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Development of copper nanoparticles and their prospective uses as antioxidants, antimicrobials, and anti-cancer agents in the pharmaceutical sector

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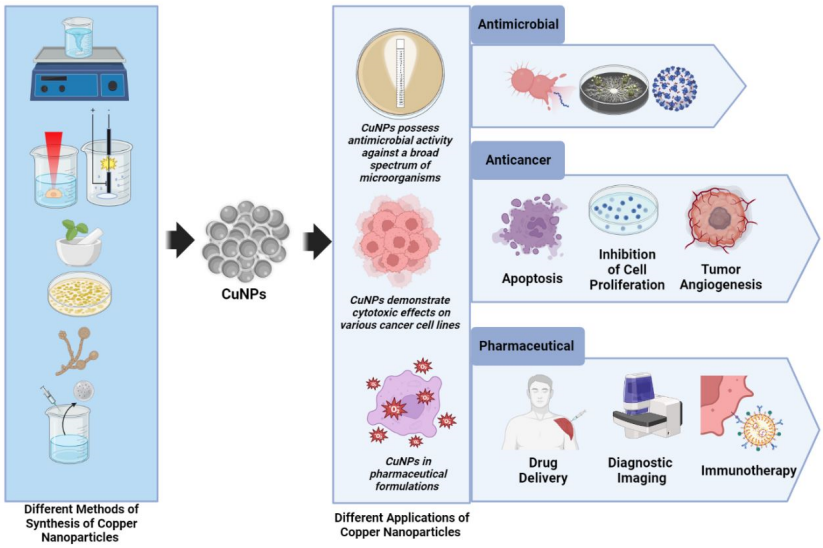
Graphical Abstract



Abstract

In this study, we review the synthesis of copper nanoparticles (CuNPs) and their future uses as antioxidants, antimicrobials, and anti-cancer agents in the pharmaceutical sector. CuNPs could be created through various methods, including chemical reduction, green synthesis, physical methods, electrochemical deposition, and the microemulsion method. These methods make it possible to precisely create nanoparticles with the necessary shapes, sizes, and surface properties, affecting how well they perform biologically. CuNPs have strong antioxidant properties because they can scavenge reactive oxygen species and prevent oxidative damage. In addition to their antioxidant properties, CuNPs show antibacterial activity against many microbes, including bacteria, fungi, and viruses. The potential of CuNPs as an anti-cancer agent has also been extensively investigated. These nanoparticles have toxic effects on a variety of cancer cell lines by inducing apoptosis, inhibiting cell proliferation, and preventing tumor angiogenesis. Because of their specific toxicity towards cancer cells while protecting normal cells, they provide the fascinating potential for tailored therapy to overcome multidrug resistance. CuNPs have also been studied in relation to their usage in medications. They may be utilized to improve drug delivery systems, wound healing, diagnostic imaging, immunotherapy, and anti-inflammatory and antioxidant effects. They can also enhance pharmaceutical stability and bioavailability and provide controlled release. More research is needed to ensure their safety, enhance their synthesis processes, and explore their full potential in therapeutic situations.

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Keywords:

Copper nanoparticles, antioxidant, antimicrobial, anti-cancer agents, pharmaceuticals, reactive oxygen species

Purpose, Rationale, and Limitations

Purpose: CuNPs are attractive prospects for a variety of medical applications, including the treatment of cancer, oxidative stress, and microbial infections. In this study, we review the synthesis of copper nanoparticles (CuNPs) and their prospective uses as antioxidants, antimicrobials, and anti-cancer agents in the pharmaceutical sector.

Rationale: CuNPs were created with these specific uses in mind due to their unique characteristics. Because it scavenges free radicals and inhibits oxidation, copper, a transition metal, has strong antioxidant properties. The antibacterial qualities of CuNPs also allow them to hinder a variety of microbes, such as bacteria, fungi, and viruses. Additionally, research indicates that CuNPs selectively induce cytotoxicity in cancer cells while sparing healthy cells.

Limitations: Despite potential advantages, there are several issues that need to be resolved to use CuNPs in medicine. Concerns about toxicity, stability and reactivity, targeting and distribution, regulatory approval, and cost-effectiveness are a few of the major drawbacks. Realizing the full potential of CuNPs as antioxidants, antimicrobials, and anti-cancer medicines will require the pharmaceutical industry to address these limitations through more research and technical developments.

Summary of relevant literature

Due to its multiple potential uses in a variety of domains, including antibacterial, antioxidant, and anti-cancer effects, fungus-mediated copper nanoparticle (CuNP) manufacturing has attracted considerable attention in recent years. As natural reducing and capping agents, several fungus species are used to create these nanoparticles, producing very stable and biocompatible CuNPs [1], [2]. The antibacterial properties of CuNPs have been extensively studied and confirmed. It has been established that copper has antibacterial activity against a variety of pathogens, including bacteria, viruses, and fungi [3], [4]. CuNPs' tiny size and large surface area facilitate their contact with microbial cells, damage their membranes, and interfere with intracellular functions, which increases their antibacterial efficacy [5]. Recent research has shown that fungus-mediated CuNPs are efficient in preventing the spread of drug-resistant bacteria, making them suitable options for addressing the worldwide challenge posed by antimicrobial resistance [6], [7]. Fungus-mediated CuNPs have not only strong antibacterial activities but also powerful antioxidant activity. Numerous chronic illnesses have been linked to oxidative stress, brought on by an imbalance between the generation of reactive oxygen species (ROS) and cellular antioxidant defense systems. CuNPs' antioxidant ability can reduce oxidative stress by scavenging ROS and defending cells from damage [8], [9]. CuNPs produced utilizing fungus have recently been shown to have considerable antioxidant activity, making them potential candidates for the creation of new medicinal treatments [10].

