

# MECHANISM OF COLLOIDAL COPPER/ COPPER OXIDE NANOPARTICLES MEDIATED BACTERICIDAL ACTIVITY AND ITS MULTI- DIMENSIONAL OUTLOOK IN FUTURE

## Abstract

Copper oxide and colloidal copper nanoparticles have gained popularity as powerful antibacterial agents. These nanoparticles have recently shown promise in preventing the spread of antibiotic resistance, combating microbial diseases, and providing fresh approaches in a variety of fields. This thorough analysis explores the complex mechanisms behind the bactericidal action of copper oxide and colloidal copper nanoparticles, illuminating their multifaceted use and potential future uses. Due to their outstanding antibacterial qualities, colloidal copper and copper oxide nanoparticles have attracted a lot of attention in the domains of nanotechnology, materials science, and biomedicine. These nanoparticles have come to light as possible substitutes and additives in response to the growing concern over antibiotic resistance and the requirement for sustainable antibacterial solutions. The purpose of this review is to examine the multi-dimensional potential of copper oxide and colloidal copper nanoparticles in various applications and to clarify the mechanism underlying their bactericidal activity. Through mechanisms involving ROS production, cell membrane rupture, intracellular absorption, and antibacterial synergy, colloidal copper and copper oxide nanoparticles demonstrate strong bactericidal action. Their numerous uses include biomedicine, water filtration, food packaging, agriculture, and even possible antiviral properties. For their successful integration into diverse industries, it is essential to solve issues with biocompatibility, resistance, regulation, and scalability. These nanoparticles have the potential to revolutionise the fight against bacterial

## Authors

### **Mou Das**

Department of Applied Biology  
Maulana Abul Kalam Azad  
University of Technology  
West Bengal, India

### **Milon Banik**

Ph.D  
Assistant Professor  
Co-Ordinator M.Sc. Biotechnology  
Department of Applied Biology  
Maulana Abul Kalam Azad  
University of Technology  
Haringhata, West Bengal, India.

MECHANISM OF COLLOIDAL COPPER/ COPPER OXIDE NANOPARTICLES MEDIATED  
BACTERICIDAL ACTIVITY AND ITS MULTI-DIMENSIONAL OUTLOOK IN FUTURE

illnesses and contribute to a safer and more sustainable future with continued study and innovation.

**Keywords:** Bactericidal action, antimicrobial mechanisms, Copper, and Copper oxide, colloidal nanoparticles, multi-dimensional applications.

## I. INTRODUCTION

The revolutionary field of nanotechnology, also known as "nano," studies how to manipulate and control matter on a very small scale, or the nanoscale. Materials display special characteristics and behaviours that set them apart from their bulk counterparts at this minute scale. Nanotechnology is the process of precisely controlling the design, manufacture, and use of structures, devices, and systems at the nanoscale scale, or roughly on the order of one billionth of a metre.

The name "nano" comes from the Greek word "nanos," which means "dwarf" and it perfectly convulsions the field of nanotechnology, in which scientists and engineers deal with extremely small structures and particles that recurrently fit inside the range of individual molecules and atoms. Across a wide range of disciplines, comprising Physics, Chemistry, Biology, Engineering, and Medicine, this is the capacity to control matter at such a tiny scale which further opens up a world of innovative opportunities.

The need for innovative, powerful antibacterial drugs has been emphasized with the rise of germs that are already becoming resistant to the traditional antibiotics. Due to their distinctive physical and chemical enigmatic characteristics, especially their improved antibacterial activity, metallic nanoparticles have drawn a lot of attention. Different metallic nanoparticles (NP), such as Copper nanoparticles have shown potential antibacterial activities to wide ranges of bacterial strain including *Escherichia coli*. In order to effectively fight bacterial illnesses, the current research intends to establish very upfront, potent and reliable approach for the manufacture of highly antibacterial copper nanoparticles.

