



## Green Synthesis of CuNPs and their Significance with Respect to Antibacterial and Anti-cancer Activity

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### ABSTRACT

Nanotechnology offers a fascinating path to copper nanoparticles (CuNPs) for their unique qualities, which can be explored in different sectors. Among all metallic nanoparticles (MNPs), CuNPs secured a central point due to their specific properties, such as being reliable as drug conjugates and drug carriers. Copper is a valuable metal found as a transition element and abundant in its free metallic state in nature. Copper is a super conductor and is present as a trace element in living cells, so it is easily adjusted to proceed in vivo in the form of CuNPs for therapeutic purposes. Copper can be used to synthesize CuNPs from green route in the form of oxides, halides, and sulphates. Due to their specific properties, CuNPs gain a lot of focus from researchers in nanotechnological studies. CuNPs proved their capacities as anti-bacterial, anti-viral, and anti-inflammatory agents in therapeutics. CuNPs were very good anti-cancer agents used in cancer therapy due to their specificity to cleave DNA in cancer cells. CuNPs have excellent capacity for wound healing and have good pesticidal effects, so that CuNPs are a significant key factor in the fields of pharmaceutical industries, agriculture, and medicine specifically. Instead of all this copper is an essential trace element of living cells in the human body, which is very supportive for enzymatic mechanisms and catalytic processes related to the digestive system, important for energy generation. CuNPs were a prime part of the dental cement used in oral and dental treatment mechanisms. CuNPs can be directly applicable in biomedical applications such as tailored surfaces with an anti-microbial effect in wound dressings.

**Keywords:** Anti-cancer activity, Copper nanoparticles, Green Synthesis, Plant extracts, Therapeutics.

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### INTRODUCTION

Nanotechnology is one of the most important beneficial and rapidly developing technologies, which have proven itself as an effective part in therapeutic systems. In order to innovate the latest drug delivery system, nanotechnology is an emerging discipline. Furthermore, the role of nanoparticles is pivotal in pharmaceutical industries, medicinal interests, and other anti-microbial measures<sup>1,2</sup>. MNPs are new factors of importance and utility in agriculture, medicine, and the pharmaceutical industries.

CuNPs have excellent antibacterial effects among all other MNPs and recent antibiotics. Instead of all this, CuNPs hold antifungal, antiviral, and anti-cancer effects have also been investigated<sup>3-5</sup>. In order to synthesize CuNPs from plant-originated resources were nontoxic or of a less toxic nature to normal cells, and better toleration has attained attention from the researchers regarding therapeutics<sup>6,7</sup>. CuNPs attained focus because of their application in wound dressings and biocidal effect<sup>8,9</sup>. In the present

scenario, microorganisms have developed resistance against antibiotics. In this context, the two most significant bacteria, *Staphylococcus aureus* and *E. coli*, have become resistant to conventional antibiotics.

Therefore, CuNPs have been thought to be another option for antibacterial factors due to their antibacterial and antifungal competencies. Due to the biologically active part of MNPs, they can affect the body in small doses compared to heavy metal quantities, they have excellent distribution morphology, a specific size, and a high surface-to-volume ratio for acting efficiently<sup>10-12</sup>. MNPs synthesized from plant resources with a green route contain a broad range of applications of industrial interest and contain drug efficacy with negligible hazards<sup>13-15</sup>.

CuNPs were highly impactful against a wide range of microorganisms due to their specialty of generating high concentrations of reactive oxygen species (ROS) within living bacterial cells to conduct cell lysis (cytolysis). Moreover, all these CuNPs were enriched with anti-cancer, antiviral, antifungal, and wound healing capacities also<sup>16-18</sup>. In the present scenario, CuNPs were framed to transport anti-cancer drugs, nucleic acids, DNA, and RNA to cancerous tissues, which is a milestone in the cancer treatment sector and therapeutics. The MNPs were organic and inorganic compounds with reliable applications in cancer therapy due to their recombinant proteins and antimalignant activity. CuNPs, with their specialty of creating a microenvironment surrounding cancerous tissue, help with the accumulation of specific



tumor points<sup>19,20,21</sup>. MNPs have shown their anti-cancer activity since long back. There is an abundance of natural metals and metal oxides in sufficient quantity in nature, and their processing is cost-effective and the synthesis protocol is affordable. Scientists believed that MNPs, including CuNPs, were more effective particles due to their physical and chemical impact, as well as having a much higher adsorption capacity than other minerals and NPs<sup>22,23,24</sup>. Copper is a pivotal component of living cells in animals and plants, where it initiates so many enzymatic and catalytic processes within the cells. Instead of, CuNPs also exhibit several applications such as electronics, textile coating, plant disease management, and can be suitable for antimicrobials.