Additionally, the potential of fungus-mediated CuNPs as anti-cancer drugs has attracted enormous interest in cancer research. Uncontrolled cell growth and division characterize the complicated illness known as cancer. The creation of efficient anti-cancer treatments with few side effects is still a difficult task. However, cytotoxic properties of CuNPs against several cancer cell lines have been emphasized by recent investigations. Through a variety of processes, including the production of ROS, the induction of apoptosis, and the disruption of cellular signaling pathways, these nanoparticles kill cells [11], [12]. CuNPs produced utilizing fungus have special qualities that hold considerable promise for effective and targeted cancer treatment [12], [13]. A potential method for creating stable, biocompatible CuNPs is the fungus-mediated synthesis of CuNPs. These nanoparticles are appealing candidates for a variety of uses in the sectors of medicine and biotechnology due to their antibacterial, antioxidant, and anti-cancer capabilities. The discovery of new therapeutic treatments can be facilitated by comprehending the methods of synthesis and investigating the underlying mechanisms of their bioactivities.

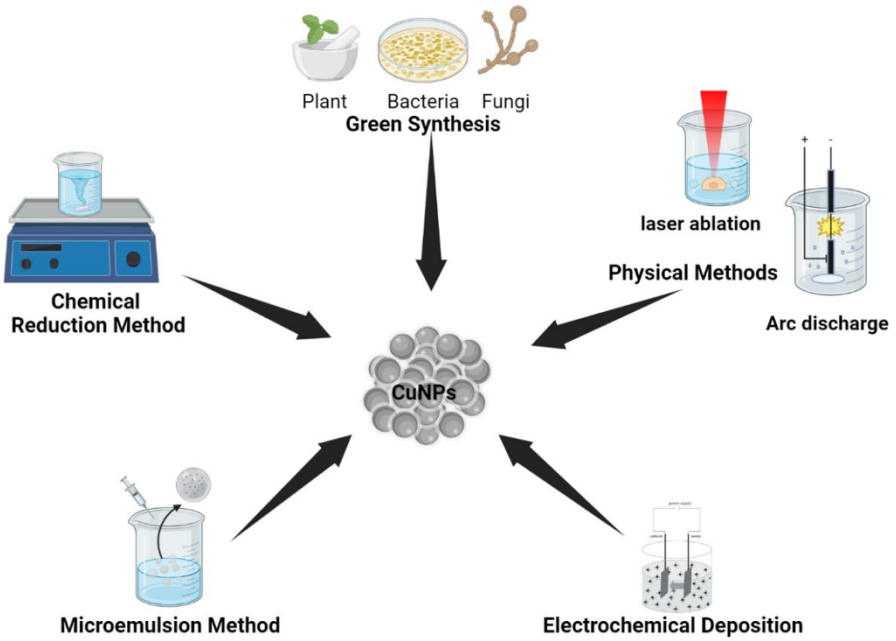

Figure 1: Different Methods of Copper Nanoparticle Synthesis

Methods of copper nanoparticle synthesis:

CuNPs may be created using a variety of techniques. The preferred nanoparticle size, shape, surface characteristics, and application all play a role in the technique selection (Fig 1).

Chemical Reduction Method:

This process includes utilizing a reducing agent in the presence of a stabilizing agent to reduce a copper precursor, such as copper salts (copper chloride or copper sulfate). Citric acid, hydrazine, and sodium borohydride are typical reducing agents. The stabilizing agent regulates the size and dispersity of the nanoparticles as well as prevents agglomeration.

Green Synthesis:

Green synthesis techniques use natural sources as reducing and stabilizing agents, such as plant extracts, microbes, or biomolecules. These techniques for synthesizing nanoparticles are sustainable and kind to the environment. Plant extracts high in polyphenols, flavonoids, or proteins are frequently utilized to reduce copper ions and create CuNPs.

Physical Methods:

Physical procedures are also used to create CuNPs. These techniques include thermal breakdown, arc discharge, and laser ablation. A high-energy laser beam is focused on a copper target that is submerged in a liquid media in laser ablation, which produces nanoparticles. To create nanoparticles, an electric arc with a high current is passed through copper electrodes submerged in a liquid. High temperatures are used to thermally decompose copper compounds, which produces nanoparticles as a by-product.

Electrochemical Deposition:

An electric current is used in the controlled synthesis process of electrochemical deposition to decrease copper ions onto an electrode surface, producing CuNPs. Through careful control of variables, including current density, electrode potential, and deposition duration, this technique enables fine control over nanoparticle size and shape.

