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REVIEW

Hydrothermal Synthesis Methods for Copper Nanoparticles: A Mini-Review

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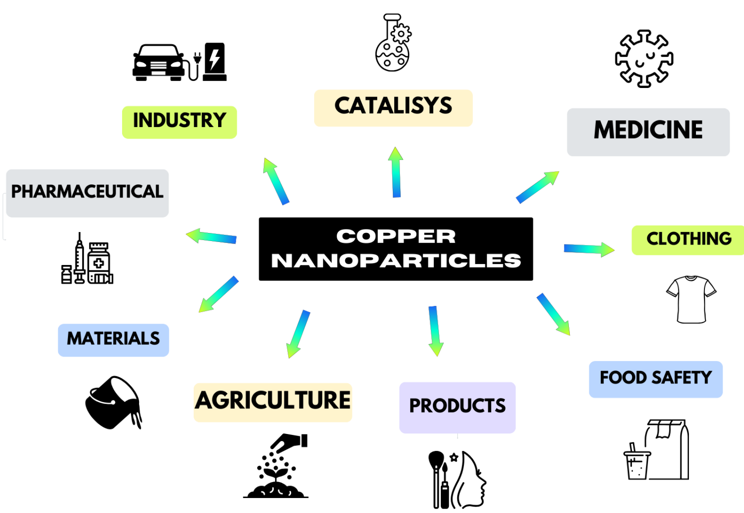

This Mini-Review focus on the production of metallic copper nanoparticles trough hydrothermal synthesis, which represents the most applied method for metallic nanoparticles synthesis. These nanoparticles stand out for their diverse applications in various scientific and technological fields, and among these, copper nanoparticles (CuNPs) are particularly notable for their unique properties, including catalytic, optical and electronic characteristics. These properties are influenced by the size, shape and structure of the particles. Then, the influence of precursor salts, reducing agents, and stabilizers are discussed inside this Mini-Review on the size and shape of CuNPs. Additionally, in recent years, green synthesis methods have gained prominence due to their environmental compatibility and sustainability, but require more robust methods to be implemented. Routes using metal reducing agents such as extracts from plants, flowers, stems are already found in the literature, and some examples are presented in such Mini-Review. Furthermore, we explore the potential applications of CuNPs in areas such as catalysis, antibacterial agents, medical diagnostics, and bioanalytics.

Keywords: CuNP synthesis, nanoparticles, green synthesis, copper nanoparticles

INTRODUCTION

Metallic nanoparticles, characterized by their small size, ranging from 1 to 100 nanometers, were first observed by Michael Faraday when investigating colored glass, who then attributed their colors to the presence of metallic gold in colloidal form.[1] However, it was only in 1908 that the phenomenon of metallic nanoparticles received a more complete formalism, thanks to the work of Gustav Mie, who introduced a theory that describes the scattering of light by spherical particles at the nanoscale. This theory, known

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as the “Mie theory” or “Mie solution,” considers Maxwell’s equations for the absorption and scattering of electromagnetic radiation by spherical particles.[2] Mie’s model assumes that the concentration of nanoparticles in the sample is low and that they are approximately spherical. One of the most relevant optical properties of metallic nanoparticles explained by Mie’s scattering theory is plasmon excitation. This excitation is related to the coherent oscillation of plasma, arising from the movement of free electrons present in the metal structure.[3]

Since then, metallic nanoparticles have had a wide range of applications, as exemplified in Figure 1, in various scientific and technological fields, notably in catalysis[4] detection[5] optoelectronics and biomedicine[6] due to characteristics such as absorption sensitivity, electrical, magnetic and catalytic properties, which are influenced by the size, shape and structure of the particles.[7] Its relevance is associated with unique physicochemical properties, such as high surface-to-volume ratio, high dispersion capacity and improved electrical and thermal conductivities. These characteristics make nanoparticles versatile and efficient materials in various applications.[8]