## II. DIFFERENT TECHNIQUES FOR COPPER AND COPPEROXIDE NANO-PARTICLE PREPARATION

The creation of copper and copper oxide nanoparticles is possible using a variety of ways. The complexity, scalability, and characteristics of the nanoparticles produced by these processes can differ based on their preparation methodologies. The following techniques are typical for creating copper and copper oxide nanoparticles: [1-9]

**Chemical Reduction Techniques:** There are numerous reports of Cu/CuO nanoparticles synthesis by different mechanism.

- 1. Solvent Reduction:** In this copper nanoparticles synthesis process, a copper precursor (basically copper salts) is first dissolved in a solvent or in aqueous medium and a reducing agent is applied. Copper salts are reduced in a polyol solvent at high temperatures, frequently with the help of stabilisers, in the polyol process. In another version named Hydrothermal Synthesis, Copper salts and reducing agents react under high pressure and temperature to produce nanoparticles. [10]
- 2. Approach of Precipitation:** In this approach, copper ions are precipitated from a solution to create copper oxide nanoparticles. In general, mixing copper salt solutions with a precipitator, such as sodium hydroxide or ammonia, is a very preferred method. Copper hydroxide initially forms as the black precipitating agent is added to the copper salt solution. CuO nanoparticles can be created through the controlled oxidation and

dehydration of copper hydroxide. Sometimes, oxidation can also be performed in presence of stabilising agents.

- 3. Solution-phase Synthesis:** The most frequent method for creating copper and copper oxide nanoparticles with specific characteristics is the solution-phase synthesis. These techniques provide different parameter control like size, form, and traits. Chemical reduction, the polyol approach, solvothermal/hydrothermal synthesis, the micro-emulsion method, electrochemical deposition, copper salt oxidation, and seed-mediated growth are very well established and commonly used methods. The resultant nanoparticles can be fine-tuned to meet particular application requirements by modifying variables including precursor concentrations, reaction conditions, and stabilising agents[11]. However, while working with chemicals and at high temperatures, safety precautions must be considered to avoid any casualties.

Electrochemical Technique is another preferred method to prepare CuNP. By controlling the deposition parameters, copper ions from a solution are deposited onto an electrode surface, where they can ultimately form nanoparticles. Copper ions in a solution are reduced at an electrode surface to create nanoparticles by an electrochemical reduction process.

In Thermal decomposition process, the Copper salts precursors have been used for the breakdown and creation of nanoparticles. When copper-containing precursors are heated to high temperatures, tiny CuNP is formed. In another version, precursors are hydrolysed to create a sol, which is then condensed to create a gel that contains nanoparticles. Water-in-Oil Surfactants stabilise the water and oil phases in a micro emulsion for the development of CuNP, where copper ions are reduced to produce nanoparticles. Sol-Gel Technique is another well-established method for metallic NP generation.

- 4. Sonochemical Technique:** There are two variations of this approach. One is Ultrasonic Irradiation performed by the creation of cavitation bubbles with ultrasonic waves in high temperatures and pressures, which encourage the reduction of copper ions followed by very small CuNP generation. Synthesis with NP can also be conducted in Microwave Assistance Irradiation where quickly heating the reaction mixture with microwaves resulting nanoparticles formation.
- 5. Green Synthesis:** The synthesis of Cu or CuO NP in biological procedure has been reported by different scientific groups. In Biological techniques: reducing copper ions and forming nanoparticles are performed using microorganisms/ fungal or enzymes. In Plant-Mediated Synthesis, CuNP or CuONPs are produced using extracts from a variety of plants. The phenolic and flavonoids from this plant extracts are cast-off both as stabilisers and reducing agents.

Regarding particle size management, cost, scalability, reproducibility, and restrictions, each of these methods has its own benefits and shortcomings. The preferred features of the nanoparticles and the particular application for which they will be employed will determine the method to be used. Additionally, while creating copper oxide nanoparticles, oxidation procedures can be used to produce the desired oxide form,

such as copper oxide nanoparticles like CuO or Cu<sub>2</sub>O, frequently made by heating copper nanoparticles in the presence of oxygen.

