828 **(2017)**

7. Amjad R., Mubeen B., Ali S.S., Imam S.S., Alshehri S., Ghoneim M.M., Alzarea S.I., Rasool R., Ul-lah I., Nadeem M.S. and Kazmi I., Green Synthesis and Characterization of Copper Nanoparticles Using Fortunella Margarita Leaves, *Polymers (Basel)*, **13(24)**, 1–12 **(2021)**

8. Andualem W.W., Sabir F.K., Mohammed E.T., Belay H.H. and Gonfa B.A., Synthesis of Copper Oxide Nanoparticles Using Plant Leaf Extract of *Catha edulis* and Its Antibacterial Activity, *J. Nanotechnol.*, **2020**, 1–10 **(2020)**

9. Angeline Mary A.P., Thaminum Ansari A. and Subramanian R., Sugarcane Juice Mediated Synthesis of Copper Oxide Nanoparticles, Characterization and Their Antibacterial Activity, *J. King Saud Univ. Sci.*, **31(4)**, 1103–1114 **(2019)**

10. Araya-Castro K., Chao T.C., Durán-Vinet B., Cisternas C., Ciudad G. and Rubilar O., Green Synthesis of Copper Oxide Nanoparticles Using Protein Fractions from an Aqueous Extract of Brown Algae Macrocystis Pyrifera, *Processes*, **9(1)**, 1–10 **(2021)**

11. Asghar M.A. et al, Iron, Copper and Silver Nanoparticles: Green Synthesis Using Green and Black Tea Leaves Extracts and Evaluation of Antibacterial, Antifungal and Aflatoxin B1 Adsorption Activity, *LWT*, **90**, 98–107 **(2018)**

12. Bayda S. et al, The History of Nanoscience and Nanotechnology: From Chemical–Physical Applications to Nanomedicine, *Molecules*, **25(112)**, 1–15 **(2020)**

13. Bordbar M., Sharifi-Zarchi Z. and Khodadadi B., Green Synthesis of Copper Oxide Nanoparticles/ Clinoptilolite Using *Rheum palmatum* L. Root Extract: High Catalytic Activity for Reduction of 4-Nitrophenol, Rhodamine B and Methylene Blue, *J. Sol-Gel Sci. Technol*., **81(3)**, 724–733 **(2017)**

14. Bose D. and Chatterjee S., Biogenic Synthesis of Silver Nanoparticles Using Guava (Psidium Guajava) Leaf Extract and Its Antibacterial Activity against Pseudomonas Aeruginosa, *Appl. Nanosci.*, **6(6)**, 895–901 **(2016)**

15. Buazar F., Sweidi S., Badri M. and Kroushawi F., Biofabrication of Highly Pure Copper Oxide Nanoparticles Using Wheat Seed Extract and Their Catalytic Activity: A Mechanistic Approach, *Green Process. Synth*., **8(1)**, 691–702 **(2019)**

16. Bukhari S.I., Hamed M.M., Al-Agamy M.H., Gazwi H.S.S., Radwan H.H. and Youssif A.M., Biosynthesis of Copper Oxide Nanoparticles Using Streptomyces MHM38 and Its Biological Applications, *J. Nanomater.*, **2021**, 1-16 **(2021)**

17. Camacho-Flores B.A., Martínez-Álvarez O., Arenas-Arrocena M.C., Garcia-Contreras R., Argueta-Figueroa L., De La Fuente-Hernández J. and Acosta-Torres L.S., Copper: Synthesis Techniques in Nanoscale and Powerful Application as an Antimicrobial Agent, *J. Nanomater*., **2015**, 1–10 **(2015)**

18. Chand Mali S., Raj S. and Trivedi R., Biosynthesis of Copper Oxide Nanoparticles Using *Enicostemma axillare* (Lam.) Leaf Extract, *Biochem. Biophys. Reports*, **20**, 100699 **(2019)**

19. Cheirmadurai K., Biswas S., Murali R. and Thanikaivelan P., Green Synthesis of Copper Nanoparticles and Conducting Nanobiocomposites Using Plant and Animal Sources, *RSC Adv.*, **4(37)**, 19507–19511 **(2014)**

20. Chinnadurai G., Subramanian R. and Ahamed M., Fish Mucus Mediated Biosynthesis of Copper Oxide Nanoparticles: Spectral Characterization, Morphology and Biological Activity, *Mater. Res. Express*., **7(12)**, 125012 **(2020)**

21. Chowdhury R., Khan A. and Rashid M.H., Green Synthesis of CuO Nanoparticles Using *Lantana camara* Flower Extract and Their Potential Catalytic Activity towards the Aza-Michael Reaction, *RSC Adv.*, **10(24)**, 14374–14385 **(2020)**