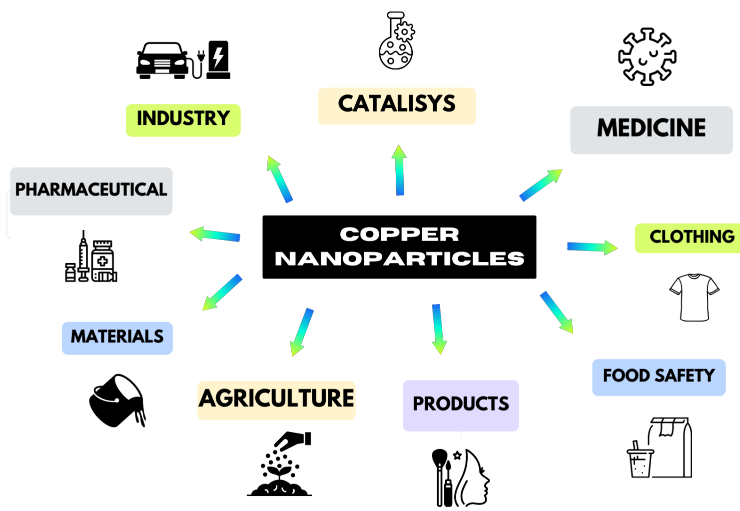

Figure 1. Areas of nanoparticles applications.

For example and in a general way, in the pharmaceutical industry, metallic nanoparticles are used in topical creams to treat infections due to their anti-fungal and antibacterial properties.[9] These properties have also contributed to the food safety industry, where smart packaging can currently be seen to extend the shelf life of a food in the supermarket.[10] In the area of agriculture, metallic nanoparticles are found to combat pests and strengthen plants.[11] Furthermore, heavily applied in the area of bioanalytics, these nanoparticles are found in biosensors for molecules such as glucose, uric acid and dopamine.[12] The use for identifying pathogens such as viruses and bacteria was also evidenced in some studies.[13] In addition, they are applied in catalytic reactions,[14] colorimetric detections for identifying mercury and lead in biological samples[15] and often used as drug delivery for targeted delivery of medications.[16]

Among metallic nanoparticles, copper nanoparticles (CuNPs) stand out for their wide availability, relatively low cost and exceptional properties. They have strong antimicrobial activity, high electrical and thermal conductivity, and are effective in catalyzing several chemical reactions.[17] Due to the high demand for this type of nanoparticle material, methods for synthesizing CuNPs have been widely studied and classified in physical, chemical and biological approaches.[18] Physical methods such as laser evaporation and ion beam deposition are known to produce nanoparticles with high purity and size control. Chemical methods, such as chemical reduction, thermal decomposition and electrodeposition, are the most used due to their simplicity, scalability and ability to tune specific particle characteristics. Recently, biological methods, which use plant extracts, microorganisms or enzymes, have gained prominence as sustainable alternatives, combining synthesis efficiency with lower environmental impact.[19]

As can be seen, the choice of method depends on the type of application desired, with control over the size, morphology and properties of the nanoparticles being crucial factors in maximizing their performance.[20] Based on this information, this Mini-Review brought a compilation of different types of syntheses for metallic CuNPs, discussing the advantages and limitations of each method, as well as their applications already described in the literature.

METHODS OF SYNTHESIS

To synthesize CuNPs, physical, biological and chemical methods are employed, but only chemical methods with a focus on hydrothermal approaches will be addressed in depth in this Mini-review. This is due to the advantages that hydrothermal methods have over other methods mentioned, whether physical, biological or chemical. These advantages are due, for example, to the growth of high-quality crystalline materials due to the combination of high temperatures and pressures, the dissolution of insoluble precursors under normal conditions, the possibility of using a wide range of temperatures and pressures, offering flexibility for different types of syntheses, among others.[21]

When comparing hydrothermal techniques to different techniques existing in the literature, such as the chemical synthesis of metal nanoparticles by the microemulsion process, for example, one can observe the limitations of such methods. The microemulsion technique is efficient, but it is performed in different stages (preparation of the microemulsion, confinement in nanoreactors and chemical reduction of metal ions), which requires a longer reaction time and may cause losses during the process. For the microemulsion stage, the aqueous phase, containing water-soluble metal precursors (such as nitrates or metal chlorides) is mixed with a non-polar organic phase (such as hexane or toluene). Subsequently, this mixture is added to compound surfactants (such as CTAB, Triton X-100 or AOT) that stabilize the interfaces between the aqueous and oily phases. The use of co-surfactants (alcohol or butanol) can also be performed to achieve microemulsion stability. After this process, micrometric-sized droplets act as confined chemical reactors, where homogeneous reactions occur. These droplets, together with a known reducing agent (hydrazine, sodium borohydride, ascorbic acid), provide a reducing environment for metal ions in a small space.[22] As can be seen, this synthesis technique using the microemulsion process requires high surfactant concentration, long steps and is associated with high synthesis costs, which is a disadvantage compared to hydrothermal processes in which they often occur in a single step and do not require surfactants.[23]