### III. MECHANISM OF Cu-BASED NP MEDIATED CELL CYTOTOXICITY

The antibacterial action of copper nanoparticles is linked to a number of phenomena that work together to compromise the integrity of bacterial membrane and operation of bacterial cellular activities. These mechanisms, by which a NP could interact with the bacterial cells in a variety of ways are practically originated from the nanoparticles itself distinct physicochemical characteristics. Strong antibacterial action has been shown by copper and copper oxide nanoparticles against a wide variety of microorganisms, including bacteria, viruses, and fungus. Their antimicrobial action involves a number of crucial activities. The following are the primary processes by which copper nanoparticles could exert their antibacterial efficacy:

- 1. Cell Membrane Damage:** Copper nanoparticles possess a high surface area to volume ratio and sharp edges and corners, which can cause cell membrane damage. [12] When in contact with moisture or biological fluids, copper nanoparticles release copper ions (Cu<sup>2+</sup>), which is one of the primary reason underlying their antibacterial activity. These characteristics give them the ability to engage with and pierce bacterial cell membranes. Copper contents are eventually released from the nano-structures whenever they come into surface of the cell membrane and cytosol. Microorganisms are extremely poisonous to these ions. These ions which are already released can systematically interact with the membrane and ultimately can damage the lipid bilayer of the cell membrane, resulting in the release of intracellular substances. They have the capacity to compromise the integrity of the cell membrane, resulting in cellular contents leakage and eventual cell death. In addition, copper ions disturb vital biological functions by attaching to trans-membrane proteins and enzymes that contain the sulphur atom. [13]
- 2. Production of Reactive Oxygen Species (ROS):** Copper nanoparticles have the ability to cause bacterial cells to produce reactive oxygen species (ROS). By producing reactive oxygen species (ROS) through procedures like Fenton-type reactions, copper and copper oxide nanoparticles can cause oxidative stress in microbial cells. Highly reactive chemicals called ROS, including hydrogen peroxide and superoxide radicals, lead to oxidative stress in cells. Naturally cells have the defence mechanism to neutralise the ROS generated from its regular biochemical pathways. But when NPs interact with the cell, the extent of ROS is so high that cell cannot mitigate it. The elevated amount of ROS ultimately destroys the essential protein and lipid inside the cell. Cellular malfunction and eventual death can result from an excessive stockpile of ROS, which can harm proteins, lipids, and DNA. [14-22]
- 3. DNA Damage:** Interactions between copper nanoparticles and bacterial DNA can result in oxidative damage and strand breakage. There are several reports that ROS can degrade the DNA into nucleotide and ultimately destroy the genetic elements. Basically the developed ROS cleaves the phosphor-diester bonds in the nucleic acid. The degradation of DNA neither harms the replication and transcription of DNA but also immediately impairing the bacterial survival and growth. [23-24]

