

Recent Advances on Antimicrobial Properties and Biomedical Applications of Copper Nanoparticles

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Abstract— This study provides an overview of the increasing importance and focus that copper nanoparticles (Cu-NPs) are gaining in medical laboratory settings. This paper thoroughly examines Cu-NPs, including essential topics such as environmental consequences. Furthermore, the paper investigates Cu-NPs' natural ability to fight pathogenic threats, connecting the materials to their potential applications. Moreover, provides an overview of recent research on the antibacterial properties of Cu-NPs. Examining the applications in a practical sense, the section demonstrates how these nanoparticles are utilized to manage infections and their adaptability to various settings. The research dives into surface coatings and biomedical applications, describing unique approaches to improving biomedical materials with Cu-NPs. Additionally, the paper thoroughly examines the potential effects and safety issues associated with the use of Cu-NPs, taking into account the bigger ramifications, and highlights the potential of Cu-NPs as antimicrobial agents by investigating their toxicity mechanisms.

Index Terms—copper nanoparticles, biomedical, antimicrobial, nanotechnology.

I. INTRODUCTION

Recent decades have seen tremendous progress in nanotechnology, which necessitates the capacity to measure, forecast, and synthesize matter at the atomic and molecular levels. It is imperative to define the "nanoscale" scale, which is the range of 1 to 100 nm, to accurately define and comprehend nanotechnology [1]. Because of their many advantages, such as their increased surface area and their biological, thermal, chemical, and optical qualities, metal nanoparticles are becoming more and more popular. They are essential in several domains, including as tissue biotechnology, antisense, gene engineering, drug delivery systems, cosmetics, and healthcare [2, 3]. Due to their many applications, Cu-NPs are becoming more and more popular in their synthesis because of their special antibacterial qualities and cheaper cost when compared to precious metals like gold and silver [4]. The potential of Cu-NPs in medical laboratories and healthcare is driving research into them. These minuscule metallic particles are transforming biomedical research, treatments, and diagnostics, opening up new possibilities for advancement [5-8].

Antimicrobial activity was demonstrated by synthesized Cu-NPs [3]. When compared to other common antibiotics, antimicrobial nanoparticles have the advantage of reducing acute toxicity, lowering cost, and overcoming resistance. A significant change in how we approach healthcare and biomedical research is indicated by the rise of Cu-NPs in

medical labs. Cu-NPs are very promising for a variety of applications due to their special physicochemical properties, which include an amazing surface area-to-volume ratio, excellent adsorptive efficiency for wastewater treatment [5], and intrinsic antimicrobial properties. Drug delivery systems [9], wound healing [6], cancer therapy [7], and the creation of antimicrobial coatings for medical devices [8] are just a few of their numerous functions.

This paper offers a reference regarding the growing significance and attention that Cu-NPs are receiving in medical labs. It seeks to advance healthcare and nanomedicine through facilitating the exchange of knowledge and encouraging responsible research and application.

II. METHODS FOR SYNTHESIZING CU-NPs

A key stage in nanotechnology is the creation of nanoparticles, which enables the use of special material properties at the nanoscale. Physical synthesis [10], chemical synthesis [11], biochemical synthesis [12], biological synthesis [13], and green synthesis [14] are among the techniques used. Chemical synthesis depends on exact control over reaction parameters and chemical reactions [11], whereas physical synthesis modifies outside forces or situations [10]. Proteins and enzymes act as catalysts in biochemical synthesis, enabling fine-grained control over the characteristics of nanoparticles and benign reaction environments. Living things are used in biological synthesis to create a variety of nanoparticle properties [1]. Green synthesis places a strong emphasis on using sustainable resources and eco-friendly processes. More control over the structure of nanoparticles is made possible by the production of metastable intermediates, which provide intermediate states with unique properties. Targeting particular nanoparticle characteristics, such as size or shape, and carefully altering them to meet the necessary specifications is the goal of selective synthesis [15].

III. ANTIMICROBIAL PROPERTIES OF CU-NPs

The potential of Cu-NPs, a multipurpose metal with antibacterial qualities, is being investigated in several sectors. These Cu-NP-based nanoparticles are used to cleanse water and

preserve food by inhibiting the growth of microorganisms. For metabolic functions including respiration, photosynthesis, hormone synthesis, growth, and development, copper is necessary. On the other hand, high concentrations may be dangerous because they can produce ROS, which can damage DNA, lipids, and proteins. Because drug-resistant pathogenic bacteria and fungi are on the rise, antimicrobial medicines are essential for controlling microbial illnesses. It has been possible to stop the spread of infections and stop the formation of bacterial biofilms by using copper surfaces, both ionic and solid. Because copper surfaces are more affordable than other metals, they are being employed in clinical and hospital environments more and more. To increase the antibacterial activity of copper, it is essential to comprehend these toxicity processes [16-18].

A. Mechanisms of Antimicrobial Action

Cu-NPs have antibacterial capabilities that include the ability to deactivate enzymes, produce hydrogen peroxide, and perhaps damage bacterial cells. They disrupt the structure of DNA and biochemical reactions, whereas copper oxide nanoparticles harm cell membranes and reduce the survival of bacteria. The precise mechanism is yet unclear. According to Chang et al. [7], three pathways account for the harmful effects of copper oxide nanoparticles on eukaryotic cells: nonhomeostasis effects, coordination effects, and oxidative stress. Ion channels, cell membrane apertures, or transporter proteins in the plasma membrane are some of the ways that nanoparticles might enter the body.

A few toxicity pathways, including oxidative stress, DNA damage, lipid peroxidation, membrane damage, mitochondrial damage, potential meta-ion leaching, and dissolution, are covered in the literature that is currently available. Nanoparticle-induced cell damage is commonly associated with toxicological mechanisms such as oxidative stress and the formation of reactive oxygen species (ROS). CuO nanoparticles in small amounts can produce a lot of ROS, including O_2^- , OH, and H_2O_2 . CuO NPs cause disruption of the membrane and the production of ROS as soon as they reach the mitochondria. Particle size, surface area, pH, temperature, chemical composition, and organic matter are all connected to particle dissolution. CuO NPs that penetrate the nucleic acid have the potential to release additional Cu^{2+} , which can cause DNA damage and oxidative damage. Figure 1 depicts the CuO NPs' method of action. All of the toxicity pathways discussed above are shown in Figure 1.

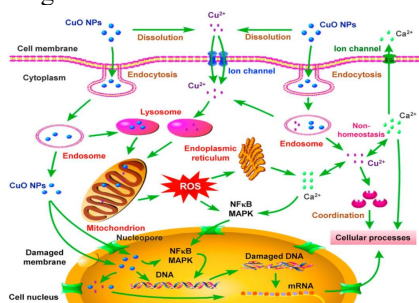


Figure 1 Schematic overview of the different pathways inducing cellular toxicity by copper oxide nanoparticles. [Reproduced with permission from Ref. 19]

The antibacterial properties of copper-based nanoparticles against bacteria, fungus, viruses, and algae have been the subject of more investigation. CuO/Cu₂O, CuS, and CuO nanoparticles have been described along with other variants. CuO/Cu₂O NPs can degrade plasmid DNA in bacterial strains, as shown in Figure 2, based on the amount and concentration of ions produced [18].