Now-a-days, CuNPs can be easily synthesized from various plant seed extracts as base materials<sup>25,26</sup>. CuNPs hold excellent high electrical conductivity and a specific optical effect with biological competency regarding antifungal, antimicrobial, and anti-inflammatory activities<sup>27,28,29</sup>. In the process of CuNPs synthesis, when practiced through polymeric absorbents, CuO and Cu<sub>2</sub>O are deposited in the basic macro-reticular anion exchanger. It is due to radically demolish the porosity of the CuNPs with respect to resource<sup>30,31,32</sup>. Copper is a microelement found in block D of the periodic table, which contains plant development and growth essentials. Definitely, it is a significant cofactor of superoxide, phenol oxidase, and ascorbate oxidase, parts of regulatory proteins, with strong involvement in the electron transport system with the processes of respiration and photosynthesis (the green procedure). CuNPs are also used to build bioactive layers for liquid filtration and air purification, sensors, skin products, lubricant oils, inks, and textile materials<sup>33,34</sup>. CuNPs are synthesized from *Fortunella margarita* leaf extract, and during the process, visual observation of a color change from dark green to bluish green shows the instant and spontaneous formation of CuNPs<sup>35,36</sup>. The CuNPs shows multi-utility as they have been of industrial and medicinal interest. They also have been exhibiting their importance in DNA analysis, cancer therapy, waste water plants, biosensors, being part of solar power plants, along with antibacterial and antifungal efficacy.

CuNPs hold much importance with respect to other nanoparticles, such as platinum, gold, iron oxide, silicon oxide, and nickel, which have not shown bactericidal effects in studies with *E. coli*<sup>37,38,39</sup>. CuNPs have a much larger antibacterial zone of inhibition than silver and are also less expensive. In the last decade, CuNPs have been explored for their capacity to be antibacterial, their toxicity mechanism, oxidation, and copper oxide biocompatibility for medical applications. With their excellent effects of oxidation and chemical composition, CuNPs are used to treat different bacterial strains on the basis of their resistance<sup>40,41,42</sup>. In most of creatures (plants and animals), copper may be found in the forms of Cu<sup>2+</sup> and Cu<sup>+</sup>, naturally at optimum concentrations. Copper is an important co-factor for various enzymes like amino oxidase, cytochrome oxidase, and plastocyanin, and

specific concentrations may led to the formation of structural components of numerous regulatory proteins, which are participants of the photosynthetic electron transport chain, mitochondrial respiration, oxidative stress response, cell wall metabolism, hormone signaling, iron mobilization, and some other vital activities<sup>43,44</sup>.

### Green Synthesis of CuNPs

The process of synthesizing CuNPs is cost-effective and has very few side effects. CuNPs are too much applicable in catalytic optical, electrical, antifungal, and antibacterial processes. CuNPs exhibit a surface-enhanced Raman scattering effect, so that it is more significant than other MNPs<sup>45,46</sup>. When we are going to synthesize CuNPs through physical, thermal, and chemical reduction methods, we find that it is a completely chemical or synthetic path, but these methods are sophisticated, quite cost-taking, and possibly toxic. The synthesis of CuNPs from green routes with plant resources presents an option to solve all these issues. This green synthesis process is very cheap and stable in a natural environment<sup>36,47</sup>. In order to synthesize CuNPs, physical methods (mechanical milling, laser ablation, and sputtering) were prominent, and chemical methods (solid state, liquid state, gas phase, biological methods, and other methods) were practiced in an ordinary way.

In the present scenario, the mechanochemical method for synthesis of nanoparticles requires a precursor for copper, salts for dilution, and as starting material, which are ball milled at an appropriate temperature, resulting in copper oxide (II) nanoparticles covered in salt matrix, further of which were washed by distilled water in an ultrasonic bath<sup>48,49,50</sup>. In the process of green synthesis of CuNPs, the alkaloids and phytochemicals specifically act as capping and stabilizing factors for CuNPs, which may be responsible for the reduction of CuO particles. However, green resources are also made up of tannins, saponins, and phenols. The CuNPs take a time slot of more than six months after the synthesis process to accumulate<sup>51,52,53</sup>.