22. Chung I., Rahuman A.A., Marimuthu S., Kirthi A.V., Anbarasan K., Padmini P. and Rajakumar G., Green Synthesis of Copper Nanoparticles Using Eclipta Prostrata Leaves Extract and Their Antioxidant and Cytotoxic Activities, *Exp. Ther. Med.*, **14(1)**, 18–24 **(2017)**

23. Cuenya B.R., Synthesis and Catalytic Properties of Metal Nanoparticles: Size, Shape, Support, Composition and Oxidation State Effects, *Thin Solid Films*, **518(12)**, 3127–3150 **(2010)**

24. Cuevas R., Durán N., Diez M.C., Tortella G.R. and Rubilar O., Extracellular Biosynthesis of Copper and Copper Oxide Nanoparticles by Stereum Hirsutum, a Native White-Rot Fungus from Chilean Forests, *J. Nanomater.*, **2015**, 1–7 **(2015)**

25. Cullity B.D., Elements of X-Ray Diffraction, 1st ed., Cohen M., ed., Addison-Wesley Publishing Company, Inc., Massachusetts **(2014)**

26. Dauthal P. and Mukhopadhyay M., Noble Metal Nanoparticles: Plant-Mediated Synthesis, Mechanistic Aspects of Synthesis and Applications, *Ind. Eng. Chem. Res.*, **55(36)**, 9557–9577 **(2016)**

27. Dayana K.S., Jothimani R. and Durai S.C.V., Green Synthesis of Copper Oxide Nanoparticles from *Catharanthus roseus* Plant Leaf Extract and Its Investigation, *J. Nano Electron. Phys*., **13(1)**, 1014–1015 **(2021)**

28. Dayana K.S., Mani R.J. and Durai S.C.V., *Morinda citrifolia* Leaf Extract Mediated Green Synthesis of Copper Oxide Nanoparticles and Its Potential and Antibacterial Studies, *Rasayan J. Chem*., **14(2)**, 861–870 **(2021)**

29. Deepthi P., Kumar P.N. and Prema P., Synthesis of Copper Oxide Nanoparticles Using Leaf Extract of Simaroubaglauca and Its Antibacterial Study, *Indian J. Chem. Technol.*, **28(1)**, 123–127 **(2021)**

30. Devipriya D. and Roopan S.M., *Cissus quadrangularis* Mediated Ecofriendly Synthesis of Copper Oxide Nanoparticles and Its Antifungal Studies against *Aspergillus niger*, *Aspergillus Flavus*, *Mater. Sci. Eng. C*., **80**, 38–44 **(2017)**

31. Długosz O., Chwastowski J. and Banach M., Hawthorn Berries Extract for the Green Synthesis of Copper and Silver Nanoparticles, *Chem. Pap.*, **74(1)**, 239–252 **(2020)**

32. Dulta K., Ko G., Chauhan P., Jasrotia R., Chauhan P.K. and Ighalo J.O., Multifunctional CuO Nanoparticles with Enhanced Photocatalytic Dye Degradation and Antibacterial Activity, *Sustain. Environ. Res*., **32(2)**, 1–15 **(2022)**

33. Eustis S. and El-Sayed M.A., Why Gold Nanoparticles Are More Precious than Pretty Gold: Noble Metal Surface Plasmon Resonance and Its Enhancement of the Radiative and Nonradiative Properties of Nanocrystals of Different Shapes, *Chem. Soc. Rev.*, **35(3)**, 209–217 **(2006)**

34. Fardood S.T. and Ramazani A., Black Tea Extract Mediated Green Synthesis of Copper Oxide Nanoparticles, *Karaj Branch J. Appl. Chem. Res*., **12**, 8–15 **(2018)**

35. Fuku X., Modibedi M. and Mathe M., Green Synthesis of Cu/Cu_2O/CuO Nanostructures and the Analysis of Their Electrochemical Properties, *SN Appl. Sci.*, **2(5)**, 1–15 **(2020)**

36. Ganesan K., Jothi V.K., Natarajan A., Rajaram A., Ravichandran S. and Ramalingam S., Green Synthesis of Copper Oxide Nanoparticles Decorated with Graphene Oxide for Anticancer Activity and Catalytic Applications, *Arab. J. Chem.*, **13(8)**, 6802–6814 **(2020)**

37. Garcia M.A., De La Venta J., Crespo P., Llopis J., Penadés S., Fernández A. and Hernando A., Surface Plasmon Resonance of Capped Au Nanoparticles, *Phys. Rev. B. Condens. Matter Mater. Phys.*, **72(24)**, 2–5 **(2005)**

38. Gaurav Sharma R., Pterocarpus Marsupium Derived Phyto-Synthesis of Copper Oxide Nanoparticles and Their Antimicrobial Activities, *J. Microb. Biochem. Technol.*, **7(3)**, 140–144 **(2015)**