Microemulsion Method:

In microemulsion, copper salts are dissolved with surfactants and co-surfactants in water-immiscible solvents. In the confined water droplets of the stable microemulsion system created by the combination, copper ions are reduced, forming CuNPs. The choice of surfactants and co-surfactants greatly influences the stability and size of the nanoparticles.

These are some of the ways that are frequently used to create CuNPs. Each method has its advantages and limitations, and the selection

depends on the desired properties and intended applications of the nanoparticles.

Fungus-mediated CuNPs synthesis:

A sustainable and environmentally friendly method for making CuNPs (CuNPs) with the different synthesis methods and their applications. The steps in the procedure of copper nanoparticle synthesis from fungal cultures are as follows:

Fungal Strain Selection:

It is decided on an appropriate fungus strain that can reduce copper ions and produce nanoparticles. Various fungi, including *Aspergillus, Fusarium, Penicillium*, and *Trichoderma*, have been employed in producing CuNPs.

Fungal Growth:

The chosen fungus strain is cultivated in an appropriate growth medium under ideal temperature, pH, and nutrient availability conditions. When growth is in its logarithmic phase, biomass is collected.

Preparation of Fungal Extract:

After being extracted from the growing medium, the fungal biomass is washed to eliminate any remaining components. After that, it is processed to create a fungal extract using methods like grinding, sonication, or enzymatic treatment. The extract includes bioactive substances, including proteins, enzymes, and metabolites, which are essential for stabilizing and reducing CuNPs.

Synthesis of CuNPs:

An appropriate concentration of the fungal extract is combined with the copper precursor solution (such as copper sulfate). Because of the bioactive properties of the extract, copper ions are reduced into metallic CuNPs. Usually, the reaction is carried out at room temperature while being watched for color changes that signify the synthesis of CuNPs. The utilization of non-toxic and freely accessible fungal biomass, gentle reaction conditions, and the possibility for mass manufacturing are only a few benefits of the fungus-mediated synthesis of CuNPs. The bioactive substances in the fungal extract help to stabilize and regulate the properties of the nanoparticles. Additionally, compared to conventional methods for synthesizing nanoparticles, our approach requires less dangerous chemicals and energy-intensive procedures (Table 1).

Antimicrobial Potential of Fungus-mediated CuNPs:

Developing CuNPs by fungus-mediated synthesis has shown promise for producing antimicrobials with broad-spectrum action. CuNPs' antibacterial potential has been thoroughly studied, and current research has shown that they are quite effective against various microbes when produced by fungi. Copper is known to have inherent antibacterial capabilities. However, copper nanoparticles, which have a much larger surface area and distinct physicochemical features, show improved activity [35], [36]. CuNPs with strong antibacterial properties may be produced using a scalable and ecologically friendly method called fungus-mediated synthesis. It has been shown that employing fungus like the Aspergillus species to produce CuNPs through extracellular biosynthesis is a successful way to produce nanoparticles [37]. CuNPs' small size and large surface area allow for intimate contact with microbes, which causes cell membranes to rupture and therefore inhibits microbial development [38].

Additionally, the antibacterial effectiveness of fungus-mediated CuNPs against bacteria, viruses, and fungi has been studied. When CuNPs interact with microbial cells, copper ions are released. These ions can pass through the cell membrane, produce oxidative stress, and damage DNA, all of which can result in the death of the microbial cells [39]. CuNPs produced by fungi have further demonstrated encouraging antiviral efficacy by preventing virus multiplication and adhesion to host cells [36]. CuNPs produced by fungi may be used as antibacterial agents, which have vast applications in agriculture, medicine, and environmental cleanup. It is crucial to be able to fight off germs that are resistant to common antibiotics and lessen reliance on them.

More study is required to improve synthesis procedures, clarify the processes behind CuNPs' antibacterial action, and assess their long-term effects. Their improved antibacterial activity is a result of the special physicochemical characteristics of CuNPs in combination with the reducing and capping abilities of fungus.

Table 1: Copper Nanoparticles: Methods of Synthesis and Their Applications

Types of Copper Nanoparticles	Sizes	Methods of Synthesis	Synthesis From	Applications	References
Copper oxide nanoparticles	5-100 nm	Green synthesis using plant extracts	Plant extracts containing copper ions	Antimicrobial coatings, catalysis, electronics	[14], [15]
Copper sulfide nanoparticles	5-50 nm	Green synthesis using natural sources	Copper salts and sulfur-containing compounds from natural sources	Evaluation of in vivo therapeutic effective-ness, antibacterial activity, Photothermal therapy, imaging, energy storage	[16]–[18]
Copper nanowires	Diameter: 50-500 nm, Length: Few μmeters	Bio fabrication method using bacteria	Copper-reducing bacteria	Transparent conductive films, flexible electronics	[19]
Copper nanoparticles	10-100 nm	Green synthesis using algae	Algal biomass or extracts	Anti-cancer therapy, antibacterial agents, environmental remediation	[20], [21]
Copper nanoparticles	5-50 nm	Green synthesis using fungi	Fungal cultures	Antimicrobial agents, antioxidant activity, anti-cancer therapy	[22], [23]
Copper nanoparticles	10-100 nm	Green synthesis using biomolecules	Biomolecules (proteins, peptides)	Biomedical imaging, drug delivery, biosensing	[24]
Copper nanoparticles	5-50 nm	Green synthesis using fruit extracts	Fruit extracts rich in copper ions	Antioxidant applications, food packaging, functional materials, adsorption of triphenylmethane dye, and antibacterial assay	[25]–[27]
Copper nanoparticles	10-100 nm	Green synthesis using microorganisms	Bacteria, yeast	Water purification, antimicrobial agents, nanocomposites	[28]
Copper nanoparticles	5-50 nm	Green synthesis using leaf extracts	Leaf extracts containing copper ions	Catalysis, sensors, environmental remediation	[15], [29], [30]
Copper nanoparticles	Varies	Green synthesis using waste materials	Copper-containing waste materials	Sustainable synthesis, waste utilization, catalysis	[31], [32]
Copper nanoparticles	10-100 nm	Green synthesis using marine sources	Marine algae, seaweed extracts	Biomedical applications, environmental remediation, drug delivery	[33], [34]