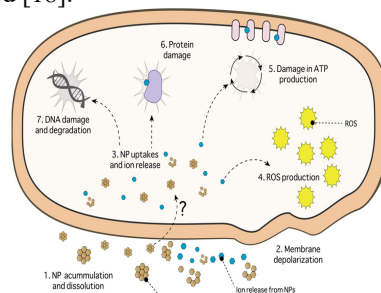


Figure 2. The overall toxicity mechanism of nanoparticles based on copper.

(1) The build-up, disintegration, and cell entry of nanoparticles. (2) The buildup of nanoparticles on the cell surface causes depolarization and membrane rupture. (3) Cu (II) ion release and nanoparticle entry into cells as a result of NP destabilization. The following reactions are brought on by the release of ions: (4) production of reactive oxygen species (ROS), lipid peroxidation, and protein oxidation; (5) reduction in ATP production; (6) protein damage from oxidation and iron replacement by copper in proteins with Fe-S centers; and (7) damage and degradation of DNA. [Reproduced with permission from Ref. 18]

B. Mechanism of Antiviral Toxicity

Viruses are particularly susceptible to copper-mediated toxicity because they do not have metal response or repair systems. There is no connection, according to research, between the type, family, genetic composition, or properties of the virus envelope and copper susceptibility. Numerous studies have been conducted on the application of Cu-NPs (CuO, Cu₂O, CuO, CuS, and CuI) as antiviral agents. These nanoparticles work by interacting with the surface of viruses, influencing their adhesion and ability to enter cells, and preventing their penetration. Additionally, they disrupt capsid proteins and inhibit Hepatitis B virus infections in CuS NPs through their antiviral action. The harm done to the viral DNA, the prevention of replication and protein synthesis, and the formation and discharge of virions are all linked to the toxicity mechanisms of copper-based NPs on viruses. The toxicity of NPs on viruses may be explained by either NP instability or dissolution-independent processes. For RSV, CMV, HadV, and HRV-2, the common factor shared by all Cu-NPs relates to "virus neutralization" [8]. Figure 3 shows the mechanisms of antiviral toxicity of copper-based nanoparticles.

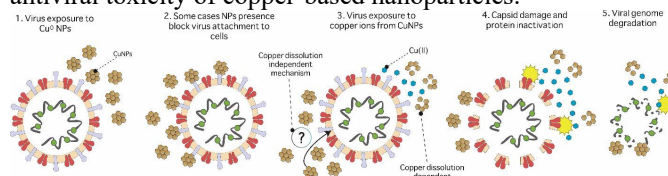


Figure 3: Copper-based nanoparticles' antiviral toxicity pathways.

(1) The virus is introduced to copper-based nanoparticles. NPs may occasionally stop the virus from attaching itself to cells by blocking or deactivating proteins involved in the attachment process. (3) The relationship between the virus and copper-based NPs is not well understood, yet it's plausible that NPs could lead to an instability of the capsid membrane (left). Conversely, copper-based NPs release copper ions (right). Every scenario involves the virus being exposed to high concentrations of localized copper exposure, which causes capsid damage, deactivation of proteins, and degradation of genetic material. [Reproduced with permission from Ref. 18]

IV. RECENT RESEARCH ON ANTIMICROBIAL EFFICACY

An antimicrobial is a chemical that either kills bacteria (microbicide) or prevents them from growing (bacteriostatic agent). Based on the bacteria that antimicrobial medications primarily target, they can be classed. Antifungals are used to treat fungi, whereas antibiotics are used to treat bacteria. They can also be divided into groups according to their objectives. Antimicrobial prophylaxis refers to the use of antimicrobial drugs to ward against infection, while antimicrobial chemotherapy deals with the treatment of infection [20]. The antibacterial qualities of Cu-NPs are briefly covered in this section.

A. Antibacterial activity

Studies have indicated that there is an increase in antibiotic resistance and that certain microbes become resistant to several of the approved antimicrobial drugs. Because of this, no antimicrobial agent is completely resistant to microbes. Because of this increase, doctors are now compelled to perform in vitro antibiotic susceptibility testing for diagnosis. Acquiring antimicrobial nanoparticles is essential, as they can be utilized to combat germs that are resistant to antibiotics and pose a threat to the health of humans and animals [19].

In the sphere of human healthcare, the developing antibiotic resistance of microorganisms has become a serious concern. The physical form (ions or NPs) in which copper is applied determines its antibacterial mechanisms most, followed by its concentration, application method, oxidation state, and coexistence of other pollutants. CuNPs have proven to be quite effective at treating bacterial illnesses that are resistant to drugs. Their affinity for the cellular membrane is enhanced by their high surface-to-volume ratio and positive charge, which changes the electrical potential difference of the cell and results in membrane depolarization and leakiness [21]. Additionally, bacteria find it difficult to evolve resistance against NPs due to their capacity to concurrently target several pathways and damage bacterial cells. According to a different mechanism, protein folding and stability may be impacted by copper ions, which could lead to anaerobic protein aggregation [22]. Furthermore, copper causes harm to microorganisms by producing reactive oxygen species (ROS), and substituting or attaching to the natural cofactors in metalloproteins [23]. CuNPs have become a promising therapeutic option in the fight against bacterial infections, providing a means of addressing the growing issue of antibiotic resistance and reducing dependency on traditional antibiotics for the treatment of bacterial

infections. Salmonella, Pseudomonas aeruginosa, Escherichia coli, and Staphylococcus aureus are a few examples of bacteria that exhibit sensitivity to CuNPs [24].

Although copper ions have been employed to protect crops, the buildup of Cu²⁺ ions in soils will cause issues and pose a threat to the environment. CuNPs are therefore suggested as a potential agricultural solution because of their antibacterial and antifungal qualities. A novel method of disease management in agriculture is nanotechnology [25]. Because of their capacity to harm cell membranes and interfere with pathogens' metabolic activities, Cu-NPs be effective as a control agent against phytopathogens [26].

CuONPs made with extracts from *Athrixia phyllicoides* have been shown by Kaningini et al. (2023) to be a viable substitute for treating bacterial infections brought on by *Staphylococcus aureus* and *Bacillus cereus*. Furthermore, these NPs did not cause any harm to human cells [27]. CuNPs have demonstrated the ability to block oral germs that cause cavities and other dental issues from growing. It has been noted that bacteria such as *Lactobacillus acidophilus*, *Aggregatibacter actinomycetemcomitans*, and *S. mutans* are growing [28]. This is why researchers are interested in using NPs in dental implants, prosthetics, and medications that prevent oral diseases. Their studies using *Escherichia coli* showed that the production of reactive oxygen species (ROS), which leads in DNA destruction, lipid peroxidation, and protein oxidation, is what causes cell death. Transmission electron microscopy (TEM) study of CuNPs produced by green synthesis utilizing extract from the leaves of *Angelica keiskei* revealed that CuNPs clung to and destroyed the cell walls of both Gram-positive and Gram-negative bacteria, resulting in their cell death [29].