39. Ghidan A.Y., Al-Antary T.M. and Awwad A.M., Green Synthesis of Copper Oxide Nanoparticles Using *Punica granatum* Peels Extract: Effect on Green Peach Aphid, *Environ. Nanotechnol. Monit. Manag.*, **6**, 95–98 **(2016)**

40. Ghorbani H.R., Chemical Synthesis of Copper Nanoparticles, *Orient. J. Chem*., **30(2)**, 803–806 **(2014)**

41. Goh E.G., Xu X. and McCormick P.G., Effect of Particle Size on the UV Absorbance of Zinc Oxide Nanoparticles, *Scr. Mater.*, **78(79)**, 49–52 **(2014)**

42. Honary S., Barabadi H., Gharaei-Fathabad E. and Naghibi F., Green Synthesis of Copper Oxide Nanoparticles Using Penicillium Aurantiogriseum, Penicillium Citrinum and Penicillium Waksmanii. Dig., *J. Nanomater. Bio-structures,* **7(3)**, 999–1005 **(2012)**

43. Hosseinzadeh R., Mohadjerani M. and Mesgar S., Green Synthesis of Copper Oxide Nanoparticles Using Aqueous Extract of *Convolvulus percicus* L. as Reusable Catalysts in Cross-Coupling Reactions and Their Antibacterial Activity, *IET Nanobiotechnol*., **11(6)**, 725–730 **(2017)**

44. Huang W. et al, Optimised Green Synthesis of Copper Oxide Nanoparticles and Their Antifungal Activity, *Micro. Nano. Lett*., **16(7)**, 374–380 **(2021)**

45. Huq M.A., Ashrafudoulla M., Rahman M.M., Balusamy S.R. and Akter S., Green Synthesis and Potential Antibacterial Applications of Bioactive Silver Nanoparticles: A Review, *Polymers (Basel)*, **14(4)**, 1–22 **(2022)**

46. Ijaz F., Shahid S., Khan S.A., Ahmad W. and Zaman S., Green Synthesis of Copper Oxide Nanoparticles Using Abutilon Indicum Leaf Extract: Antimicrobial, Antioxidant and Photocatalytic Dye Degradation Activities, *Trop. J. Pharm. Res.*, **16(4)**, 743–753 **(2017)**

47. Isaac R.S.R., Sakthivel G. and Murthy C., Green Synthesis of Gold and Silver Nanoparticles Using Averrhoa Bilimbi Fruit Extract, *J. Nanotechnol.*, **5(3)**, 223–228 **(2013)**

48. Ismail M.I.M., Green Synthesis and Characterizations of Copper Nanoparticles, *Mater. Chem. Phys.*, **240**, 1–25 **(2020)**

49. Jayakumarai G., Gokulpriya C., Sudhapriya R., Sharmila G. and Muthukumaran C., Phytofabrication and Characterization of Monodisperse Copper Oxide Nanoparticles Using Albizia Lebbeck Leaf Extract, *Appl. Nanosci.*, **5(8)**, 1017–1021 **(2015)**

50. Jayarambabu N., Akshaykranth A., Venkatappa Rao T., Venkateswara Rao K. and Rakesh Kumar R., Green Synthesis of Cu Nanoparticles Using Curcuma Longa Extract and Their Application in Antimicrobial Activity, *Mater. Lett.*, **259**, 126813 **(2020)**

51. Jeeffin Blessikha R. and Isac Sobana Raj C., Green Amalgamation of Copper Nanoparticles of Assorted Size exploiting Lawsonia inermis Leaf: Biological Assay and Photocatalytic Activity, *Res. J. Chem. Environ*., **27(6)**, 8-17 **(2023)**

52. Kapoor R.T., Salvadori M.R., Rafatullah M., Siddiqui M.R., Khan M.A. and Alshareef S.A., Exploration of Microbial Factories for Synthesis of Nanoparticles – A Sustainable Approach for Bioremediation of Environmental Contaminants, *Front. Microbiol*., **12**, 1–16 **(2021)**

53. Kasi S.D. et al, Biogenic Synthesis of Copper Oxide Nanoparticles Using Leaf Extracts of *Cissus quadrangularis* and *Piper betle* and Its Antibacterial Effects, *Micro. Nano. Lett*., **16(8)**, 419–424 **(2021)**

54. Kato H., *In Vitro* Assays: Tracking Nanoparticles inside Cells, *Nat. Nanotechnol*., **6(3)**, 139–140 **(2011)**

55. Kaur P., Thakur R. and Chaudhury A., Biogenesis of Copper Nanoparticles Using Peel Extract of Punica Granatum and Their Antimicrobial Activity against Opportunistic Pathogens, *Green Chem. Lett. Rev.*, **9(1)**, 33–38 **(2016)**