Continued research in this area holds a lot of potential for the creation of powerful substitutes for traditional antibacterial agents.

Antioxidant properties of Fungus-mediated CuNPs:

CuNPs have strong antioxidant potential, and fungus-mediated production is a viable way to take advantage of their positive benefits. Due to their unique physicochemical characteristics, they are effective scavengers of free radicals and ROS, resulting in antioxidant activity [40], [41]. Fungus-mediated synthesis offers a renewable and sustainable way of creating CuNPs with increased antioxidant potential. Utilizing a variety of assays, including DPPH radical scavenging, reducing power, and total antioxidant capacity tests, the antioxidant capability of fungus-mediated CuNPs has been assessed. The capacity of the CuNPs to neutralize free radicals was demonstrated by their considerable DPPH radical scavenging activity [42], [43]. Similarly, other researchers described the use of fungus in manufacturing CuNPs, showing off their potent reducing power and overall antioxidant potential [44]. Due to their capacity to donate electrons and scavenge free radicals, CuNPs have antioxidant properties that protect cells from oxidative damage and preserve cellular redox equilibrium [45]. CuNPs are potent antioxidants due to their tiny size and wide surface area, which improve their interactions with ROS and free radicals. CuNPs produced by fungi have antioxidant qualities that are used in medicine, food preservation, and cosmetics. Numerous disorders are linked to oxidative stress, and using CuNPs as antioxidants may help treat these conditions. Additionally, by suppressing lipid peroxidation and halting oxidative degradation, CuNPs can be used as natural antioxidants to increase the shelf life of food goods [46].

Anti-cancer properties of fungus-mediated CuNPs:

CuNPs have unique physicochemical characteristics that enable them to target cancer cells and inhibit tumor development [12], [47]. Their tiny size and high surface-to-volume ratio make it easy for cancer cells to pick them up and interact with them. Additionally, it has been demonstrated that CuNPs have intrinsic cytotoxic effects on several cancer cell types. Utilizing both in vitro and in vivo models, the anti-cancer potential of CuNPs has also been studied, with aspects such as cell viability, apoptosis induction, and tumor growth suppression being evaluated [48], [49]. For instance, CuNPs created by Gupta et al. and tested for their cytotoxic effects on breast cancer cells resulted in decreased cell viability and the activation of apoptosis [50] [5].

Similarly, Al-zharani et al. showed that CuNPs had an anti-cancer impact on human breast and colon cancers [51]. CuNPs' anti-cancer effects are caused by several processes, including activating apoptotic pathways, developing oxidative stress, and preventing angiogenesis [52], [53]. CuNPs can produce ROS inside cancer cells, resulting in oxidative stress and cell death. Additionally, it has been demonstrated that CuNPs can alter apoptotic pathways, causing cancer cells to undergo apoptosis while sparing healthy cells. They also have anti-angiogenic qualities, essential for preventing metastasis and tumor development. CuNPs have the potential to be effective anti-cancer treatments due to their focused drug delivery, low toxicity to healthy cells, and improved therapeutic effectiveness. Additionally, the surface functionalization of CuNPs enables the conjugation of targeting ligands and anti-cancer medications, enabling precise tumor targeting and synergistic effects. Silica-based organic-inorganic hybrid nanoparticles and nanoconjugates for enhanced anti-cancer drug delivery are also possible [54].

Discussion

Role and Application of copper nanoparticles in the pharmaceutical industry

Because of their distinctive characteristics and possible uses, CuNPs have attracted much attention in the pharmaceutical industry (Figure 2). The following are some of the functions and benefits of copper nanoparticles in the pharmaceutical sector:

Drug Delivery Systems:

CuNPs can be used as carriers for drug delivery systems. They have a large surface area, which allows for high drug-loading capacity. CuNPs can encapsulate drugs and release them in a controlled manner, improving the efficiency and targeted delivery of therapeutic agents.