B. Antimycotic activity

The application of copper as an antibacterial agent is widespread. CuNPs have been shown in several investigations to exhibit antibacterial action against a variety of fungus [24]. According to Oussou-Azo et al. [25], hyphal development was reduced in a dose-dependent manner by all types of copper that were examined. Additionally, they stated that the most potent inhibitory effects against fungal infections were demonstrated by Cu-NPs and CuO NPs. Cu-NPs are thought to be useful in preventing *Colletotrichum gloeosporioides* from growing and forming colonies. Copper particle toxicity is contingent upon multiple parameters, including concentration, duration of exposure, humidity, and temperature. Through its interactions with microbes, copper can modify a variety of processes leading to cell death, including denaturation of nucleic acids, protein modification, membrane lipid peroxidation, and cell membrane permeabilization. Copper surface coatings have the potential to have antifungal properties as well [26].

Through the production of free radicals, particularly nitric oxide radicals, the CuO NPs demonstrated the strongest antibacterial and antifungal properties against human clinical pathogens [27]. Cu-NPs with antifungal properties against *F. solani*, *Neofusicoccum* sp., and *F. oxysporum* were produced using green synthesis. These Cu-NPs worked by rupturing the pathogens' cell membranes and causing the mycelium to produce ROS intracellularly [28]. Using sucrose as a capping agent, copper oxide nanocomposites (CuO/C nanocomposites) with a particle size of 50 nm have also been created. Potential

antifungal action against *A. niger* and *A. flavus* species was demonstrated by CuO/C nanocomposites [29].

CuNPs with a round to polygonal form and a size range of 23–82 nm also showed possible antifungal efficacy against *Phytophthora parasitica* and *F. oxysporum*, two plant diseases that cause rotting [30]. CuO NPs with a spherical form and an average diameter of 7–10 nm were produced by microwave-mediated synthesis, and they demonstrated strong antifungal action against *Cladosporium herbarum* [31]. Nanoparticles with antifungal properties against *F. oxysporum* were also produced by aqueous-phase assisted synthesis of copper/copper oxides. A significant proportion of inhibition of radial growth (IGR) was demonstrated by both of these nanoparticles [32].

Microscopic examination showed that CuNP and nanowire treatment changed the shape of the cell and the cell wall, which finally causes the yeast to completely collapse. CuNPs and nanowires showed possible antifungal action against *C. albicans* through the release of free Cu²⁺ ions, which functioned as a biocide. Furthermore, the sharp edges of the nanostructures resembling marigold petals could damage the yeast's cell wall and membrane, ultimately leading to its demise. CuNPs with antifungal properties against *Candida albicans* and *Candida krusei* were synthesized using starch and sodium alginate [33]. In a dose-dependent way, CuO NPs dramatically inhibited the mycelial development of *P. oryzae* and *A. alternata* [34].

C. Antiviral activity

Viral evolution proceeds extremely quickly and effectively, which presents a growing global concern. Hence, it is imperative to devise novel and inventive tactics to counteract them, optimize the efficacy of current medications, and investigate alternative methods that disrupt viral replication processes. Anti-dengue and anti-chikungunya virus activity were demonstrated by various solvent extracts from *Plumeria alba*, *Ancistrocladus heyneanus*, *Bacopa monnieri*, *Anacardium occidentale*, *Cucurbita maxima*, *Simarouba glauca*, and *Embelia ribes* [35]. *Artemisia cina* flower extract shown to encourage antiviral efficacy against the highly pathogenic zoonotic influenza virus [36]. *Ficus rubiginosa* may be a valuable natural source of antiviral chemicals that are effective against HCoV-229E and HSV-1 [37].

To assess the transfer of antiviral capacity to the generated NPs and thereby aid in the development of new potentiated antiviral alternatives, it would be highly interesting to investigate conjugation plant extracts from these plants, such as those mentioned above with antiviral activity, in green nanoparticle synthesis processes. Several attempts have been undertaken to produce NPs that possess antiviral properties. Silver nanoparticles (AgNPs) have been successfully identified as antiviral agents against SARS-CoV-2 [38], HIV [39], chikungunya virus [40], and herpes virus [41], among other viruses, among the different NPs biosynthesized with plant extracts. Biosynthesized SNPs have an unknown antiviral mechanism; however, it has been hypothesized to be caused by SNPs binding to viral envelope glycoproteins, which stops the virus from penetrating the host cell, damaging the viral coat proteins, or fixing to the viral DNA [42].

Significant antiviral action of biosynthesized CuNPs has not been reported in numerous investigations. We go over a few

documented incidents below. The green husk of *Juglans regia* was used to biosynthesize CuNPs. When combined with FeNPs, the generated CuNPs caused a 4.5 TCID₅₀ reduction in the herpes simplex virus's viral titer when compared to the virus control. It is noteworthy to add that the antiviral activity of the green CuNPs was potentiated, as evidenced by the evaluation of the FeNPs' individual antiviral activity, which was measured with a decrease of 3.5 times the reduction of the viral titer. CuNPs did not exhibit antiviral action on their own [43].

Research on AgNPs and AuNPs suggests that they could be used as antivirals [44], however, there aren't many studies on CuNPs. Hang et al., 2015 [45] have suggested that these can bind to the virion and inhibit cell receptors. If not, it has been suggested that the mechanisms are comparable to those seen in bacteria that produce harmful species [46, 47]. Escoffery et al. (2020) suggested an intriguing use for CuNPs: impregnating face masks to prevent SARS-CoV-2 infections [48].

Cu2ONPs have been shown by Hang et al. (2015) to be able to block hepatitis C infection in its early stages, although they stop working after two hours [45]. As of right now, three primary antiviral mechanisms have been identified: breaking down the disulfide bonds that hold viral proteins together, causing denaturation of proteins, nucleic acids, and lipids by producing reactive oxygen species (ROS), and preventing viruses from binding to host cells by inhibiting their surface proteins [49]. To properly understand how CuNPs affect viruses, more research on this topic is necessary.

V. APPLICATIONS OF CU-NP IN INFECTION CONTROL

The inherent antibacterial qualities of copper have long been known. The foundational reference is the work of Rai et al. [50], which clarifies the antibacterial capability of silver nanoparticles, a feature that Cu-NPs also possess. This realization serves as the cornerstone for comprehending Cu-NPs' basic antibacterial capabilities. Cu-NPs are being used in antimicrobial applications more and more, although there are worries regarding their possible toxicity. Therefore, studying their distribution and permeability in cell membranes is essential to comprehending their toxicity mechanisms. An investigation into the impact of ultra-small Cu-NPs on phospholipid membranes was conducted using phosphatidylcholine-based large unilamellar vesicles, which were designed to resemble biological membranes. Cu-NPs have been found to cause phospholipid membrane degradation, resulting in aggregation or rupture [51].