56. Keabadile O.P., Aremu A.O., Elugoke S.E. and Fayemi O.E., Green and Traditional Synthesis of Copper Oxide Nanoparticles—Comparative Study, *Nanomaterials*, **10(12)**, 1–19 **(2020)**

57. Khani R., Roostaei B., Bagherzade G. and Moudi M., Green Synthesis of Copper Nanoparticles by Fruit Extract of Ziziphus Spina Christi (L.) Wild.Application for Adsorption of

Triphenylmethane Dye and Antibacterial Assay, *J. Mol. Liq.*, **255**, 541–549 **(2018)**

58. Khatami M., Heli H., Jahani P.M., Azizi H. and Nobre M.A.L., Copper/Copper Oxide Nanoparticles Synthesis Using *Stachys lavandulifolia* and Its Antibacterial Activity, *IET Nanobiotech*., **11(6)**, 709–713 **(2017)**

59. Kiruba Daniel S.C.G., Vinothini G., Subramanian N., Nehru K. and Sivakumar M., Biosynthesis of Cu, ZVI and Ag Nanoparticles Using Dodonaea Viscosa Extract for Antibacterial Activity against Human Pathogens, *J. Nanoparticle Res.*, **15(1)**, 1319 **(2013)**

60. Kouhkan M., Ahangar P., Babaganjeh L.A. and Allahyari-Devin M., Biosynthesis of Copper Oxide Nanoparticles Using Lactobacillus Casei Subsp. Casei and Its Anticancer and Antibacterial Activities, *Curr. Nanosci*., **16(1)**, 101–111 **(2019)**

61. Kouvaris P., Delimitis A., Zaspalis V., Papadopoulos D., Tsipas S.A. and Michailidis N., Green Synthesis and Characterization of Silver Nanoparticles Produced Using Arbutus Unedo Leaf Extract, *Mater. Lett.*, **76**, 18–20 **(2012)**

62. Krishna B.A., Kumar P.N. and Prema P., Green Synthesis of Copper Oxide Nanoparticles Using *Cinnamomum malabatrum* Leaf Extract and Its Antibacterial Activity, *Indian J. Chem. Technol*., **27**, 525–530 **(2021)**

63. Kumar B., Smita K., Cumbal L. and Debut A., Ultrasound Agitated Phytofabrication of Palladium Nanoparticles Using Andean Blackberry Leaf and Its Photocatalytic Activity, *J. Saudi Chem. Soc.*, **19(5)**, 574–580 **(2015)**

64. Kurkure R.V., Jaybhaye S. and Sangle A., Synthesis of Copper / Copper Oxide Nanoparticles in Eco-Friendly and Non-Toxic Manner from Floral Extract of *Caesalpinia pulcherrima*, *Int. J. Recent Innov. Trends Comput. Commun.*, **4(4)**, 363–366 **(2016)**

65. Li X.Q., Elliott D.W. and Zhang W.X., Zero-Valent Iron Nanoparticles for Abatement of Environmental Pollutants: Materials and Engineering Aspects, *Crit. Rev. Solid State Mater. Sci.*, **31(4)**, 111–122 **(2006)**

66. Liu Z., Jiang W., Nam J., Moon J.J. and Kim B.Y.S., Immunomodulating Nanomedicine for Cancer Therapy, *Nano Lett.*, **18(11)**, 6655–6659 **(2018)**

67. Mahmood R.I., Kadhim A.A., Ibraheem S., Albukhaty S., Mohammed-Salih H.S., Abbas R.H., Jabir M.S., Mohammed M.K.A., Nayef U.M., AlMalki F.A., Sulaiman G.M. and Al-Karagoly H., Biosynthesis of Copper Oxide Nanoparticles Mediated Annona Muricata as Cytotoxic and Apoptosis Inducer Factor in Breast Cancer Cell Lines, *Sci. Rep*., **12(1)**, 1–10 **(2022)**

68. Mahmoudvand H., Khaksarian M., Ebrahimi K., Shiravand S., Jahanbakhsh S., Niazi M. and Nadri S., Antinociceptive Effects of Green Synthesized Copper Nanoparticles Alone or in Combination with Morphine, *Ann. Med. Surg.*, **51**, 31–36 **(2020)**

69. Malik P., Shankar R., Malik V., Sharma N. and Mukherjee T.K., Green Chemistry Based Benign Routes for Nanoparticle Synthesis, *J. Nanoparticles*, **2014**, 1–14 **(2014)**

70. Manasa D.J., Chandrashekar K.R., Kumar D.J.M. and Niranjana M., *Mussaenda frondosa* L.Mediated Facile Green Synthesis of Copper Oxide Nanoparticles – Characterization, Photocatalytic and Their Biological Investigations, *Arab. J. Chem*., **14(6)**, 103184 **(2021)**