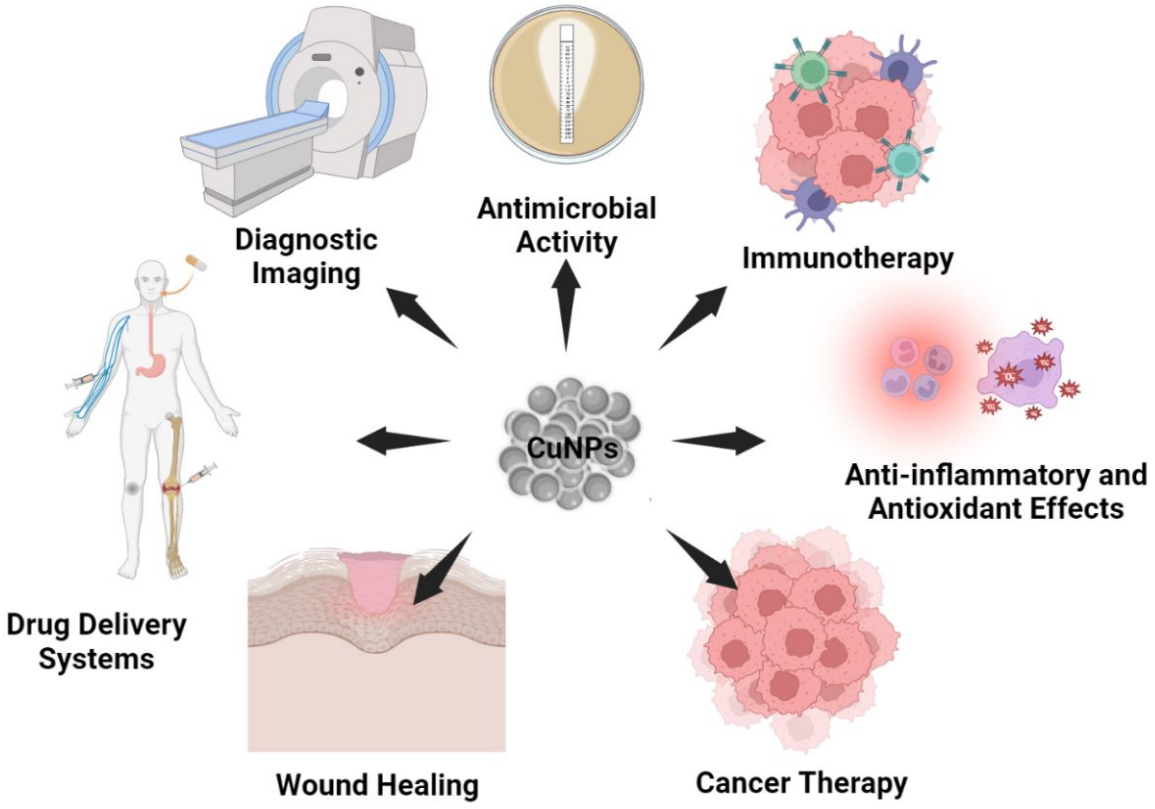

Figure 2: Different Applications of Copper Nanoparticles

Additionally, their small size facilitates cellular uptake and enhances bioavailability.

Antimicrobial Activity:

Antibacterial solid effects against bacteria, viruses, and fungi are present in CuNPs. They can damage pathogens' cell membranes, which renders them inactive or kills them. CuNPs have demonstrated efficacy against drug-resistant bacteria, making them a possible alternative to conventional antibiotics for treating infections.

Wound Healing:

The ability of CuNPs to heal wounds has been studied. They can encourage angiogenesis, which is the growth of new blood vessels, collagen production, and cell proliferation, all of which are vital steps in the healing process. CuNPs can be added to creams or dressings to speed up wound healing and stop infections.

Anti-inflammatory and Antioxidant Effects:

CuNPs have been shown to have antioxidant and anti-inflammatory properties. ROS and inflammatory cytokines, which are linked to several disorders, can be produced less. The development of treatments for inflammatory diseases like arthritis or inflammatory bowel disease may involve CuNPs.

Cancer Therapy:

CuNPs have shown promise as a cancer treatment. Through several processes, such as oxidative stress, DNA damage, and a reduction in cell growth, they can cause cancer cells to die. For improved therapeutic benefits, CuNPs can be utilized alone or with other anti-cancer drugs.

Diagnostic Imaging:

Applications of CuNPs in diagnostic imaging have been investigated. They can be functionalized with imaging agents like fluorescent dyes or contrast agents to improve imaging modalities like magnetic resonance imaging, computed tomography, or fluorescence imaging. CuNPs increase the sensitivity and specificity of imaging, allowing for more accurate disease monitoring and diagnosis.

Immunotherapy:

The potential of CuNPs for immunotherapy has been investigated. They can influence the immune system by improving antigen presentation, boosting immunological responses, and activating immune cells. To increase the effectiveness of immunotherapeutic drugs in treating illnesses like cancer and autoimmune disorders, CuNPs may be employed in conjunction with them.

In vivo fate and possible side effects of copper nanoparticles

When assessing them for biomedical applications, it is critical to consider CuNPs' in vivo fate and potential side effects. The following is a list of their in vivo fate and possible drawbacks.

Distribution:

After being administered, CuNPs can spread throughout the body through various methods, including inhalation, oral consumption, injection, and topical application. Particle size, surface coating, method of administration, and interactions with biological systems all impact how widely they are distributed [55].