Cu-NPs exhibit potent antioxidant and antibacterial effects, having been synthesized by diverse ways. Because they are harmful to cancer cells while sparing healthy cells, they may have use as anti-cancer agents. Cu-NPs have anti-inflammatory properties, improved immunotherapy, wound healing, drug delivery, and diagnostic imaging. They can also improve the bioavailability and stability of pharmaceuticals. To guarantee safety, improve synthesis procedures, and investigate their complete therapeutic potential, more study is required [52].

A study has been conducted by Orabi et al. [53] to explore the use of plant extracts in the environmentally friendly manufacture of metal nanoparticles. The researchers used

purified tamarixinin A (TA) ellagitannin from *Tamarix aphylla* galls to make Cu-NPs. The end product, Cu-NPs, exhibited antibacterial activity against a range of bacterial and fungal species and was stable. The researchers concluded that Cu-NPs mediated by TA can be used in several fields to combat bacterial and fungal species, such as *Aspergillus flavus*, *Pseudomonas aeruginosa*, and *Candida albicans*.

Jardón-Maximino et al. [54] used a chemical reduction approach to demonstrate Cu-NPs in an aqueous media. The most stable nanoparticles were those produced when the PEI/AAM mixture was present. The NPs showed strong antibacterial activity against *S. aureus* and *P. aeruginosa* bacteria, proving to be oxidation stable, oxide-free, and producing a large yield.

Aegle marmelos leaf powder was used in a cost-effective method to synthesize Cu-NPs in a recent study. These plant biomolecules serve as stabilizing and capping agents in addition to their medicinal uses. The NPs were verified using UV-visible spectroscopy and photoluminescence. The size ranged from 20 to 40 nm on average. It was also investigated whether the NPs' antimicrobial action extended to both Gram-positive and Gram-negative bacteria. These nanoparticles may find use as antibacterial agents, according to the findings [55].

Cu-NPs were synthesized utilizing leaf extract from *Manilkara zapota* in one of the most recent investigations by Kiriyathan et al. [56]. The antibacterial activities of the nanoparticles were demonstrated against both bacterial and fungal species. Furthermore, the development of innovative periodontal therapeutic materials that can be utilized to treat bacterial infections in place of antibiotics has demonstrated the promise of nanoparticles. In one study, mesoporous silica nanomaterial combinations with 11 different metals were aged, dried, and calcined to produce 16 unique combinations. Four distinct susceptibility tests were used to evaluate the antibacterial qualities of these nanoparticles: MIC and MBC assays, a colony-forming unit assay, and a growth kinetics investigation. The results show that sol-gel generated silver- and zinc-doped silica nanoparticles can be effective antibacterial agents against microorganisms that cause periodontitis, which could be useful in the fight against a variety of infectious disorders [57].

Recent studies have examined the application of Cu-NPs' antibacterial properties in the textile sector. The use of Cu-NPs for antibacterial functionalization on polyester textiles (PES) is investigated in a study. Cu-NPs were produced onto PES in the presence or absence of chitosan by the scientists using safe, reasonably priced materials. The results showed that whereas fewer Cu-NPs were maintained and agglomerated in the presence of chitosan, Cu-NPs stabilized onto PES in the absence of chitosan [58]. In another work, a unique technique for changing textile materials was developed by combining nanoparticles in dendrimers with N-methyldiethanolamine and Eosin Y. This photochemical process lowers the concentration of copper ions, which increases the antibacterial activity of the dendrimer complex. Three cotton fabrics' antibacterial qualities were examined in a study using *Bacillus cereus* as the test organism. Because of its two photosensitizers, which under the correct lighting conditions form reactive oxygen species and kill bacteria, the fabric containing Cu-NPs demonstrated the strongest antibacterial activity [59].

Furthermore, the emergence of β -lactamase is the cause of bacterial resistance, which is a serious worldwide health concern related to infections. Nanoparticles of copper and gold have shown promise in a variety of sectors, including as medication delivery systems, biology, and textiles. These nanoparticles' small size, high penetration rate, and ability to damage cells make them excellent at reducing health issues and fabric degradation. They can also be used to stop allergies in fabrics and skin irritation. The process of producing green nanoparticles is easy, economical, and environmentally beneficial. Zinc oxide nanoparticles are biocompatible, stable, and antibacterial, while Cu-NPs are antifungal and antibacterial against food-borne infections. While nano-silver is employed to fight specific bacterial strains, the graphene family of nanomaterials transfers charge from one bacterium to another. Nanoparticles are generally regarded as promising materials [60].

VI. SURFACE COATINGS AND BIOMEDICAL APPLICATIONS

The use of Cu-NPs in surface coatings for biomedical applications is examined in recent developments. Conde et al.'s thorough analysis of inorganic nanoparticle surface chemistry and biofunctionalization [61] offers insights into the creation of surfaces covered with Cu-NPs for the prevention of infection in medical environments. Metal and metallic oxide nanoparticles are being employed in dentistry more and more due to their special shape-dependent properties, antibacterial activity, and biocompatibility. Since they are cheap and simple to mix with other materials, Cu-NPs are among the most often used. Their application is advantageous for dental materials such as orthodontic archwires, dental amalgam, restorative cements, adhesives, resins, and implants [62].

Cometa et al. [63] have developed a study on a unique antibacterial coating that can be used to maintain stainless steel devices sterile and prevent infections. Two distinct trapping techniques were used to introduce copper-based nanoparticles to poly (ethylene glycol diacrylate) hydrogel thin films. These coatings were deposited quickly and easily using electrochemical polymerization on metal substrates with a high level of security. Studies on the surface composition and bactericidal activity of hydrogel coatings modified with Cu nanoparticles against *Escherichia coli* and *Staphylococcus aureus* have shown how effective these systems are at preventing bacterial infections. Drug resistance and disease can be brought on by bacterial and fungal biofilms. Size, shape, and surface treatment control the antimicrobial and antiviral properties of Ag-NPs and Cu-NPs, which have different cytotoxicities and capacities. They coat substrates like textiles, polymers, ceramics, and metals in biomedical applications. Synthetic AgCu nanoalloys with various microstructures work synergistically to inhibit bacterial growth [64].

There are significant health and financial risks associated with the formation of biofilms and bacterial adhesion on material surfaces. The need for surface coating techniques is growing due to the prevalence of antibiotic-resistant microbes. Polymer chains, hydrogels, super-hydrophobic surfaces, antimicrobial peptides, antibiotics, chitosan, or enzymes can all be included

in effective antimicrobial coatings. Additionally, they may be predicated on anti-adhesive or bactericidal mechanisms [65].

Food packaging is becoming increasingly important in terms of antibacterial properties as consumer demands for higher-quality food continue to rise. Both inorganic and organic materials can be used to package food, although the temperature stability of organic antibacterial agents is lower than that of inorganic ones [66]. The materials most frequently used in the production of antimicrobial food packaging materials include poly (vinyl alcohol), poly (ethylene glycol), poly (caprolactone), and metal nanoparticles [67, 68].