This advantage of reactions by hydrothermal routes compared to other types of synthesis can also be observed when the type of synthesis occurs using microwave irradiation methods.[24] This technique can be performed without the use of a stabilizing agent due to the rapid reduction of metal ions. However, as this reaction occurs quickly, there is no control over its size and there is a greater probability of oxide formation, which depending on the application of these nanoparticles is not viable, unlike when using the already consolidated hydrothermal methods, in which the control of the size of the nanoparticles is controlled and the formation of oxides is almost non-existent.[25]

Electrodeposition methods are also widely used for the synthesis of copper nanoparticles, however, like the other methods mentioned, this method has disadvantages compared to hydrothermal methods. One of the reasons is the need for different steps (electrolytes with the metal ions of interest for deposition, substrates that function as cathodes and a controlled electric current sufficient for the reduction of metal ions and the formation of nanoparticles).[26] In other words, hydrothermal methods that occur in a single step are superior to other methods due to their ease of implementation, low use of reagents and morphological control of the efficiently synthesized nanoparticles.

Therefore, it can be stated that hydrothermal methods are relevant in the literature due to their unique characteristics. Although hydrothermal methods have advantages over other methods, some factors can influence the quality of the synthesis of metallic copper nanoparticles.

FACTORS INFLUENCING THE HYDROTHERMAL SYNTHESIS OF COPPER NANOPARTICLES

Hydrothermal synthesis of copper nanoparticles is a widely used technique to produce particles with controlled properties, influenced by several factors that determine the size, morphology and stability of the nanoparticles. The main factors that affect this process include, for example, the concentration of the metal precursor, where the amount of copper ions in the initial solution directly influences the size of the synthesized nanoparticles. The higher the concentration of copper ions in the solution, the greater the agglomeration of these nanoparticles and the formation of larger particles. Whereas, when lower concentrations are used, these nanoparticles tend to be more uniform and smaller.[27]

Furthermore, the combination of solvents and the size of synthesized nanoparticles were evaluated. In this study it can be observed that ethanol is the most effective solvent for carrying out the synthesis of copper nanoparticles. Other solvents, such as dimethyl sulfoxide, acetonitrile, cyclohexanol, water and methanol, showed results with greater polydispersity and less stabilization of the nanoparticles. It is noted that water was considered the least suitable solvent due to the wide size distribution of the CuNPs obtained.[28]

Other substances that directly influence the formation of copper nanoparticles are reducing agents. These reducing agents have the property of reducing the metal in question. Strong reducing agents can accelerate the formation of nanoparticles, thus affecting their size and distribution. Strong reducing agents, such as hydrazine, for example, produce nanoparticles that are smaller than the others.[29] This can be seen in Table I.

Table I. Methods for the synthesis of CuNPs via hydrothermal route

	Copper salt	Reducing agent	Stabilizing agent	Size (nm)	Shape	Ref.
1	Copper sulfosuccinate	Hydrazine	Sodium sulfosuccinate	9	Sphere	30
2	Copper acetate	Sodium hydroxide	Ascorbic acid	7	Shapeless	31
3	Copper nitrate	Hydrazine	Hexadecyltrimethylammonium bromide	6	Sphere	32
4	Copper sulfate	Ascorbic acid		3900	Hexahedron	33
5	Copper sulfate	Ascorbic acid	*PVP	10	Sphere	34
6	Copper sulfate	Hydrazine	Serum albumin bovina	2,7	Sphere	35
7	Copper sulfate	Hydrazine	*PVP	9	Sphere	36
8	Copper chloride	Hydrazine	Pectin	5	Sphere	37
9	Copper sulfate	(3-Mercaptopropyl) trimethoxysilane	Histidine	11	Shapeless	38
10	Copper acetate	Hydrazine	1-Decyne	4-6	Sphere	39

*PVP: Polyvinylpyrrolidone

As previously discussed, studies using hydrazine as a reducing agent for the synthesis of copper nanoparticles (entries 1, 3, 6, 7, 8, and 10) presented nanoparticles with smaller sizes compared to other reducing agents mentioned in Table I. This result is associated with the high reducing power of hydrazine.