Biodistribution:

Various tissues or organs may get contaminated with CuNPs. Studies have revealed buildup in the gastrointestinal system, kidneys, lungs, liver, and spleen [56]. The characteristics of the nanoparticles and the clearance processes determine the amount and duration of bio-distribution.

Clearance:

There are several mechanisms for CuNPs to leave the body, including hepatic clearance, renal excretion, and phagocytic cell uptake. Nanoparticle size, surface characteristics, and the presence of surface coatings all affect the clearance rate and its underlying process [57].

Metabolism and Transformation:

CuNPs can go through metabolic processes in the body. For instance, the copper ions released from nanoparticles can be metabolized and participate in the pathways controlling copper homeostasis and metabolism [58].

Possible Side Effects of Copper Nanoparticles:

Understanding the characterization and surface modification of CuONPs, routes of exposure, and mechanisms or pathways involved in toxicity are necessary to clarify the toxicity of CuONPs.

Characterization:

The particles' size, shape, and charge are all factors in the characterization of CuO nanoparticles (NPs). There is a relationship between the size of the NPs and the surface-to-volume ratio; the ratio will be higher when the size is smaller and vice versa. A particle's size does not impact its ability to penetrate or respond. However, it has been hypothesized that NPs larger than 100 nm can enter cells by piercing the cell membrane, whereas NPs smaller than 40 nm can enter the blood and reach the cell nucleus. Cellular uptake, interaction processes, and intercellular stability are the mechanisms that are affected by NP size. The little NPs exhibit greater toxicity and are more likely to be internalized by cells due to their abbreviated size compared to large-size NPs [59]–[62].

The synthesis process:

Physical, chemical, and biological processes are the three synthetic techniques that impact the characteristics and properties of CuONPs. The physical and chemical generated CuONPs are crystalline and have an average size of 45 nm, sufficient to pierce bacterial cell membranes and result in cell disturbances at various levels. CuONPs created using the chemical vapor deposition and precipitation process had 33 nm-wide monoclinic rod-like features. For CuONPs, biological approaches such as those involving bacteria, fungi, algae, and plants have also been employed [63]–[67]. The synthesized NPs come in various sizes and forms and exhibit potent photocatalytic and antibacterial properties. The synthesized NPs have a high potential for usage in pharmaceutical, biotechnological, environmental, industrial, and therapeutic applications.

Doses/Concentrations:

NP dosage is a major element influencing toxicity. The NP dosage considers both the actual quantity of NPs that are absorbed by a single cell and the initial concentration of NPs in the cells. For in-vitro and in-vivo experimental models, it is crucial to define genuine and pertinent dosage regimes for risk evaluation in public health [68], [69]. By all

means, nanotechnologists should study the toxicity of NPs based on actual dosages rather than inflated ones to elicit a biological reaction. NP dosage is regarded as a crucial phenomenon in nanomedicines [70]. When exposed to CuONPs concentration in a dose-dependent manner (10, 25, 50 µg/ml), the human pulmonary epithelial cells (A549) showed depletion of glutathione and stimulation of lipid peroxidation, catalase and superoxide dismutase. The MIT experiment showed CuO NPs reduced cell viability to 75, 66, and 48%, respectively [71]–[73].

Reactive Oxygen Species:

CuNPs may be hazardous to living organisms. CuNPs releasing copper ions may also cause ROS and oxidative stress. This may lead to cellular malfunction, inflammation, and cell damage (Fig. 3). ROS are molecules that include oxygen, such as O_2^-, H_2O_2, and $HO^\bullet$, and are more reactive than molecular oxygen [74], [75]. The most abundant sulfhydryl group-containing molecule among antioxidants, glutathione (GSH), plays a significant function in several biological processes. It also creates the initial line of defense against oxidative damage, serves as the primary intracellular redox buffer, and is a co-substrate in the GSH peroxidase-catalyzed reaction of H_2O_2 or lipid peroxidation that depletes it [76]. The oxidation of biological components, including DNA, proteins, and lipids, directly results from superoxides, hydroxyls, hydrogen peroxide, and other oxygen radicals among ROS [77], [78]. Under normal physiological circumstances, antioxidative enzymes and non-enzymatic molecules, including catalases, superoxide dismutase, glutathione peroxidase, tocopherol, glutathione, and ascorbic acid present in the cell control damages brought on by ROS [79]. Due to an imbalance between the quantity of ROS and antioxidants that detoxify toxic intermediates and repair damages, however, increased oxygen-containing radicals produce hazardous intermediaries often to blame for oxidative stress [80], [81]. The body's defensive mechanisms fail to counteract oxidative stress, which causes biomolecules to malfunction [82]–[84], the amount of antioxidant enzymes to vary, glutathione to be depleted, and mitochondria to become perturbed. DNA is also damaged, leading to cell death[85].