Generally speaking, ionic or covalent attachment of antimicrobials to polymer surfaces and adsorption of antimicrobial agents on the polymer surface are the two approaches used to enhance antimicrobial food packaging [67]. CuO has also been shown in food packaging research to be a stable nanometal with good antibacterial properties. However, it is legally mandated to precisely identify and quantify the quantity of antimicrobial compounds released from the container to the product to utilize it for food packaging that lasts a long time [69, 70]. Low-density polyethylene/Cu films were made by the solvent evaporation method, and the mechanical and antibacterial qualities of the films were successfully enhanced by the incorporation of Cu nanoparticles [71]. Moreover, montmorillonite/CuO nanocomposites enhance chitosan films' antibacterial qualities [72].

VII. ENVIRONMENTAL

The development and application of novel, low-cost methods for pollution detection, degradation, and removal depend heavily on environmental nanotechnology. Cu-NPs have been used to remove pollutants from wastewater samples that were obtained from water treatment plants utilizing mixed samples and particles. Furthermore, it has been demonstrated that pollutants like sulfur and phosphorus, which impair aquatic life, may be extracted and utilized to eliminate pollutants from coal mines and household wastewater factories [73, 74].

Cu-NPs are a cost-effective agricultural solution because they can be used as fungicides, insecticides, micronutrients, and fertilizers. In addition to being safe for the environment, they can be used as antimicrobials in food packaging, to prevent diseases caused by stress and drought, and to increase the content of anthocyanin, chlorophyll, and carotenoid pigments, which can lead to an increase in the number of seeds produced, grain yield, wastewater management, and biomedical applications [75].

The growing usage of nanoparticles raises important questions about safety and the environment. The Singh et al. article [76] addresses the environmental issues related to micro/nanoplastics and offers a framework for assessing the possible environmental effects of Cu-NPs. Cu-NPs' potential use in agriculture stress management has piqued interest in recent years. Using bioactive substances present in plants to create Cu-NPs is one particularly important technique.

Consequently, plant crops benefit from a multitude of beneficial characteristics due to their environmentally benign nature. Cu-NPs derived from plant materials have been found to positively influence plant growth and development in earlier studies. In a

similar vein, these have demonstrated their ability to act as a buffer against unfavorable environmental conditions such as air dryness. The nanoparticles work as a barrier to prevent the oxidation reaction damages brought on by unfavorable circumstances. Cu-NPs have a significant impact on plants' stress response genes, strengthening their ability to withstand environmental fluctuations. They cause the synthesis of proteins and osmoprotectants for cellular defense and water retention, which in turn activates stress tolerance systems. This eco-friendly method encourages photosynthesis and plant development. Cu-NPs can be identified by their electrical and thermal conductivity, antimicrobial properties, and catalytic activity. They are used in microchip technology, medical applications, and environmental remediation. Their ability to serve several purposes makes them desirable for incorporation into different industries and technologies, which promotes more study and testing [77].

The work by Pawar and Takke (2023) investigates the kinds, regulatory issues, and bioapplications of metallic nanoparticles with an emphasis on airborne transmission. Understanding how Cu-NPs can be added to air filtration systems to stop the spread of airborne illnesses is made possible in large part by this source [78].

VIII. PERSPECTIVES AND OUTLOOK FOR THE FUTURE

Prospective investigations may concentrate on improving the synthesis processes for Cu-NPs to augment efficaciousness, expandability, and durability. The creation of innovative and improved synthesis methods could lead to more uses and accessibility in medical laboratory settings. Future research into the usefulness of Cu-NPs in the treatment of infections seems very promising. Future studies ought to investigate and broaden the range of applications since this could result in the creation of focused and efficient infection control methods. Exciting opportunities arise from the novel methods of enhancing biological materials by using copper nanoparticle surface coatings. Subsequent initiatives might concentrate on advancing innovation in biomedical applications, which could result in the creation of better medical equipment and materials with higher performance and safety. It is essential to conduct a comprehensive analysis of the environmental effects and safety concerns related to Cu-NPs. Future studies should focus more on comprehending and reducing possible environmental effects to guarantee the ethical and sustainable usage of Cu-NPs in medicinal applications. To maximize the antibacterial activity of Cu-NPs, it is imperative to investigate their toxicity mechanisms. Further investigation could yield a more comprehensive comprehension of the mechanisms by which Cu-NPs counteract infections, thereby enabling the creation of antimicrobial drugs that are both more precise and effective. The real-world impact depends on how well research findings are applied in the real world. Subsequent endeavors ought to concentrate on closing the knowledge gap between research and practice, which could eventually result in the incorporation of Cu-NPs for infection control into standard medical procedures.

CONCLUSION

Cu-NPs are becoming more and more popular and useful, which highlights their expanding importance in medical laboratories and other fields including healthcare, nanomedicine, and other fields. Cu-NPs have been shown to alter biomedical research, treatments, and diagnostics; this proposes a paradigm shift in the way we approach biomedical research and healthcare. Cu-NPs have a wide range of applications, ranging from cancer therapy and wound healing to drug delivery systems, demonstrating their adaptability and promise to tackle challenging healthcare issues. Synthesized Cu-NPs have been shown to have antibacterial action, and this, together with benefits like less acute toxicity, decreased cost, and resistance-busting, makes them a viable substitute for conventional antibiotics. Cu-NPs are now being studied in medical labs, which suggests that more research is needed to fully comprehend their characteristics, uses, and possible ramifications. Cu-NPs are thought to have a wide range of uses, and this, together with their inherent qualities, points to a fertile ground for future research that could result in advances in nanomedicine, healthcare, and other related fields.

DECLARATION OF COMPETING INTEREST

The author declares that they have no known competing financial and conflicts of interest or personal relationships that could have appeared to influence the work reported in this paper.