71. Manjari G., Saran S., Arun T., Vijaya Bhaskara Rao A. and Devipriya S.P., Catalytic and Recyclability Properties of Phytogenic Copper Oxide Nanoparticles Derived from Aglaia Elaeagnoidea Flower Extract, *J. Saudi Chem. Soc*., **21(5)**, 610–618 **(2017)**

72. Mohamed E.A., Green Synthesis of Copper and Copper Oxide Nanoparticles Using the Extract of Seedless Dates, *Heliyon*, **6(1)**, e03123 **(2020)**

73. Murthy H.C.A., Desalegn T., Kassa M., Abebe B. and Assefa T., Synthesis of Green Copper Nanoparticles Using Medicinal Plant *Hagenia abyssinica* (Brace) JF. Gmel. Leaf Extract: Antimicrobial Properties, *J. Nanomater.*, **2020**, 1–12 **(2020)**

74. Muthu B., Phytosynthesis of Copper Oxide Nanoparticles from *Opuntia ficus* and Its Antibreast Cancer Activity against MCF-7 Cell Line (Invasive Ductal Carcinoma), *Malaya Journal of Matematik.*, **S(2)**, 4414-4419 **(2020)**

75. Nabila M.I. and Kannabiran K., Biosynthesis, Characterization and Antibacterial Activity of Copper Oxide Nanoparticles (CuO NPs) from Actinomycetes, *Biocatal. Agric. Biotechnol*., **15**, 56–62 **(2018)**

76. Nagar N. and Devra V., Green Synthesis and Characterization of Copper Nanoparticles Using *Azadirachta indica* Leaves, *Mater. Chem. Phys*., **213(1)**, 44–51 **(2018)**

77. Narasaiah P., Mandal B.K. and Sarada N.C., Biosynthesis of Copper Oxide Nanoparticles from Drypetes Sepiaria Leaf Extract and Their Catalytic Activity to Dye Degradation, IOP Conf. Ser. Mater. Sci. Eng., **263(2)**, 022012 **(2017)**

78. Nasrollahzadeh M. and Mohammad Sajadi S., Green Synthesis of Copper Nanoparticles Using Ginkgo Biloba L. Leaf Extract and Their Catalytic Activity for the Huisgen [3+2] Cycloaddition of Azides and Alkynes at Room Temperature, *J. Colloid Interface Sci.*, **457**, 141–147 **(2015)**

79. Nasrollahzadeh M., Mohammad Sajadi S. and Rostami-Vartooni A., Green Synthesis of CuO Nanoparticles by Aqueous Extract of Anthemis Nobilis Flowers and Their Catalytic Activity for the A3 Coupling Reaction, *J. Colloid Interface Sci*., **459**, 183–188 **(2015)**

80. Nasrollahzadeh M., Sajadi S.M. and Khalaj M., Green Synthesis of Copper Nanoparticles Using Aqueous Extract of the Leaves of Euphorbia Esula L and Their Catalytic Activity for Ligand-Free Ullmann-Coupling Reaction and Reduction of 4-Nitrophenol, *RSC Adv.*, **4(88)**, 47313–47318 **(2014)**

81. Nasrollahzadeh M., Sajadi S.M., Rostami-Vartooni A. and Hussin S.M., Green Synthesis of CuO Nanoparticles Using Aqueous Extract of Thymus Vulgaris L. Leaves and Their Catalytic Performance for N-Arylation of Indoles and Amines, *J. Colloid Interface Sci.*, **466**, 113–119 **(2016)**

82. Naveen Kumar J., Ashok Reddy V., Roji Marjorie S. and Thanikaikarasan S., Structural, Compositional and Optical

Properties of Copper Oxide Nanoparticles by Sol-Gel Method, *Mater. Today Proc.*, **33**, 2961–2963 **(2020)**

83. Noory V. and Saeedy R., Green Synthesis of Copper Oxide Nanoparticles Using *Citrus limetta* (Sweet Lime) Peel Waste, *Magna Sci. Adv. Biol. Pharm*., **2(2)**, 010–013 **(2021)**

84. Nzilu D.M., Madivoli E.S., Makhanu D.S., Wanakai S.I., Kiprono G.K. and Kareru P.G., Green Synthesis of Copper Oxide Nanoparticles and Its Efficiency in Degradation of Rifampicin Antibiotic, *Sci. Rep*., **13(1)**, 1–18 **(2023)**

85. Pansambal S., Gonade S., Ghotekar S., Oza R. and Deshmukh K., Green Synthesis of CuO Nanoparticles Using *Ziziphus mauritiana* L. Extract and Its Characterizations, *IJSRST*, **3(8)**, 1388–1392 **(2017)**

86. Peternela J., Silva M.F., Vieira M.F., Bergamasco R. and Vieira A.M.S., Synthesis and Impregnation of Copper Oxide Nanoparticles on Activated Carbon through Green Synthesis for Water Pollutant Removal, *Mater. Res*., **21(1)**, 1–11 **(2018)**