### Characterization of CuNPs: Techniques and Pathways

In order to characterize the structural and functional properties of CuNPs, researchers prefer scanning electron microscopy (SEM), transmission electron microscopy (TEM), X-ray diffraction (XRD), and Fourier-transform infrared spectroscopy (FTIR). However, optical specification is also explored by these methods<sup>39,54</sup>. The pure phase of CuONPs with monoclinic symmetry is confirmed after green synthesis through X-ray diffraction. Instead of conventional techniques, the results of SEM, TEM, and FTIR were much more accurate regarding the characterization of biosynthesized NPs. In the process of green synthesis of NPs from plant extract, analysis can be done with the help of a UV-visible spectrophotometer via a photodiode array. Having a quartz cell in absorbance mode while holding a tungsten lamp at 200–800 nm of wavelength the experiment can be done with liquid forms of green resources (aqueous solutions)<sup>55,56</sup>.



CuNPs were characterized with the help of different multi-techniques; among all conventional techniques, FTIR analysis is much more accurate and confirms the functional groups of phenolic compounds as well as those of other reducing agents. These reducing agents reduce Cu<sup>2+</sup> to CuNPs<sup>57,58</sup>. During characterization after synthesis, CuNPs first study factor is to analyze its chemical composition and crystalline structure. The analytical tools of scanning electron microscopy (SEM), tunneling electron microscopy (TEM), dynamic light scattering (DLS), particle analyzers, and field emission scanning electron microscopy (FESEM) were the milestones in the field of evaluation of morphology and physiology regarding the size and shape of CuNPs. However, UV-visible spectroscopy (UV-vis), X-ray diffraction (XRD), Fourier transform infrared spectroscopy (FTIR), surface plasmon resonance, and energy dispersive X-ray spectroscopy (EDS) were applicable for the evaluation of the overall chemical and elemental consistency of CuNPs<sup>59,60,61</sup>.

#### **UV-Vis Spectroscopy:**

CuNPs were characterized by UV-Visible spectroscopy from an aqueous solution obtained from the filtration of the original basic reaction solutions in the process of green synthesis from plant extract<sup>55,62</sup>. UV-Visible spectroscopy is simply molecular spectroscopy through UV-Visible light. When electromagnetic waves are also involved to measure plasmon resonance and oscillations of electrons, it becomes a much more effective technique. It is also applied for surface plasmon resonance (SPR), during UV-visible spectroscopy analysis; a beam of light is split into two halves, with one part analyzing the compounds inside the transparent cell. In contrast, the other part examines the reference molecules. Under UV-visible assessment, the optical effect, sensitive concentrations of MNPs, the agglomeration effect, shape, and size can be detected. The SPR range of CuNPs is between 200 and 400 nm. The specific peak appears at a particular wavelength of light because of the electrons present on the surface of MNPs<sup>54,60</sup>.

#### **X-ray diffraction (XRD):**

The X-ray diffraction is suitable to evaluate the crystalline structure of green synthesized NPs. In order to evaluate the major composition of MNPs, the base is taken in powdered form, homogenized, and in a specific quantity<sup>63,64</sup>. XRD is a prime technique to study NPs, as it is a novel method regarding material science and solid state chemistry; it is accurate in finding out a unit cell's size and shape<sup>65</sup>. After X-ray diffraction, an X-ray diffractometer is the ideal tool for identifying perfect CuNPs after MNP preparation. The X-ray diffraction technique is also used to identify the nanoparticles through crystallographic examination under specific radiation. X-ray energy-dispersive spectroscopy is also an exact method to examine the overall chemical consistency of prepared NPs<sup>60</sup>.

#### **Fourier-transform infrared spectroscopy (FTIR):**

FTIR spectroscopy analysis was applied to evaluate the stabilization, reduction, and capping procedures for plant leaf extract during the green synthesis of CuNPs<sup>66</sup>. FTIR analysis is performed to find the bioactive molecules responsible for the reduction reaction of Cu<sup>2+</sup> ions to CuNPs<sup>67</sup>. The green resource or plant extract performs the roles of reducing and capping agents to confirm the presence of functional groups on CuNPs via FTIR analysis<sup>68</sup>.