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REFERENCES

- [1] Nasrollahzadeh, M., Sajadi, M.S., Atarod, M., Sajjadi, M. and Isaabadi, Z., 2019. An introduction to green nanotechnology. Academic Press.
- [2] Dashora, A. and Sharma, K., 2018. Green synthesis of nanoparticles and their applications. *Advanced Science, Engineering and Medicine*, 10(6), pp.523-541.
- [3] Thakur, S., Sharma, S., Thakur, S. and Rai, R., 2018. Green synthesis of copper nano-particles using *Asparagus adscendens roxb.* Root and leaf extract and their antimicrobial activities. *Int. j. curr. microbiol. appl. sci.*, 7(4), pp.683-694.
- [4] Khan, I., Saeed, K. and Khan, I., 2019. Nanoparticles: Properties, applications and toxicities. *Arabian journal of chemistry*, 12(7), pp.908-931.
- [5] Al-Hakkani, M.F., 2020. Biogenic copper nanoparticles and their applications: A review. *SN Applied Sciences*, 2(3), p.505.
- [6] Fahimirad, S., Satei, P., Ganji, A. and Abtahi, H., 2023. Wound healing performance of PVA/PCL based electrospun nanofiber incorporated green synthesized CuNPs and *Quercus infectoria* extracts. *Journal of Biomaterials Science, Polymer Edition*, 34(3), pp.277-301.
- [7] Amatya, R., Lee, D., Sultana, M., Min, K.A. and Shin, M.C., 2023. Albumin-coated copper nanoparticles for photothermal cancer therapy: Synthesis and in vitro characterization. *Heliyon*, 9(7).
- [8] Krukiewicz, K., 2023. Development of Copper Nanoparticles Based Antimicrobial Coatings Mediated by *Zingiber Officinale* to Combat Antimicrobial Resistance. *Applied Medical Informatics*, 45, pp. S28-S28.
- [9] Woźniak-Budych, M.J., Staszak, K. and Staszak, M., 2023. Copper and Copper-Based Nanoparticles in Medicine—Perspectives and Challenges. *Molecules*, 28(18), p.6687.
- [10] Jamkhande, P.G., Ghule, N.W., Bamer, A.H. and Kalaskar, M.G., 2019. Metal nanoparticles synthesis: An overview on methods of preparation, advantages and disadvantages, and applications. *Journal of drug delivery science and technology*, 53, p.101174.
- [11] Shah, K.W. and Lu, Y., 2018. Morphology, large scale synthesis and building applications of copper nanomaterials. *Construction and Building Materials*, 180, pp.544-578.
- [12] Varghese, B., Kurian, M., Krishna, S. and Athira, T.S., 2020. Biochemical synthesis of copper nanoparticles using *Zingiber officinalis* and *Curcuma longa*: Characterization and antibacterial activity study. *Materials Today: Proceedings*, 25, pp.302-306.
- [13] Santhoshkumar, J., Agarwal, H., Menon, S., Rajeshkumar, S. and Kumar, S.V., 2019. A biological synthesis of copper nanoparticles and its potential applications. In *Green Synthesis, Characterization and Applications of Nanoparticles* (pp. 199-221). Elsevier.
- [14] Akintelu, S.A., Folorunso, A.S., Folorunso, F.A. and Oyebamiji, A.K., 2020. Green synthesis of copper oxide nanoparticles for biomedical application and environmental remediation. *Heliyon*, 6(7).
- [15] Akintelu, S.A., Oyebamiji, A.K., Olugbeko, S.C. and Latona, D.F., 2021. Green chemistry approach towards the synthesis of copper nanoparticles and its potential applications as therapeutic agents and environmental control. *Current Research in Green and Sustainable Chemistry*, 4, p.100176.
- [16] Solioz, M., 2018. Copper and bacteria: evolution, homeostasis and toxicity (p. 88). Cham, Switzerland: Springer International Publishing.
- [17] Pontin, K.P., Borges, K.A., Furian, T.Q., Carvalho, D., Wilmann, D.E., Cardoso, H.R.P., Alves, A.K., Chitolina, G.Z., Salle, C.T.P., de Souza Moraes, H.L. and do Nascimento, V.P., 2021. Antimicrobial activity of copper surfaces against biofilm formation by *Salmonella Enteritidis* and its potential application in the poultry industry. *Food Microbiology*, 94, p.103645.
- [18] Ramos-Zúñiga, J., Bruna, N. and Pérez-Donoso, J.M., 2023. Toxicity Mechanisms of Copper Nanoparticles and Copper Surfaces on Bacterial Cells and Viruses. *International Journal of Molecular Sciences*, 24(13), p.10503.
- [19] Crisan, M.C., Teodora, M. and Lucian, M., 2021. Copper nanoparticles: Synthesis and characterization, physiology, toxicity and antimicrobial applications. *Applied Sciences*, 12(1), p.141.
- [20] Leekha, S., Terrell, C.L. and Edson, R.S., 2011, February. General principles of antimicrobial therapy. In *Mayo clinic proceedings* (Vol. 86, No. 2, pp. 156-167). Elsevier.
- [21] Mitra, D., Kang, E.T. and Neoh, K.G., 2019. Antimicrobial copper-based materials and coatings: potential multifaceted biomedical applications. *ACS applied materials & interfaces*, 12(19), pp.21159-21182.
- [22] Zuily, L., Lahrach, N., Fassler, R., Genest, O., Faller, P., Sénèque, O., Denis, Y., Castanié-Cornet, M.P., Genevaux, P., Jakob, U. and Reichmann, D., 2022. Copper induces protein aggregation, a toxic process compensated by molecular chaperones. *MBio*, 13(2), pp. e03251-21.
- [23] Ma, X., Zhou, S., Xu, X. and Du, Q., 2022. Copper-containing nanoparticles: Mechanism of antimicrobial effect and application in dentistry—a narrative review. *Frontiers in Surgery*, 9, p.905892.
- [24] Chalandar, H.E., Ghorbani, H.R., Attar, H. and Alavi, S.A., 2017. Antifungal effect of copper and copper oxide nanoparticles against *Penicillium* on orange fruit. *Biosciences Biotechnology Research Asia*, 14(1), pp.279-284.