87. Phang Y.K., Aminuzzaman M., Akhtaruzzaman M., Muhammad G., Ogawa S., Watanabe A. and Tey L.H., Green Synthesis and Characterization of CuO Nanoparticles Derived from Papaya Peel Extract for the Photo-catalytic Degradation of Palm Oil Mill Effluent (POME), *Sustain*., **13(2)**, 1–15 **(2021)**

88. Pradeep T., NANO: The Essentials Understanding Nanoscience and Nanotechnology, 1st Edition, Pradeep T., Ed., Tata McGraw-Hill Publishing Company Limited, New Delhi **(2007)**

89. Pradhan S., Shrestha R. and Bhandari K., Effect of Various Parameters on Bio-Synthesis of Copper Nano-particles Using *Citrus medica* Linn (Lemon) Extract and Its Antibacterial Activity, *Amrit Res. J.*, **1(1)**, 51–58 **(2020)**

90. Prakash M.V.D., Sampath S., Amudha K., Nadeem A., Lopes B.S., Durga B. and Muthupandian S., Eco-Friendly Green Synthesis of Copper Nanoparticles from *Tinospora cordifolia* Leaves: Optical Properties with Biological Evaluation of Anti-Microbial, Anti-Inflammatory and Anti-Oxidant Applications, *Mater. Technol.*, **38(1)**, 2247908 **(2023)**

91. Prasad K.S., Patra A., Shruthi G. and Chandan S., Aqueous Extract of Saraca Indica Leaves in the Synthesis of Copper Oxide Nanoparticles: Finding a Way towards Going Green, *J. Nanotechnol.*, **2017**, 1-6 **(2017)**

92. Raghunandan D. et al, Biosynthesis of Stable Polyshaped Gold Nanoparticles from Microwave-Exposed Aqueous Extracellular Anti-Malignant Guava (*Psidium guajava*) Leaf Extract, *Nanobiotechnology*, **5(1–4)**, 34–41 **(2009)**

93. Rajesh K.M., Ajitha B., Reddy Y.A.K., Suneetha Y. and Reddy P.S., Assisted Green Synthesis of Copper Nanoparticles Using Syzygium Aromaticum Bud Extract: Physical, Optical and Antimicrobial Properties, *Optik (Stuttg)*, **154**, 593–600 **(2018)**

94. Ramalechume C., Shamili P., Krishnaveni R. and Swamidoss C.M.A., Synthesis of Copper Oxide Nanoparticles Using Tree Gum Extract, Its Spectral Characterization and a Study of Its Anti-Anti-Bactericidal Properties, *Mater. Today Proc*., **33**, 4151–4155 **(2020)**

95. Ramzan M., Obodo R.M., Mukhtar S., Ilyas S.Z., Aziz F. and Thovhogi N., Green Synthesis of Copper Oxide Nanoparticles Using *Cedrus deodara* Aqueous Extract for Antibacterial Activity, *Mater. Today Proc.*, **36**, 576–581 **(2019)**

96. Rathod A., Siddesh M.R., Prakruthi S., Nagaraj V. and Kiran S.C.R., A Review on Green Synthesized Copper Nanoparticles and Their Applications, *Int. J. Eng. Res. Technol*., **9(15)**, 45–49 **(2021)**

97. Rehana D., Mahendiran D., Kumar R.S. and Rahiman A.K., Evaluation of Antioxidant and Anticancer Activity of Copper Oxide Nanoparticles Synthesized Using Medicinally Important Plant Extracts, *Biomed. Pharmacother.*, **89**, 1067–1077 **(2017)**

98. Renuga D., Jeyasundari J., Shakthi Athithan A.S. and Brightson Arul Jacob Y., Synthesis and Characterization of Copper Oxide Nanoparticles Using Brassica Oleracea Var. Italic Extract for Its Antifungal Application, *Mater. Res. Express.*, **7(4)**, 45007 **(2020)**

99. Sackey J., Nwanya A.C., Bashir A.K.H., Matinise N., Ngilirabanga J.B., Ameh A.E., Coetsee E. and Maaza M., Electrochemical Properties of *Euphorbia pulcherrima* Mediated Copper Oxide Nanoparticles, *Mater. Chem. Phys*., **244**, 122714 **(2020)**

100. Sankar R., Manikandan P., Malarvizhi V., Fathima T., Shivashangari K.S. and Ravikumar V., Green Synthesis of Colloidal Copper Oxide Nanoparticles Using Carica Papaya and Its Application in Photocatalytic Dye Degradation, *Spectrochim. Acta - Part A Mol. Biomol. Spectrosc.*, **121(75)**, 746–750 **(2014)**