FTIR spectrophotometers contain long wave-lengths to determine functional groups on NPs. In contact with FTIR light, the bond of atoms or vibrational frequency conducts absorption at a specific resonant frequency. The absorption of energy by inorganic substances is based on their molecular energy, vibrational coupling, and molecular mass. The peaks have prior value in the cases of CuONPs and O–H, C=O, C–N, C–H, and C=C. The rectification on the surface of green synthesized CuNPs is evaluated by FTIR chemicals mixed with plant extract or green resource<sup>60</sup>. FTIR observations also identify the proteins and phenolic group during the formation of CuNPs<sup>67</sup>. The reading of FTIR determines the consumption of bioactive compounds obtained from plant extracts during CuNPs formation<sup>69</sup>.

#### **Scanning Electron Microscope (SEM):**

Scanning electron microscopy (SEM) is applied for the determination of the chemical composition, proper morphology, shape, size, structure, and basic orientation of NPs. Under SEM evaluation, the liquid state of NPs is transformed to a dry power form<sup>70</sup>. This powder of nanomaterials is mounted on an SEM machine, and a fine beam of electrons is thrown on the sample, which results in the release of secondary electrons that will find out the surface specificity. The dispersion of electrons from nanomaterials altered regarding the surface quality, due to which degradation and aggregation of surface material can be analyzed and the morphology of NPs can be detected. The proper pellets should be used to perform SEM, and thin films of sample were mounted on a carbon-coated grid of copper, with a small quantity of sample loaded on the grid for proper evaluation<sup>71,72</sup>.

#### **Transmission electron microscopy (TEM):**

Transmission electron microscopy (TEM) is applied to visualize the nanomaterials by using an electron beam; it is also used to find out the size of NPs. The accurate size distribution of NPs is estimated properly under the TEM machine. By using TEM in the case of CuNPs from *Persea Americana* seed extract, the size of CuNPs ranges between 40-95 nm, and they got rounded in shape. After being characterized through TEM, the picture of CuONPs shows that CuNPs were crystalline in structure with a spherical, rounded shape with a radius of 20 nm<sup>73</sup>.

**Table 1:** Characterization techniques, morphological effects and applications of CuNPs synthesized from plant sources<sup>38</sup>.

Plants	Part	Techniques	Sizes	Shapes	Applications
<i>Cissus arnotiana</i>	Leaf	UV, SEM, TEM, XRD	60-90	spherical	Antibacterial
Guava	Leaf	UV, FTIR, XRD, SEM	15-30	Flakes	Antibacterial
<i>Datura innoxia</i>	Leaf	UV, FTIR, EDX, SEM	90-200	Spherical	Antibacterial
Arevalanata	Leaf	UV, FTIR, TEM SEM	40-100	Spherical	Antimicrobial
<i>Rhus coriaria L.</i>	Fruit	UV, TEM, FTIR, XRD	7-10	spherical	Antifungal
<i>Phaseolus vulgaris</i>	Seed	UV, FTIR, TEM	26.6	spherical	Anti-cancer
<i>Azadirachta indica</i>	Leaf	UV, FTIR, XRD, SEM, TEM	12	spherical	Anti-cancer
Walnut	Shell	UV, FTIR, SEM	15-22	spherical	Anti-cancer
<i>Acalypha indica L.</i>	Leaf	SEM, TEM, XRD, FTIR	66	spherical	Catalytic
Green coffee	Bean	TEM, UV, FTIR, XRD, SEM	5-8	Spherical	Catalytic