In addition, regardless of the metal precursor used (such as copper sulphate, copper acetate, among others), the sizes of the synthesized nanoparticles remained small, reinforcing the determining influence of the reducing agent in the synthesis.

Another relevant aspect is the influence of stabilizing agents in the synthesis process. Studies in entries 4 and 5, both using copper sulphate as a metal precursor and ascorbic acid as a reducing agent, highlighted the difference in nanoparticle size due to the presence or absence of the stabilizing agent. When PVP (polyvinylpyrrolidone) was used as a stabilizer, the nanoparticles formed did not show agglomeration. In contrast, under the same reaction condition but without the use of a stabilizing agent, the nanoparticles presented an estimated size of 3900 nm. This significant increase in size is due to agglomeration resulting from reaction instability, highlighting the importance of using stabilizing agents to avoid uncontrolled particle growth.

The influence of the precursor salt on the morphology of nanoparticles is notable too (see Figure 2), with fibrous nanoparticles growing in size when the salt used is copper acetate, copper chloride, or copper sulfate, especially in the presence of NaOH. The use of ascorbic acid as a reducing agent also significantly impacts the shape and size of the nanoparticles, resulting in variations ranging from rods to triangular, tetrahedral, and spherical forms, depending on the type of copper salt employed.[40]

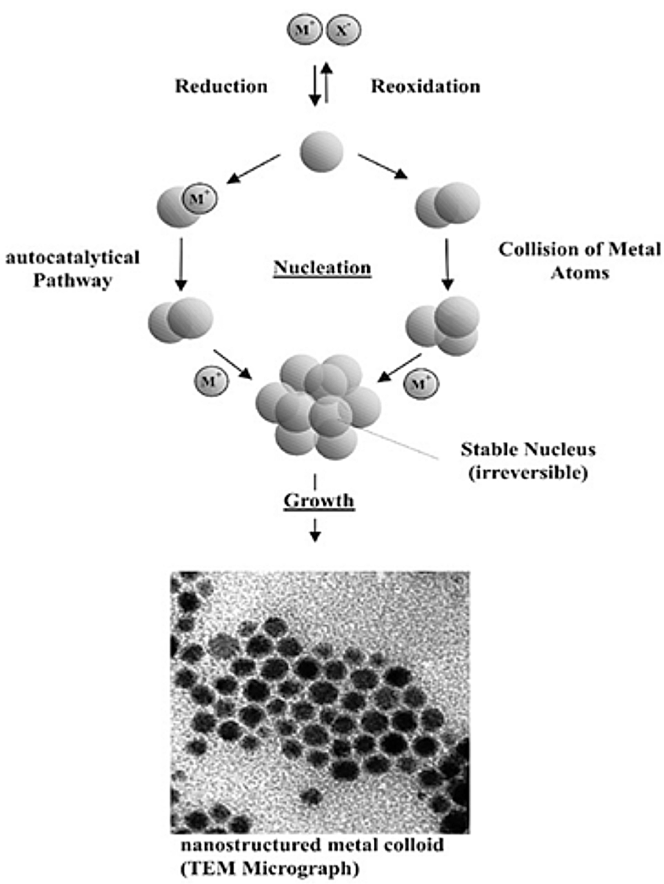

Figure 2. Formation of nanostructured metal colloids by the ‘‘salt reduction’’ method.

From ‘Bönnemann, H.; Richards, R. M. Nanoscopic metal particles – Synthetic methods and potential applications. *Eur. J. Inorg. Chem.* **2001**, *2001* (10), 2455–2480’.[40] Copyright © License No. 5863721378835, [2024] [John Wiley and Sons].