101. Sankara Narayanan V.P., Kathirason S.G., Elango P., Subramanian R., Sivagurusundar R. and Gurusamy A., *Emilia sonchifolia* Leaf Extract-Mediated Green Synthesis, Characterization, in-vitro Biological Activities, Photocatalytic Degradation and in-vivo *Danio rerio* Embryo Toxicity of Copper Nanoparticles, *RSC Adv.*, **13(24)**, 16724–16740 **(2023)**

102. Santhoshkumar J. and Shanmugam V., Green Synthesis of Copper Oxide Nanoparticles from *Magnolia champaca* Floral Extract and Its Antioxidant & Toxicity Assay Using Danio Rerio, *Int. J. Recent Technol. Eng.*, **8(5)**, 5444–5449 **(2020)**

103. Saravanakumar K., Shanmugam S., Varukattu N.B., MubarakAli D., Kathiresan K. and Wang M.H., Biosynthesis and Characterization of Copper Oxide Nanoparticles from Indigenous Fungi and Its Effect of Photothermolysis on Human Lung Carcinoma, *J. Photochem. Photobiol. B Biol*., **190**, 103–109 **(2019)**

104. Sebeia N., Jabli M., Ghith A. and Saleh T.A., Eco-Friendly Synthesis of *Cynomorium coccineum* Extract for Controlled Production of Copper Nanoparticles for Sorption of Methylene Blue Dye, *Arab. J. Chem*., **13(2)**, 4263–4274 **(2020)**

105. Selvam K., Sudhakar C., Selvankumar T., Senthilkumar B., Selva Kumar R. and Kannan N., Biomimetic Synthesis of Copper Nanoparticles Using Rhizome Extract of Corallocarbus Epigaeus and Their Bactericidal with Photocatalytic Activity, *SN Appl. Sci*., **2(6)**, 1–7 **(2020)**

106. Shammout M.W. and Awwad A.M., A Novel Route for the Synthesis of Copper Oxide Nanoparticles using Bougainvillea Plant Flowers Extract and Antifungal Activity Evaluation, *Int. Sci. Organ*., **7**, 71–78 **(2021)**

107. Shiravand S. and Azarbani F., Phytosynthesis, Characterization, Antibacterial and Cytotoxic Effects of Copper Nanoparticles, *Green Chem. Lett. Rev*., **10(4)**, 241–249 **(2017)**

108. Singh A., Patil R., Anand A., Milani P. and Gade W.N., Biological Synthesis of Copper Oxide Nanoparticles Using *Escherichia Coli*, *Curr. Nanosci.*, **6(4)**, 365–369 **(2010)**

109. Sorbiun M., Shayegan Mehr E., Ramazani A. and Taghavi Fardood S., Green Synthesis of Zinc Oxide and Copper Oxide Nanoparticles Using Aqueous Extract of Oak Fruit Hull (Jaft) and Comparing Their Photocatalytic Degradation of Basic Violet 3, *Int. J. Environ. Res*., **12(1)**, 29–37 **(2018)**

110. Srinivasan S. and Rani P., Biological Synthesis of Copper Nanoparticles Using Pseudomonas Fluorescens, *Int. J. Curr. Microbiol. Appl. Sci.*, **3**, 374–383 **(2016)**

111. Sriramulu M., Shanmugam S. and Ponnusamy V.K., Agaricus Bisporus Mediated Biosynthesis of Copper Nanoparticles and Its Biological Effects: An in-Vitro Study, *Colloids Interface Sci. Commun.*, **35**, 100254 **(2020)**

112. Subbaiya R., Saravanan M., Priya A.R., Shankar K.R., Selvam M., Ovais M., Balajee R. and Barabadi H., Biomimetic Synthesis of Silver Nanoparticles from Streptomyces Atrovirens and Their Potential Anticancer Activity against Human Breast Cancer Cells, *IET Nanobiotechnology*, **11(8)**, 965–972 **(2017)**

113. Suganeswari M. et al, Nano Particles: A Novel System in the Current Century, *Int. J. Pharm. Biol. Arch.*, **2(2)**, 847–854 **(2011)**

114. Sukumar S., Rudrasenan A. and Nambiar P.D., Green-Synthesized Rice-Shaped Copper Oxide Nanoparticles Using *Caesalpinia bonducella* Seed Extract and Their Applications, *ACS Omega*, **5(2)**, 1040–1051 **(2020)**

115. Thakkar K.N., Mhatre S.S. and Parikh R.Y., Biological Synthesis of Metallic Nanoparticles, *Nanomedicine: Nanotech. Biol. Med*., **6(2)**, 257–262 **(2010)**

116. Thakur S., Sharma S., Thakur S. and Rai R., Green Synthesis of Copper Nano-Particles Using *Asparagus adscendens Roxb*. Root and Leaf Extract and Their Antimicrobial Activities, *Int. J. Curr. Microbiol. Appl. Sci*., **7(4)**, 683–694 **(2018)**