### CuNPs and their anomalous effects

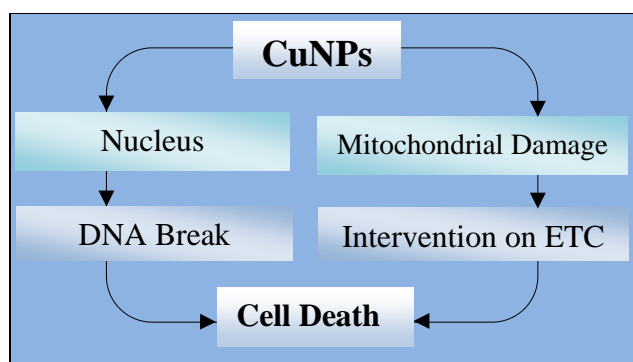
In the present scenario, the observations with gram-negative bacteria (*E. coli* and *P. Gingivalis*) proved that CuNPs hold definite antioxidant and antibacterial activities themselves. CuNPs exhibit antibiotic and obstructive activity against *S. aureus* and *E. coli* when synthesized from ginger extract from the green route<sup>74,75</sup>. In order to focus on the chemical and pharmaceutical specialties of CuNPs, endodontic therapy decreases the amount of bacteria when antimicrobial agents are applied for wound healing. Although the process of disinfection of the overall canal system is tough, due to the complexity of antimicrobial actions, this may lead to the suppression of the endodontic system. CuNPs contain excellent antimicrobial effects against diverse pathogens and resistant strains. During the ex-vivo multispecies biofilm study, observation shows that CuNPs were much more effective than  $\text{Ca(OH)}_2$ <sup>76</sup>. The combined pharmacological complexes made up of CuNPs were reliable antibacterial, antifungal, and antiviral factors. Studies show that CuNPs contain antimicrobial and antiviral properties with appropriate mechanisms of action such as the release of ions, reactive oxygen species (ROS), contact killing, immunostimulants, and apoptosis. In the case of CuNPs, AgNPs, and their derivatives, explore antimicrobial activities and cytotoxicities on the basis of their shape, size, and surface treatment<sup>77,78</sup>. The transition-element-based NPs exhibit excellent antibacterial activity due to their synergistic effect<sup>79,80</sup>. Researchers prefer CuO to synthesize CuNPs due to its low cost, wide abundance, lower toxicity to mammalian cells, higher stability, and positive tendency towards the environment. Moreover, CuNPs exhibit significant antifungal and antibacterial activity and have been found lethal for ticks, mites, and many mosquito species. Regarding antibacterial activity against *E. coli* and *Bacillus subtilis*, the zone of inhibition of CuNPs-based drugs is 70nm to 20 nm<sup>66,81</sup>. When we are going to concentrate on the effects of metal copper and CuNPs on fish organs with different physicochemical standards, it is found to be completely different for different fish organs. In the present

condition, different derivatives of CuNPs and copper itself have specific and effective utilizations; for e.g,  $\text{Cu}_5\text{O}_4$  is a very good pesticide to control the growth of algae and other water weeds in various water bodies. On the other hand, the deactivation of fungal spores from germination is caused by a free cupric ion, which is a most toxic form of copper. However, complexes of copper and CuNPs may or may not be completely biocompatible for fish and other aquatic animals<sup>82,83</sup>. When we are talking about the anomalous effect of green synthesized CuNPs, we found that they are sustainable in nature, cost-effective, pollution-free, biofavorable, low-toxic, and hold different applications in medicine<sup>84</sup>. The green synthesized CuNPs were extremely firm, rounded, and bore a particle size near about 14nm. In the case of Hippophae rhamnoides stem, the antioxidant activity was found to be increased at higher levels. The green synthesized CuNPs from stem extract show multiple functions and a significant antioxidant effect, so that they can be used in place of an obstructing drug for ailments<sup>84,85</sup>. In case of human body part copper is an important trace element and is essential for the development of bones. Copper stimulates the functioning of the lysyl oxidase enzyme, which is the key to the deposition process of calcium and phosphorus in human bones. A copper deficiency may lead to weak bones and fractures. The process of cross-linking of collagen and elastin fibers takes place due to the presence of copper. Instead of collagen, which is significant for bones, cartilage, and muscles<sup>86,87</sup>. There are several forms of copper-based nanomaterials, such as copper ions, copper nanoparticles, copper oxides, and copper alloys that are used in therapeutics. The invasion of copper into the base materials of MNPs gives rise to significant effects on mechanical strength, proper porosity, and cross-linking of scaffolds, as well as degradation. Copper is an element full of virtues related to biological activities regarding cell migration, cell adhesion, osteogenesis, chondrogenesis, angiogenesis, antibacterial activities, and other procedures. CuNPs contain wonderful physicochemical, biological, and optical properties that are applicable to bones, cartilages, and dental issues<sup>88,89</sup>. CuNPs synthesized from CuO also show