BIOGENICS HIDROTHERMAL SYNTHESIS

Besides the synthesis using stabilizing agents, another important method, and which has gained the attention, is the green synthesis of CuNPs, once it is also recognized for its safety and lower environmental impact, which currently uses natural materials as reducing agents. The transition to more sustainable methods is illustrated by the preference for using plants in the synthesis of metallic nanoparticles due to their availability, cost-effectiveness, and environmentally friendly nature.[41]

There are two main ways in which biogenic synthesis can be carried out by living organisms: intracellular (endogenous) and extracellular (exogenous) synthesis. Endogenous biosynthesis depends on the ability of microorganisms and plant cells to hyperaccumulate metals in their environment. Metals are reduced within the cell cytosol and retained as nanosized particles. Exogenous biosynthesis depends on the secretion of secondary metabolites by plant roots under metal stress.[42] These metabolites chelate metal ions and reduce them into nanosized particles. Although the methods described above have not actually been validated, these studies have produced progress in developing new procedures to synthesize and refine control over nanoparticle morphology and size. The main issue of the study is that the interaction of the protection agent (biomolecules or secondary metabolites) with a certain facet of a metal or metal oxide crystal actually produces nanometric particles. In nature, there are abundant biological resources (plants and microorganisms, among others) that can potentially be used as reducing agents for the synthesis of NPs.[43]

For example, *Laurus nobilis* L. extract has been used as both a reducing and stabilizing agent in the synthesis of these nanoparticles. The synthesis consists of first synthesizing an extract with 10 g of the plant (*Laurus nobilis* L.) at a temperature of 60 ºC and stirring for 10 min. Subsequently, this extract is added to 50 mL of 0.1 mM $CuSO_4$ and heated again for 60 min at 90 °C. This synthesis produced metallic copper nanoparticles with an average size estimated at 10 nm. It can be observed that this type of synthesis can be carried out easily, with little use of instrumentation and is more environmentally friendly, as it does not use reducing agents and toxic stabilizing agents.[44]

Kaur et al.[45] also developed metallic copper nanoparticles using agro-industrial waste (banana peel, potato peel and pea waste), for the synthesis of the reducing extract and subsequent formation of nanoparticles. The first step in the synthesis was drying the residues at high temperature and adding 100 mL of water to synthesize the extract. Subsequently, this extract with high reducing power was added to copper nitrate and heated for 4 h, 400 °C. After this solution is filtrate and the nanoparticles obtained. In this study, the nanoparticles synthesized with potato peels were those with the smallest diameter when compared to other waste that the group in question used, such as banana peel and pea waste.[45]

Artabotrys odoratissimus has also been used as a reducing agent in the synthesis of CuNPs from $CuSO_4$ at 95 °C, resulting in particles with sizes ranging from 109 to 135 nm.[30] The literature mentions the use of *Nerium oleander* and L-ascorbic acid as stabilizing and reducing agents.[42,46] The leaf extract of *Datura metel* has been utilized under ambient conditions for nanoparticle formation, while potato starch has been noted as a stabilizer in the presence of L-ascorbic acid, acting as an antioxidant, and NaOH, as a catalyst.[42] Many syntheses involving plant extract reducing agents and stabilizing agents can be seen in Table II.

Table II. Methods of synthesis by plant extract

	Copper salt	Reducing agent	Stabilizing agent	Size (nm)	Shape	Ref.
1	Copper sulphate	*Picea glauca*	Starch	20	Sphere	47
2	Copper nitrate	*Terminalia arjuna*	-	27	Spheres	48
3	Copper sulphate	*Sapindus mukorossi* + curd	-	25	Shapeless	49
		Sapindus mukorossi + *Tamarindus indica*	-	27		
		Sapindus mukorossi + *Phyllanthus emblica*	-	37		
		Phyllanthus emblica + curd	-	49		

(continues on the next page)

Table II. Methods of synthesis by plant extract (continuation)

	Copper salt	Reducing agent	Stabilizing agent	Size (nm)	Shape	Ref.
4	Copper sulphate	*Citrus medica*	-	10-60	-	50
5	Copper chloride	*Citrus limon* Osbeck	-	60-100	Sphere	51
6	Copper sulphate	*Datura metel*	-	15-20	Sphere	52
7	Copper sulphate	*Artabotrys odoratissimus*	-	135	Sphere	53
8	Copper acetate	*Aloe vera*	-	40	Sphere	54
9	Copper sulphate	*Eucalyptus* sp.	-	38-62	Sphere	55