- [25] Oussou-Azo, A.F., Nakama, T., Nakamura, M., Futagami, T. and Vestergaard, M.D.C.M., 2020. Antifungal potential of nanostructured crystalline copper and its oxide forms. *Nanomaterials*, 10(5), p.1003.
- [26] Arendsen, L.P., Vig, S., Thakar, R. and Sultan, A.H., 2019. Impact of copper compression stockings on venous insufficiency and lipodermatosclerosis: a randomised controlled trial. *Phlebology*, 34(4), pp.224-230.
- [27] Mani, V.M., Kalaivani, S., Sabarathinam, S., Vasuki, M., Soundari, A.J.P.G., Das, M.A., Elfasakhany, A. and Pugazhendhi, A., 2021. Copper oxide nanoparticles synthesized from an endophytic fungus *Aspergillus terreus*: Bioactivity and anti-cancer evaluations. *Environmental Research*, 201, p.111502.
- [28] Pariona, N., Mtz-Enriquez, A.I., Sánchez-Rangel, D., Carrión, G., Paraguay-Delgado, F. and Rosas-Saito, G., 2019. Green-synthesized copper nanoparticles as a potential antifungal against plant pathogens. *RSC advances*, 9(33), pp.18835-18843.
- [29] Roopan, S.M., Priya, D.D., Shanavas, S., Acevedo, R., Al-Dhabi, N.A. and Arasu, M.V., 2019. CuO/C nanocomposite: Synthesis and optimization using sucrose as carbon source and its antifungal activity. *Materials Science and Engineering: C*, 101, pp.404-414.
- [30] Ammar, H.Y. and Badran, H.M., 2019. Effect of CO adsorption on properties of transition metal doped porphyrin: A DFT and TD-DFT study. *Heliyon*, 5(10).
- [31] Henam, S.D., Ahmad, F., Shah, M.A., Parveen, S. and Wani, A.H., 2019. Microwave synthesis of nanoparticles and their antifungal activities. *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*, 213, pp.337-341.
- [32] Hermida-Montero, L.A., Pariona, N., Mtz-Enriquez, A.I., Carrión, G., Paraguay-Delgado, F. and Rosas-Saito, G., 2019. Aqueous-phase synthesis of nanoparticles of copper/copper oxides and their antifungal effect against *Fusarium oxysporum*. *Journal of hazardous materials*, 380, p.120850.
- [33] Akturk, A., Güler, F.K., Taygun, M.E., Goller, G. and Küçükbayrak, S., 2020. Synthesis and antifungal activity of soluble starch and sodium alginate capped copper nanoparticles. *Materials Research Express*, 6(12), p.1250g3.
- [34] Consolo, V.F., Torres-Nicolini, A. and Alvarez, V.A., 2020. Mycosynthetized Ag, CuO and ZnO nanoparticles from a promising *Trichoderma harzianum* strain and their antifungal potential against important phytopathogens. *Scientific Reports*, 10(1), p.20499.
- [35] Alagarasu, K., Patil, P., Kaushik, M., Chowdhury, D., Joshi, R.K., Hegde, H.V., Kakade, M.B., Hoti, S.L., Cherian, S. and Parashar, D., 2022. In vitro antiviral activity of potential medicinal plant extracts against dengue and chikungunya viruses. *Frontiers in Cellular and Infection Microbiology*, 12, p.866452.
- [36] Hegazy, A., Mostafa, I., Elshaier, Y.A., Mahmoud, S.H., Abo Shama, N.M., Shehata, M., Yahya, G., Nasr, N.F., El-Halawany, A.M., Ali, M.A. and Ali, M.A., 2022. Robust antiviral activity of santonica flower extract (*Artemisia cina*) against avian and human influenza A viruses: In vitro and chemoinformatic studies. *ACS omega*, 7(45), pp.41212-41223.
- [37] Antonio-Pérez, A., Durán-Armenta, L.F., Pérez-Loredo, M.G. and Torres-Huerta, A.L., 2023. Biosynthesis of Copper Nanoparticles with Medicinal Plants Extracts: From Extraction Methods to Applications. *Micromachines*, 14(10), p.1882.
- [38] Karthik, C., Punnaivalavan, K.A., Prabha, S.P. and Caroline, D.G., 2022. Multifarious global flora fabricated phytosynthesis of silver nanoparticles: a green nanoweapon for antiviral approach including SARS-CoV-2. *International Nano Letters*, 12(4), pp.313-344.
- [39] Kumar, S.D., Singaravelu, G., Ajithkumar, S., Murugan, K., Nicoletti, M. and Benelli, G., 2017. Mangrove-mediated green synthesis of silver nanoparticles with high HIV-1 reverse transcriptase inhibitory potential. *Journal of Cluster Science*, 28, pp.359-367.
- [40] Sharma, V., Kaushik, S., Pandit, P., Dhull, D., Yadav, J.P. and Kaushik, S., 2019. Green synthesis of silver nanoparticles from medicinal plants and evaluation of their antiviral potential against chikungunya virus. *Applied microbiology and biotechnology*, 103, pp.881-891.
- [41] Haggag, E.G., Elshamy, A.M., Rabeh, M.A., Gabr, N.M., Salem, M., Youssif, K.A., Samir, A., Bin Muhsinah, A., Alsayari, A. and Abdelmohsen, U.R., 2019. Antiviral potential of green synthesized silver nanoparticles of *Lampranthus coccineus* and *Malephora lutea*. *International journal of nanomedicine*, pp.6217-6229.
- [42] Naikoo, G.A., Mustaqeem, M., Hassan, I.U., Awan, T., Arshad, F., Salim, H. and Qurashi, A., 2021. Bioinspired and green synthesis of nanoparticles from plant extracts with antiviral and antimicrobial properties: A critical review. *Journal of Saudi Chemical Society*, 25(9), p.101304.
- [43] Ahmadi, M., Elikaei, A. and Ghadam, P., 2023. Antiviral activity of biosynthesized copper nanoparticle by *Juglans regia* green husk aqueous extract and Iron nanoparticle: molecular docking and in-vitro studies. *Iranian Journal of Microbiology*, 15(1), p.138.
- [44] Ermini, M.L. and Voliani, V., 2021. Antimicrobial nano-agents: The copper age. *ACS nano*, 15(4), pp.6008-6029.
- [45] Hang, X., Peng, H., Song, H., Qi, Z., Miao, X. and Xu, W., 2015. Antiviral activity of cuprous oxide nanoparticles against Hepatitis C Virus in vitro. *Journal of virological methods*, 222, pp.150-157.
- [46] Ishida, T., 2018. Antiviral activities of Cu²⁺ ions in viral prevention, replication, RNA degradation, and for antiviral efficacies of lytic virus, ROS-mediated virus, copper chelation. *World Scientific News*, (99), pp.148-168.
- [47] Sucipto, T.H., Churrotin, S., Setyawati, H., Kotaki, T., Martak, F. and Soegijanto, S., 2017. Antiviral activity of copper (II) chloride dihydrate against dengue virus type-2 in vero cell. *Indonesian Journal of Tropical and Infectious Disease*, 6(4), pp.84-87.
- [48] Escoffery, C.C., Dunn, I., Patel, H., Yan, S. and Shukla, S., 2020. A Novel Approach to Antiviral COVID-19 Masks.
- [49] Alavi, M., Kamarasu, P., McClements, D.J. and Moore, M.D., 2022. Metal and metal oxide-based antiviral nanoparticles: Properties, mechanisms of action, and applications. *Advances in Colloid and Interface Science*, p.102726.
- [50] Rai, M., Yadav, A., & Gade, A. (2009). Silver nanoparticles as a new generation of antimicrobials. *Biotechnology Advances*, 27(1), 76-83.
- [51] Izzi, M., Oliver, M., Mateos, H., Palazzo, G., Cioffi, N. and Miró, M., 2023. Analytical probing of membranotropic effects of antimicrobial copper nanoparticles on lipid vesicles as membrane models. *Nanoscale Advances*, 5(23), pp.6533-6541.
- [52] Tyagi, P.K., Arya, A., Mazumder, A.M. and Tyagi, S., 2023. Development of copper nanoparticles and their prospective uses as antioxidants, antimicrobials, anticancer agents in the pharmaceutical sector. *Precis. Nanomed*, 6, pp.1048-1065.
- [53] Orabi, M.A., Salem-Bekhit, M.M., Taha, E.I., Abdel-Sattar, E.S., Alqahtani, O.S., Al-Joufi, F.A., Abdel-Wahab, B.A., Alshabi, A.M., Alyami, H.S., Ahmad, J. and Hatano, T., 2022. Design, characterization, and antimicrobial evaluation of copper nanoparticles utilizing tamarixinin a ellagitannin from galls of *Tamarix aphylla*. *Pharmaceuticals*, 15(2), p.216.
- [54] Jardón-Maximino, N., Pérez-Alvarez, M., Cadenas-Pliego, G., Lugo-Uribe, L.E., Cabello-Alvarado, C., Mata-Padilla, J.M. and Barriga-Castro, E.D., 2021. Synthesis of copper nanoparticles stabilized with organic ligands and their antimicrobial properties. *polymers*, 13(17), p.2846.
- [55] Tanwar, S., Parauha, Y.R., There, Y. and Dhoble, S.J., 2023. Green synthesis-assisted copper nanoparticles using *Aegle marmelos* leaves extract: physical, optical, and antimicrobial properties. *Luminescence*, 38(11), pp.1912-1920.
- [56] Kiriyanthan, R.M., Sharmili, S.A., Balaji, R., Jayashree, S., Mahboob, S., Al-Ghanim, K.A., Al-Misned, F., Ahmed, Z., Govindarajan, M. and Vasecharan, B., 2020. Photocatalytic, antiproliferative and antimicrobial properties of copper nanoparticles synthesized using *Manilkara zapota*