synergy towards the carboxyl and amine groups found in a living cell's superficial area. The CuNPs may invade DNA molecules after crossing the cell and cleave the helical structure by cross-linking with nucleic acid. CuNPs exhibit antimicrobial activity through direct interaction with bacterial or fungal cell membranes and obstruct the formation of biofilm, which may lead to strong antimicrobial property<sup>90,91</sup>. CuNPs captured the prime space among so many MNPs with respect to their antimicrobial, anti-inflammatory, and anti-proliferative effects<sup>92</sup>. Basic metal copper and copper oxide nanoparticles exhibit anti-cancerous effects against HeLa cells, MD A-MB-231 (human breast cancer cell lines), Caco-2 (human colon cancer cells), HepG2 cells (hepatic cancer cells), MCF-7 breast cancer cells, and some other kinds of malignant tissues. CuNPs have wound healing capacity with a proper increase in fibrocytes forming collagen for repair; this was seen in living cells *in vivo* studies. CuNPs also explored wound healing capacity on the Cutaneous layer when observed *in vivo* by the synthesis of CuNPs from *Falcaria vulgaris* leaf extract and also showed potent cytotoxicity, antioxidant, antifungal, and antibacterial activities with their specific potential in therapeutics<sup>92,93</sup>.

#### Anti-cancer Activity of CuNPs:

Cancer is characterized by unlimited cell proliferation with different biochemical and enzymatic standards; this is the general manner of cancer cells. Green synthesized CuNPs are utilized to destroy cancer cells by interfering with the cell cycle mechanism. Moreover, plant based metal and metal oxide nanoparticles have the capacity to affect different types of cancer cell lines, such as HeLa, Hep-2, and HCT 116 cell lines, as well as some other animal cancer cells and tissues. There were so many studies that proved that CuNPs have excellent anti-cancer properties and can control cancer cell growth<sup>94,95</sup>.



**Figure 1:** Diagrammatic representation of the hypothetical mechanism for the anticancer activity of copper nanoparticles<sup>98</sup>.

To design an ideal anti-cancer system Nanostructured device have been developed for specific drug transport and chemotherapy. CuNPs have a large specific area and high reactive energy, so they are appropriate anti-cancer agents. CuNPs and CuONPs have potential applications in different fields, such as heterogeneous catalysis, antibacterial, anti-cancer, antioxidant, antifungal, antiviral, imaging agents,

drug delivery agents in biomedicine and pest control measures in agriculture. CuONPs explore different physical effects such as high temperature, superconductivity, electron correlation, and spin dynamics, which can be very useful in cancer therapy<sup>96,97</sup>.

In the treatment of cancer, inhibition of cancer cell proliferation and apoptosis induction are thought to be innovative streams of chemotherapy. High toxicity of anti-cancer agents may also damage the normal cells of the body, so CuNPs were incorporated. CuNPs synthesized from plant resources via the green route hold anti-cancer activity against breast, cervical, colon, epithelial, liver, lung, and skin cancers, as well as other normal tumours<sup>98,99</sup>. CuNPs have the capacity to bind and modify themselves regarding surface area through conjugation with several biomolecules, so that CuNPs can cleave DNA. Because of these qualities, CuNPs have proved themselves as anti-cancer therapeutic agents with high potential<sup>100,101</sup>.

Plants	Parts	Type of Cancer Activity
<i>Centella asiatica</i>	Leaves	Lung cancer
<i>Bauhinia racemosa</i>	Bark	Against a HeLa cancer cell
<i>Catharanthus roseus</i>	Root	Breast cancer
<i>Leguminase</i>	Bark	Anti-human breast cancer cells
<i>Blumealance olaria</i>	Leaves	Anti-cancer
<i>Begonia malabarica</i>	Plant	Colon, lung, and stomach cancer
<i>Arnebia euchroma</i>	Leaves	Anti-tumor
<i>Croton tiglium</i>	Seeds	Anti-tumor S-180 and Ehrlich
<i>Euphorbia hirta</i>	Plant	Anti-MCF cancer cell line
<i>Azadirachta indica</i>	Aerial	Anti-MCF cancer Cell line
<i>Berberis aristate</i>	Bark	Anti-cancer
<i>Berberis lyceum</i>	Root	Anti-cancer
<i>Cedrus deodara</i>	Wood	Anti-cancer