Table II shows that the majority of syntheses do not use stabilizing agents and are peculiarly small in size. This demonstrates that the nanoparticles synthesized by this type of method are somehow more stable. Furthermore, it can be observed in Table II that all plants used as reducing agents have specific properties such as high antioxidant power, flavonoids, polyphenols and/or terpenes. The use of copper sulphate appears to be a more effective route in terms of synthesized nanoparticle sizes than other copper-containing reagents. All synthesized nanoparticles presented spherical morphology, and only one synthesis using copper bicarbonate presented rod-type morphology.[56]

APPLICATIONS

As previously stated, metallic copper nanoparticles have different applications due to their unique characteristics. One of them is to combat microbial contamination of water, which is a serious risk to public health. In this context, CuNPs have emerged as effective disinfectants for wastewater treatment. When stabilized on substrates such as carbon, polymers, sepiolite and polyurethane foam, they demonstrate remarkable antibacterial efficacy. Furthermore, the high affinity of CuNPs for bacterial active sites is evidenced by their effective use against *Bacillus subtilis*.[57]

Copper nanoparticles are highly valued for their catalytic properties, attributed to their high surface-to-volume ratio, renewable surface area, and variations in microelectrode potentials. Their stabilities are fundamentals to catalytic performance, especially in dye reduction processes, where factors such as number density, shape, composition and particle size play essential roles.[58] Isolated spherical particles demonstrate superior catalytic activity compared to compact hexagonal arrangements, and smaller nanoparticles exhibit greater efficiency due to their high reactivity. To optimize catalytic activity, it is crucial to increase the interaction between the reactants and the catalyst. Although copper oxide nanoparticles (CuONPs) are generally less active than pure CuNPs, their catalytic performance can be tuned through precise control of synthesis conditions.[59] In particular, smaller CuONPs exhibit greater activity due to their high negative electrochemical potentials, making them effective in specific reactions. In the area of catalysis, the choice of a support material is essential, especially when the synthesized nanoparticles have low stability or when the catalyst is used in high-demand applications, which require continuous recycling throughout the reactions. CuNPs can be supported on inert materials, such as zeolites,[60] polymers,[61] kaolinite[62] and agro-industrial waste,[63] expanding their practical applicability and recyclability.[64] For example, Siegnin et al.[62] synthesized CuNPs supported on kaolinite for the reduction of nitroaromatic compounds. The nanoparticles were produced using sodium borohydride as a reducing agent, and the reduction of nitrophenol was carried out in just 20 minutes.[62] This approach highlights the potential of supported CuNPs as efficient, sustainable and recyclable catalysts for industrial and environmental applications.

The impact of CuNPs on fluorescent materials has also been noted, which may lead to either the suppression or the amplification of fluorescence, as well as influencing the aggregation and disaggregation of dyes. These characteristics are put to use in biosensors and biolabeling techniques. In medicine, copper-based compounds are employed in the treatment of tumours and cancer cells. CuNPs have displayed promise as screening tools for hemoglobinopathies, including beta-thalassemia, and their antithrombotic and imaging attributes are under investigation. Furthermore, CuNPs find application in electrical conductivity-related uses.[65]

Deepanjan et al.[66] found that the administration of copper ions through sutures can promote the healing of incisional wounds. Additionally, copper-releasing fibers have the potential to accelerate the repair of surgical and traumatic wounds. Volodina et al.[66] developed an ointment containing CuNPs, which proved effective in the repair of skin wounds, providing a high level of skin regeneration.

Copper-containing substances have been identified as potential agents in cancer therapy, according to several investigations. Empirical evidence has established the efficacy of colloidal CuNPs, an inorganic material, in combating diverse cancer cell lineages. Valodkar et al.[67] reported that CuNPs exhibited cytotoxicity against cell lines of human lung carcinoma (A549), human liver hepatoma (HepG2), Chinese hamster ovary (CHO), human osteosarcoma (Saos), and mouse embryonic fibroblast (3T3L1) in a dose-dependent manner. The investigation demonstrated that CuNPs coated with a non-toxic aqueous latex extract could potentially be utilized directly for *in vivo* administration in cancer therapy. In another study, Harne et al.[68] observed excellent viability of CuNPs against BHK21 cells, even at concentrations of 120 μM. Anticancer studies have demonstrated that CuNPs exhibit significant *in vitro* cytotoxicity values against human colon cancer Caco-2 cells, human liver cancer HepG2 cells, and human breast cancer MCF-7 cells, and can be utilized as a photothermal treatment to eradicate cancer cells.[69]