Genotoxicity and Mutagenicity:

Genotoxicity is the term for the many mutagens that induce DNA strand breaks, oxidative DNA damage, and chromosomal abnormalities that result in mutations. The synthesis of ROS and DNA damage are correlated classically [86], [87] and NPs are taken up by cells via endocytosis, which causes the creation of ROS [88], [89]. ROS damages the DNA, which starts a signaling cascade that leads to apoptosis or cell death. Since a change to the genetic material may encourage cancer development or reproductive impairment, the genotoxicity of nanomaterials is of particular concern. As a result, the potential for mutations and genetic instability raises questions about long-term effects and likely carcinogenicity.

Environmental impact:

CuNPs released into the environment might endanger ecosystems. They may have a deleterious effect on aquatic creatures and bioaccumulate the food chain. The disposal of CuNPs may potentially cause pollution and have long-term repercussions on the ecosystem. The toxicity hazards associated with nanomaterials are strongly impacted by their chemical transformation in the environment or a biological system. NPs interact with the air, soil, and water in the environment. CuNPs released into the environment by Cu-based agricultural pesticides or wastewater treatment effluent go through several chemical changes, including sedimentation, aggregation, dissolution, interactions with natural organic matter, and redox reactions [90], [91].

Human health risks:

Concerns about copper nanoparticles' potential toxicity for human health are raised in a manner similar to how they impact the environment. Exposure to CuNPs through food, cutaneous absorption, or inhalation may have negative health effects. The main method through which NPs enter the body is by inhalation. When NPs are inhaled, they enter the lungs and interact with the epithelium, causing inflammation (Fig. 3). One of the potentially dangerous pathways for inhaled NPs to reach other bodily organs, such as the central nervous system, is the olfactory bulb [92], [93]. The endocytosis of alveolar epithelial cells

appears to be the mechanism behind the translocation of NPs [94]. Rubber and asphalt manufacturing produce industrial emissions of Cu NPs [95]. Cu NPs' capacity to stay in lung tissues for an extended period is attributed to their tiny size, which causes ROS generation, oxidative stress, and inflammatory reactions due to sensitization and irritation. It is crucial to assess the toxicity of possible risks and create appropriate safety standards to reduce potential risks. Another potential route of exposure for NPs is the gastrointestinal system. NPs are either directly or indirectly added to various foods and medications eaten orally and absorbed by the gastrointestinal tract (GIT), where they then reach lymphatic cells [96]. When considering such features of nanomaterial toxicity, greater attention should be given to analyzing negative consequences before supporting any parenteral dosage [97], [98]. The CuNPs in the meal and water were exposed to the GIT after being consumed directly or inhaled. The initial defense against NPs and other dangerous chemicals is provided by human skin. However, sweat glands and hair follicles make this barrier permeable, enabling NPs to enter. When the skin's protective barrier is damaged or destroyed, the likelihood of NP penetration increases [99]. The destiny of NPs is determined by skin penetration, which reveals their many harmful forms. They may irritate people, trigger allergies, or harm the body's cellular or subcellular components, causing a chemical reaction that creates ROS [100].

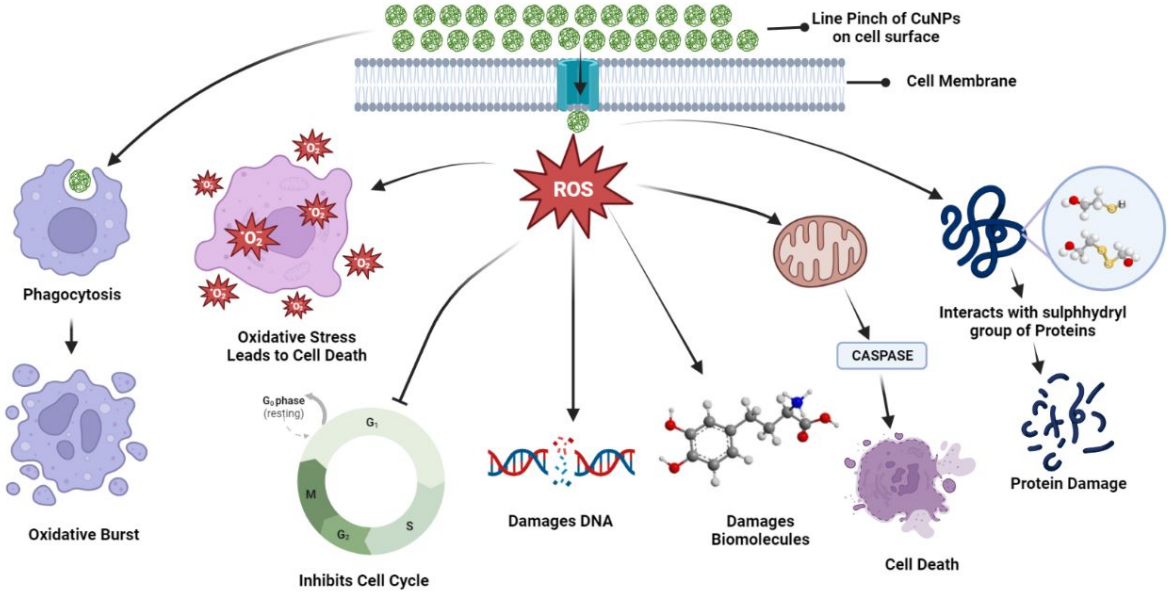

Figure 3: A schematic diagram showing the effects of Cu nanoparticles inside the cells.