**Table 2:** Different types of medicinal plants used to synthesize CuNPs regarding anti-cancer activity<sup>102</sup>.

#### Applications of CuNPs with respect to therapeutics and industrial issues

NPs are currently in high demand commercially due to their wide range of applications in industries such as electronics, environment, energy, and more particularly in biomedical fields<sup>103,104</sup>. The most significant advantage of synthesis of CuNPs via the green route (various plant extracts) by reduction of Cu ions in aqueous solution is the accuracy of the therapeutic mechanisms. However, CuNPs were eco-friendly to living cells, so they were less toxic for normal cells and human organs. Although CuNPs show some adverse effects along with their therapeutic benefits<sup>105,106</sup>. CuNPs are very effective against a variety of pathogenic microbes, while green synthesized NPs were used to remove pollutants in water (PAHs) from aqueous solutions by a bio-sorbent mechanism<sup>107,108</sup>. Green synthesized, plant extract-derived CuNPs show less toxicity towards normal living cells as compared to cancerous cells, so CuNPs can be

safer for therapeutic and pharmaceutical applications<sup>109,110</sup>. To cause cell lysis in bacterial cells, CuNPs produce reactive oxygen species (ROS) within the bacterial cell. Instead, CuNPs hold anti-cancer, anti-fungal, anti-microbial, and anti-inflammatory properties. Copper and copper nanoparticles-mediated bio-treatment plays a pivotal role in the removal of heavy metals from soil and can also be used in waste water treatment plants<sup>111,112,113</sup>. CuNPs show high oxidation rates when encapsulated with carbon; they may be capable of resisting the oxidation reaction and high temperature. On the other hand, CuNPs show tremendous compatibility with organic compounds, good feasibility for being conductive fillers, electromagnetic wave shielding factors, and good catalyst properties as well. CuNPs used with polymers or in a stabilized state have a high capacity to release ions<sup>114,115</sup>. CuNPs play an important role in treating infections such as prosthesis-induced inflammatory diseases, such as stomatitis and peri-implantitis, which pose challenges in clinical dentistry and other general dental problems. Due to the contact-killing capacity of CuNPs, they can destroy genomic and plasmid DNA. This will make them more important in therapeutics. In the theme of oral infection, CuNPs embedded as replaceable and a static partial denture framework design could be used to resolve denture-induced stomatitis<sup>116,117</sup>. CuNPs have significant applications in agriculture as anti-pest factors and disease management agents. In addition, CuNPs and CuONPs were significantly good in nanoformulations, agrochemicals, and mannered release factors of fertilizers and pesticides. CuNPs were also important for plant protection, promoting plant growth, nanosensors, and antifungal, antibacterial, and other plant-supporting mechanism<sup>118,119</sup>. CuNPs and CuONPs are used in fungicides that can represent direct and indirect exposure of CuNPs into the soil and plant. Microbial response towards exposure to larger CuONPs is anomalous in land and soil management with respect to direct copper concentration in the soil. In comparison to conventional soil treatment, nanoparticle communities were more effective<sup>120,121</sup>.

CuNPs/CuONPs
CuONPs labeling (detection of H1N1 flu virus)
Enzymatic chromogenic approach ELISA
CuO water suspension (ROS anti-cancer activity)
Gram character for different bacterial cells
CuNPs coat reduction in the viability of bacteria
CuNPs toxic for algae and fungi

**Figure 2:** CuNPs in light of technical and biological aspects<sup>98</sup>.

## CONCLUSION

CuNPs are unique and important due to their proven specificities, such as wound healing capacity, pesticide effect, anti-cancer, anti-microbial, anti-inflammatory, and tremendous adjustment capacity with living cells. They have been observed to increase the bioavailability of conventional therapeutic agents when applied as drug adjuvants. Copper is a transition metal with superconductivity and excellent corrosion resistance and is considered essential for human health because it facilitates energy transfer in living cells through enzymatic and catalytic processes. These properties open a new path of hope for anti-cancer drug development, but more research is needed to understand the molecular mechanism of the anti-cancer effects of CuNPs.

## FUTURE ASPECTS

With developmental studies in nanotechnology, scientists are emerging with innovations using CuNPs in the fields of medicine and therapeutics. The anomalous properties of CuNPs, like DNA cleavage capacity during anti-cancer mechanisms and purely antibiotic activity with a specific zone of inhibition, make them very special regarding future perspectives of nanotechnology. So that with an understanding of the measures of specific qualities of CuNPs, more research is required for further innovations in the fields of medicine, agriculture, green chemistry, and therapeutics.

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