Cancer cells are susceptible to the cytotoxic effects of copper, which also plays a role in regulating energy metabolism during anticancer treatments. Additionally, copper possesses antiangiogenic, antitumor, antibacterial, antiviral, and enzyme-inhibitory qualities. These properties are not limited to copper alone but can also be observed in copper complexes, potentially offering significant advantages in the field of cancer therapy.[70] Likewise, copper nanoparticles (CuNPs) produced through eco-friendly synthesis using *Nigella sativa* L. seed water extract showed protective effects against cell death induced by methadone in the adrenal phaeochromocytoma (PC12) cell line.[71] The small size of these nanoparticles allows for improved infiltration into tumour tissues and more efficient drug delivery to cancer cells.[72] Moreover, CuNPs exhibit inherent cytotoxicity, causing cancer cell death through oxidative stress pathways.[73] Their ability to produce reactive oxygen species (ROS) reduces side effects via the previously mentioned mechanisms, specifically targeting cancerous cells while leaving normal tissues unharmed.[74] CuNPs can also be modified with targeting ligands, enabling precise recognition and attachment to cancer cells, thus enhancing therapeutic effectiveness.[75] Their exceptional biocompatibility and biodegradability further contribute to decreased systemic toxicity and allow for safe elimination from the body. These combined attributes make CuNPs promising candidates in the development of efficient and targeted cancer treatments.

Just like in medicine, the area of drug delivery was developed to quickly and efficiently deliver drugs using metallic nanoparticles as a carrier. Thus, nanoparticles have been explored as a tool in improving gene and drug delivery due to several reasons, such as their low toxicity, targeted delivery potential, long-term stability, lack of immunogenicity, and relatively low production cost. Additionally, nanoparticles can be functionalized with ligands for specific cellular targeting, such as folic acid for cancer cells, where targeted delivery helps preserve healthy cells.[76] Singh et al.[77] proposed a synthesis of CuNPs using the coprecipitation method for use as a carrier for the drug paclitaxel. The drug was loaded using surface adsorption techniques, mixing an aliquot of the drug with a suspension of CuNPs. In this study, excellent stability, safety, biocompatibility can be verified and dispersibility when using CuNPs as a carrier. Furthermore, the junction between the drug and the nanoparticles improved the issue of biocompatibility with blood cells, which allowed greater interaction between the parts and thus better absorption of the drug paclitaxel quickly and efficiently.[77]

The effectiveness of using nanoparticles in combination with drugs for drug delivery was confirmed too in the study by Mariadoss et al.[78] In this work, CuNPs were synthesized through the reduction of a copper precursor using a plant extract from *Leontodon tuberosus*, subsequently modified with starch and functionalized with folic acid. The study demonstrated that CuNPs have low toxicity for healthy cells, regardless of the dose used, highlighting their safety for biomedical applications. Furthermore, it was proven that functionalization with folic acid, using CuNPs as a carrier, significantly increased the ability of folic acid to penetrate the cell cytoplasm. This mechanism facilitated the targeting of particles to mitochondria, inducing specific reactions that culminated in mitochondrial sequencing processes associated with programmed cell death. These results reinforce the potential of CuNPs as effective and selective carrier for drug release, combining high therapeutic efficiency with lower toxicity, which is essential for advances in targeted treatments.[78]

In agriculture, CuNPs are integrated into conventional fertilizers, plant supplements and pesticides, offering safer and more sustainable alternatives for controlling pests and diseases.[79] In addition to reducing dependence on traditional chemicals, these nanoparticles help minimize environmental impacts, promoting more responsible and efficient agricultural practices.[80] The application of CuNPs to the soil, for example, significantly reduces the incidence of red root rot disease in vineyards.[81] Just as foliar spraying of CuNPs on avocado growth has shown promise in small concentrations. Photosynthetic efficiency was improved and there were no signs of copper toxicity in the avocado plant, in addition to no ultrastructural changes being observed in the organelles.[82]

In the biopolymers sector, CuNPs play an important role in controlling the size of the materials obtained and act as stabilizing agents.[83] These metallic nanoparticles are often coated with long chains, which can be composed of polysaccharides, fundamental elements in the cellular structure of unicellular and multicellular organisms. The combination of metallic CuNPs with polysaccharides increases the environmental compatibility of production processes, making them more sustainable and less harmful to the environment.[84] Biopolymers widely used to stabilize nanoparticles include chitosan,[85] cellulose,[86] starch,[87] alginates[88] and gelatins,[84] which, in addition to being biodegradable, contribute to the efficiency and safety of the materials produced. This integration between CuNPs and biopolymers stands out as an innovative and ecologically responsible approach for the development of advanced materials with varied applications.