- leaf extract: A photodynamic approach. *Photodiagnosis and Photodynamic Therapy*, 32, p.102058.
- [57] Nawaz, M.Z., Alghamdi, H.A., Zahoor, M., Rashid, F., Alshahrani, A.A., Alghamdi, N.S., Pugazhendhi, A. and Zhu, D., 2024. Synthesis of novel metal silica nanoparticles exhibiting antimicrobial potential and applications to combat periodontitis. *Environmental Research*, 241, p.117415.
- [58] Mehravani, B., Ribeiro, A.I., Montazer, M. and Zille, A., 2022, July. Development of antimicrobial polyester fabric by a green in situ synthesis of copper nanoparticles mediated from chitosan and ascorbic acid. In *Materials Science Forum* (Vol. 1063, pp. 83-90). Trans Tech Publications Ltd.
- [59] Staneva, D., Atanasova, D., Nenova, A., Vasileva-Tonkova, E. and Grabchev, I., 2021. Cotton fabric modified with a PAMAM dendrimer with encapsulated copper nanoparticles: Antimicrobial activity. *Materials*, 14(24), p.7832.
- [60] Nawab, R., Iqbal, A., Niazi, F., Iqbal, G., Khurshid, A., Saleem, A. and Munis, M.F.H., 2023. Review featuring the use of inorganic nano-structured material for anti-microbial properties in textile. *Polymer Bulletin*, 80(7), pp.7221-7245.
- [61] Conde, J., Dias, J.T., Grazú, V., Moros, M., Baptista, P.V., & de la Fuente, J.M. (2014). Revisiting 30 years of biofunctionalization and surface chemistry of inorganic nanoparticles for nanomedicine. *Frontiers in Chemistry*, 2, 48.
- [62] Xu, V.W., Nizami, M.Z.I., Yin, I.X., Yu, O.Y., Lung, C.Y.K. and Chu, C.H., 2022. Application of copper nanoparticles in dentistry. *Nanomaterials*, 12(5), p.805.
- [63] Cometa, S., Iatta, R., Ricci, M.A., Ferretti, C. and De Giglio, E., 2013. Analytical characterization and antimicrobial properties of novel copper nanoparticle-loaded electrosynthesized hydrogel coatings. *Journal of bioactive and compatible polymers*, 28(5), pp.508-522.
- [64] Fan, X., Yahia, L.H. and Sacher, E., 2021. Antimicrobial properties of the Ag, Cu nanoparticle system. *Biology*, 10(2), p.137.
- [65] Swartjes, J.J., Sharma, P.K., Kooten, T., van der Mei, H.C., Mahmoudi, M., Busscher, H.J. and Rochford, E.T., 2015. Current developments in antimicrobial surface coatings for biomedical applications. *Current Medicinal Chemistry*, 22(18), pp.2116-2129.
- [66] Kişla, D., Gökmen, G.G., Evrendilek, G., Akan, T., Vlčko, T., Kulawik, P., Jambrak, A.R. and Özoğul, F., 2023. Recent developments in antimicrobial surface coatings: Various deposition techniques with nanosized particles, their application and environmental concerns. *Trends in Food Science & Technology*.
- [67] Dobrucka, R. and Ankiel, M., 2019. Possible applications of metal nanoparticles in antimicrobial food packaging. *Journal of Food Safety*, 39(2), p.e12617.
- [68] Valencia, G.A., Zare, E.N., Makvandi, P. and Gutiérrez, T.J., 2019. Self-assembled carbohydrate polymers for food applications: A review. *Comprehensive reviews in food science and food safety*, 18(6), pp.2009-2024.
- [69] Pour, Z.S., Makvandi, P. and Ghaemy, M., 2015. Performance properties and antibacterial activity of crosslinked films of quaternary ammonium modified starch and poly (vinyl alcohol). *International journal of biological macromolecules*, 80, pp.596-604.
- [70] Hoseinnejad, M., Jafari, S.M. and Katouzian, I., 2018. Inorganic and metal nanoparticles and their antimicrobial activity in food packaging applications. *Critical reviews in microbiology*, 44(2), pp.161-181.
- [71] Lomate, G.B., Dandi, B. and Mishra, S., 2018. Development of antimicrobial LDPE/Cu nanocomposite food packaging film for extended shelf life of peda. *Food packaging and shelf life*, 16, pp.211-219.
- [72] Jayakumar, A., Heera, K.V., Sumi, T.S., Joseph, M., Mathew, S., Praveen, G., Nair, I.C. and Radhakrishnan, E.K., 2019. Starch-PVA composite films with zinc-oxide nanoparticles and phytochemicals as intelligent pH sensing wraps for food packaging application. *International Journal of Biological Macromolecules*, 136, pp.395-403.
- [73] Haider, S., Kamal, T., Khan, S.B., Omer, M., Haider, A., Khan, F.U. and Asiri, A.M., 2016. Natural polymers supported copper nanoparticles for pollutants degradation. *Applied Surface Science*, 387, pp.1154-1161.
- [74] Naubi, I., Zardari, N.H., Shirazi, S.M., Ibrahim, N.F.B. and Baloo, L., 2016. Effectiveness of water quality index for monitoring Malaysian river water quality. *Polish Journal of Environmental Studies*, 25(1).
- [75] Bhagat, M., Anand, R., Sharma, P., Rajput, P., Sharma, N. and Singh, K., 2021. Multifunctional copper nanoparticles: synthesis and applications. *ECS Journal of Solid State Science and Technology*, 10(6), p.063011.
- [76] Singh, A.V., Sigloch, H., Laux, P., Luch, A., Wagener, S., & Tentschert, J. (2020). Micro/nanoplastics: an emerging environmental concern for the future decade. *Front. Nanosci. Nanotechnology*, 6, 1-2.
- [77] Wahab, A., Batoool, F., Muhammad, M., Zaman, W., Mikhlef, R.M. and Naeem, M., 2023. Current Knowledge, Research Progress, and Future Prospects of Phyto-Synthesized Nanoparticles Interactions with Food Crops under Induced Drought Stress. *Sustainability*, 15(20), p.14792.
- [78] Pawar, S., & Takke, A. (2023). Regulatory Aspects, Types and Bioapplications of Metallic Nanoparticles: A Review. *Current Drug Delivery*, 20(7), 857-883.