117. Tréguer-Delapierre M., Majimel J., Mornet S., Duguet E. and Ravaine S., Synthesis of Non-Spherical Gold Nanoparticles, *Gold Bull*., **41(2)**, 195–207 **(2008)**

118. Tshireletso P., Ateba C.N. and Fayemi O.E., Spectroscopic and Antibacterial Properties of CuONPs from Orange, Lemon and Tangerine Peel Extracts: Potential for Combating Bacterial Resistance, *Molecule*s, **26(586)**, 1–18 **(2021)**

119. Udayabhanu, Nethravathi P.C., Pavan Kumar M.A., Suresh D., Lingaraju K., Rajanaika H., Nagabhushana H. and Sharma S.C., *Tinospora cordifolia* Mediated Facile Green Synthesis of Cupric Oxide Nanoparticles and Their Photocatalytic, Antioxidant and Antibacterial Properties, *Mater. Sci. Semicond. Process*, **33**, 81–88 **(2015)**

120. Vanaja M., Paulkumar K., Baburaja M., Rajeshkumar S., Gnanajobitha G., Malarkodi C., Sivakavinesan M. and Annadurai G., Photocatalytic Degradation of Methylene Blue Using Silver Nanoparticles Synthesized from Gymnema Sylvestre and Antimicrobial Assay, *Nov. Res. Sci.*, **2(2)**, 1–8 **(2019)**

121. Vanathi P., Rajiv P. and Sivaraj R., Synthesis and Characterization of Eichhornia-Mediated Copper Oxide Nanoparticles and Assessing Their Antifungal Activity against Plant Pathogens, *Bull. Mater. Sci.*, **39(5)**, 1165–1170 **(2016)**

122. Veisi H., Hemmati S. and Javaheri H., N-Arylation of Indole and Aniline by a Green Synthesized CuO Nanoparticles Mediated by Thymbra Spicata Leaves Extract as a Recyclable and Heterogeneous Nanocatalyst, *Tetrahedron Lett.*, **58(32)**, 3155–3159 **(2017)**

123. Velsankar K., Aswin Kumara R.M., Preethi R., Muthulakshmi V. and Sudhahar S., Green Synthesis of CuO Nanoparticles via Allium Sativum Extract and Its Characterizations on Antimicrobial, Antioxidant and Antilarycidal Activities, *J. Environ. Chem. Eng*., **8(5)**, 104123 **(2020)**

124. Vilchis-Nestor A.R., Sánchez-Mendieta V., Camacho-López M.A., Gómez-Espinosa R.M., Camacho-López M.A. and Arenas-Alatorre J.A., Solventless Synthesis and Optical Properties of Au and Ag Nanoparticles Using *Camellia sinensis* Extract, *Mater. Lett*., **62 (17–18)**, 3103–3105 **(2018)**

125. Vinod T.P. and Jelinek R., Nanoparticles in Cosmetics: Inorganic Nanoparticles in Cosmetics, In Nano-cosmetics: From Ideas to Products, Springer Nature, Cham, Switzerland, 1–363 **(2019)**

126. Weir E., Lawlor A., Whelan A. and Regan F., The Use of Nanoparticles in Anti-Microbial Materials and Their Characterization, *Analyst*, **133(7)**, 835–845 **(2008)**

127. Yew Y.P., Shameli K., Miyake M., Kuwano N., Bt Ahmad Khairudin N.B., Bt Mohamad S.E. and Lee K.X., Green Synthesis of Magnetite (Fe_3O_4) Nanoparticles Using Seaweed (*Kappaphycus alvarezii*) Extract, *Nanoscale Res. Lett.*, **11(1)**, 1–7 **(2016)**

128. Yugandhar P., Vasavi T., Uma P. and Devi M., Bioinspired Green Synthesis of Copper Oxide Nanoparticles from Syzygium Alternifolium (Wt.) Walp: Characterization and Evaluation of Its Synergistic Antimicrobial and Anticancer Activity, *Appl. Nanosci.*, **7**, 417–427 **(2017)**

129. Zaman M.B., Poolla R., Singh P. and Gudipati T., Biogenic Synthesis of CuO Nanoparticles Using *Tamarindus indica* L. and a Study of Their Photocatalytic and Antibacterial Activity, *Environ. Nanotechnology. Monit. Manag*., **14**, 100346 **(2020)**

130. Zhou D., Abdel-Fattah A.I. and Keller A.A., Clay Particles Destabilize Engineered Nanoparticles in Aqueous Environments, *Environ. Sci. Technol*., **46 (14)**, 7520–7526 **(2012)**.

(Received 09th December 2024, accepted 10th February 2025)