Comprehensive differences between silver and copper nanoparticles

The variations in antibacterial activity, catalytic behavior, optical features, stability, and cost make copper and silver nanoparticles (AgNPs) suitable for various applications in various sectors and businesses. Finally, we examine copper and AgNPs' unique attributes and purposes (Table 2). The characteristics and uses of copper and AgNPs differ significantly in many ways. At first glance, compared to CuNPs, AgNPs have stronger antibacterial and antimicrobial properties [101]. Due to this, AgNPs are especially beneficial in healthcare and medical applications, such as antibacterial coatings and wound dressings. In contrast, CuNPs are advantageous in various industrial activities, including chemical synthesis and energy generation, because of their propensity to rapidly give and absorb electrons [102]. This makes them more effective in catalytic reactions. In addition, there are notable differences between the optical characteristics of copper and AgNPs. Strong plasmonic effects in AgNPs give them a remarkable capacity to interact with light at certain wavelengths [103]. This characteristic qualifies them for use in optical sensors and surface-enhanced Raman spectroscopy, among others. The electrical conductivity of CuNPs, however, makes them

Table 2: A Comprehensive Comparison between Silver Nanoparticles (AgNPs) and Copper Nanoparticles (CuNPs)

Parameter	Silver Nanoparticles	Copper oxide Nanoparticles
Representation	AgNPs	CuONPs
Size Range	Typically <100 nm	Typically <100 nm
Synthesis Methods	Chemical reduction, physical methods, biological synthesis	Chemical reduction, physical methods, biological synthesis
Stability	Relatively stable	Moderate stability, susceptible to oxidation and degradation over time
Surface Modification	Easily functionalized with various coatings	Can be modified with surface coatings for improved stability and function
Electrical Conductivity	Excellent	Moderate
Optical Properties	Exhibit strong plasmonic properties, giving rise to unique color	Absorb and scatter visible light
Antibacterial Activity	AgNPs have strong antibacterial properties and can effectively inhibit bacterial growth.	CuNPs also possess antibacterial activity, although they are generally less potent than Ag NPs.
Mechanism of Action	AgNPs exert antimicrobial effects through multiple mechanisms, including oxidative stress, membrane damage, and DNA binding.	CuNPs primarily target bacterial membranes and disrupt cellular functions.
Broad-Spectrum Activity	AgNPs exhibit broad-spectrum antimicrobial activity against a wide range of bacteria, fungi, and viruses.	CuNPs demonstrate antimicrobial activity against certain bacterial strains but may be less effective against other pathogens.
Stability and Aggregation	AgNPs are prone to aggregation, which can affect their antimicrobial efficacy. Proper stabilization is required to maintain their activity.	CuNPs have relatively good stability and are less prone to aggregation, ensuring consistent antimicrobial performance.
Toxicity	AgNPs have a higher potential for cytotoxicity compared to Cu NPs and may cause adverse effects on mammalian cells.	CuNPs generally exhibit lower toxicity levels and are considered safer for biological applications.
Antimicrobial Applications	AgNPs find widespread use in various antimicrobial applications, including wound dressings, coatings, and medical devices.	CuNPs have potential applications in antimicrobial coatings, water treatment, and biomedical devices.
Catalytic Properties	Excellent catalytic activity	Exhibit catalytic activity in certain reactions
Biocompatibility	Generally considered biocompatible, but depends on the size and surface coating	Biocompatible, but toxicity can be observed at higher doses
Biomedical Applications	Wound dressings, drug delivery systems, biosensors, imaging agents	Drug delivery, imaging, biosensors, tissue engineering
Environmental Impact	Low toxicity to aquatic organisms, but long-term effects uncertain	Can accumulate in ecosystems and pose risks
Cost	Relatively more expensive than CuNPs	Relatively less expensive than AgNPs

ideal for use in electronic devices and conductive inks, even though they do not show substantial plasmonic effects. The stability of copper and AgNPs also varies. Compared to AgNPs, CuNPs oxidize more quickly, which reduces their long-term stability. Because of this, AgNPs are more suited for long-term stable applications such as inks, coatings, and biomedical equipment. Eventually, there is a sizable price difference between copper and AgNPs. A valuable metal, silver is often more costly than copper. As a result, CuNPs are frequently used in processes like large-scale industrial operations and electronic manufacturing, where cost-effectiveness is important.

Conclusion:

Due to their distinctive physicochemical characteristics, CuNPs show remarkable potential as antibacterial, antioxidant, and anti-cancer agents. The variations in antibacterial activity, catalytic behavior, optical features, stability, and cost between copper and AgNPs and their unique attributes and uses allow for several applications in various sectors and companies. It's crucial to remember that research on the use of CuNPs in medications is ongoing, and studies into their potential medicinal uses are ongoing as well. Their safety, pharmacokinetics, and long-term consequences all require more research. Regulatory clearances and criteria must be followed for CuNPs to be used safely and effectively in pharmaceutical applications.

Conflict of interests

The authors declare no conflicts of interest. For a signed statement, please contact the journal office at editor@precisionnanomedicine.com.

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