In the food packaging sector, CuNPs also play an important role. Incorporated into packaging materials, they demonstrate high efficiency in inhibiting the growth of pathogenic bacteria, such as *Staphylococcus aureus*, *Bacillus subtilis*, *Shigella dysenteriae*, *Klebsiella pneumoniae*, *Salmonella typhi* and *Escherichia coli*, as well as containing phytopathogenic fungi. This application not only increases food safety, but also extends the shelf life of food, representing an innovative and sustainable solution to meet the growing demands for quality and protection in the food sector.[89]

The antibacterial and antifungal properties of CuNPs go beyond application in food packaging, covering a wide range of possibilities.[90] A study carried out by Bogdanović et al.[91] demonstrated the potential of these nanoparticles as highly effective antimicrobial agents against various microorganisms. For this, a chemical reduction method was used, in which copper salts were treated with sodium borohydride in the presence of ascorbic acid, resulting in nanoparticles that were subsequently evaluated for their antimicrobial properties. In the study, CuNPs synthesized at a concentration of 32 mg kg^{-1} were shown to be able to significantly reduce the growth of *Candida albicans*, *Staphylococcus aureus* and *Escherichia coli* in just two hours. This efficiency is related to the direct interaction of nanoparticles with the cell wall of microorganisms, promoting the release of Cu^{2+} ions. These ions are attracted to the plasma membrane and are absorbed by cells, where they trigger oxidative reactions that lead to the degradation of essential cellular components and, consequently, cell death. The study highlighted that factors such as the size, shape and specific surface area of CuNPs play a crucial role in determining their antimicrobial efficacy. Furthermore, the high toxicity presented even at very low concentrations highlights the potential of these nanoparticles for large-scale industrial applications as antibacterial agents. Another important point is that adjustments in the physicochemical properties of CuNPs can intensify their antimicrobial activity, making them even more effective in diverse applications.[91]

CONCLUSIONS AND FUTURE PERSPECTIVES

The importance of CuNPs in the current global context is demonstrated. With their unique characteristics, such as high reactivity, antimicrobial properties and functional versatility, these nanoparticles have been widely used in several areas, including medicine, agriculture, catalysis, drug delivery, among others. Their ability to offer innovative and sustainable solutions highlights the crucial role of CuNPs in the development of advanced technologies, contributing to addressing global challenges and promoting significant advances in strategic sectors.

In fact, metallic CuNPs play a fundamental role in several areas due to their unique properties, such as high reactivity and versatility. The synthesis of these nanoparticles can be carried out using different methods, with hydrothermal processes being preferred when seeking greater robustness and stability, while biosynthesis, despite presenting limitations in terms of reproducibility, stands out for the use of reducing agents of natural origin, such as polyphenols. and terpenes. The choice of synthesis method and reducing agent has a direct impact on the final characteristics of CuNPs, including shape, size and presence of oxides. Controlling parameters such as pH during synthesis is also essential to optimize the quality and functionality of nanoparticles.

In the future, the challenge will be to improve synthesis methods to achieve greater control over the size, shape and stability of CuNPs, especially in biosynthesis, where the structural variability of plant materials still represents a limitation. Exploring new natural reducing agents and environmentally friendly solvents can make production more sustainable and affordable. Furthermore, further research into the behavior of CuNPs under different environmental conditions, such as pH and temperature, will be essential to expand their practical applications.

Finally, CuNPs are expected to continue to play an essential role in emerging areas, such as nanotechnology applied to health and agriculture, driving the development of advanced materials and contributing to the construction of innovative and ecologically responsible solutions to global challenges.

Conflicts of interest

The authors declare no conflicts of interest.

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