- 4. Protein Denaturation:** By relating with amino acids that contain sulphur, copper nanoparticles can interact with bacterial proteins and alter their natural structures thereby causing denaturation. This may result in protein degradation or aggregation and loss of function, which are essential for the survival and development of bacteria. [25]
- 5. Lipid Denaturation:** One of the important mechanism nanoparticles mediated cytotoxicity is related with the oxidation of membrane lipid. The elevated amount of ROS causes lipid oxidation like protein one. The oxidation of lipid has very severe consequences. Membrane becomes rigid and also fluidity is also lost. Rigid membrane further hampers the essential cellular and biophysical activities. [22]
- 6. Disruption of Ion Homeostasis:** Copper ions emitted from the nanoparticles can interfere with the ion homeostasis of bacteria. Different cellular functions need the maintenance of distinct ion gradients across the membranes of bacterial cells. These gradients may be disturbed by the entry of copper ions, impairing vital cellular processes. [26]
- 7. Intracellular Accumulation of Copper Ions:** Bacterial cells have systems for absorbing copper ions, which are crucial trace metals for numerous cellular activities. However, an excessive build-up of copper ions can overpower these defences, resulting in cell toxicity. [27]
- 8. Nanoparticle Agglomeration:** Copper nanoparticles can aggregate on bacterial cell surfaces, forming physical barriers that obstruct nutrition intake. The bombardment of CuNP on the surface of cell membrane or bacterial outer membrane have effect the formation of big pores and compromises with its membrane integrity. Cell membrane integrity is much needed for the bacterial cell for its waste removal, and other critical bacterial growth processes. [28]
- 9. Enzymatic Activity Inhibition:** Copper nanoparticles have the ability to block important enzymatic processes in bacterial cells as CuNP can denature the intracellular proteins very often. Moreover, many enzymatic functions require the presence of di-valent metals, and copper nanoparticles can interfere with these processes by competitive inhibition mechanism, causing disrupt of cellular metabolism permanently. [29]
- 10. Intracellular Effects:** Copper nanoparticles in any form, can enter easily in different types of microbial cells. Upon entering inside the microbial cells, the stockpile of CuNPs is very often enhanced gradually and it is observed that its substantial accumulate in numerous organelles, including mitochondria may cause cellular damage. This is known as intracellular effects. This interferes with cellular energy production, organelle function, and might be with mitochondrial biogenesis. [30]
- 11. Synergistic Effects:** The synergistic effects Copper nanoparticles are also being manifested when combined with other antimicrobial substances like antibiotics or antifungal medications. The likelihood of microbial resistance is decreased and the total antibacterial action is improved by these synergistic effects.

However, it's also crucial to exactly take into account any hazards that could arise from using copper nanoparticles, including worries about the environment and cytotoxicity to human cells. Therefore, using copper and copper oxide nanoparticles for antimicrobial applications requires rigorous investigation and evaluation. Different scientific communities are also actively investigating CuNP mediated cyto-toxicity in *Caenorhabditis elegans*. [31]

#### IV. FUTURE OUTLOOKS OF COPPER AND COPPER OXIDE NANO PARTICLE

Due to their special characteristics and possible applications, copper and copper oxide nanoparticles have attracted a lot of attention in a number of sectors. Here are a few hypothetical future perspectives:

- 1. Electronics and Optoelectronics:** Due to their high electrical conductivity and possible usage in printed electronics, copper nanoparticles have showed promise in the fields of electronics and optoelectronics. They could also be used in transparent conductive films, conductive inks, and flexible and wearable electronics. Due to their semiconducting characteristics, copper oxide nanoparticles may be used in optoelectronic devices such as solar cells and light-emitting diodes (LEDs). [32]
- 2. Catalysis:** Due to their large surface area and distinctive electrical characteristics, copper nanoparticles, in particular copper oxide nanoparticles, have been investigated as catalysts in a number of chemical processes. They might be applied in procedures like pollutant degradation, hydrogenation, and oxidation. [33]
- 3. Biomedical Applications:** Antimicrobial agents, medication delivery systems, and imaging agents are just a few of the biomedical uses that copper and copper oxide nanoparticles have showed promise in. They are intriguing for battling germs that are resistant to antibiotics because of their antibacterial capabilities.
- 4. Energy Storage:** Due to their high electrical conductivity and catalytic activity, copper-based nanoparticles may be used in energy storage devices like batteries and supercapacitors. [34]
- 5. Environmental Remediation:** Due to their catalytic activity and capacity to absorb contaminants, copper oxide nanoparticles may be used in environmental applications like water purification and pollution removal. [35]
- 6. Research in Nanotechnology:** As the field develops, it's possible that copper and copper oxide nanoparticles will be used for hitherto unrecognised purposes and will exhibit novel features.

Due to their special qualities and prospective uses, copper and copper oxide nanoparticles have attracted a lot of attention in a variety of sectors, including medicine. An overview of the prospective future for copper and copper oxide nanoparticle utilisation in human therapeutics is given below: [36]

- 7. Antibacterial and Antimicrobial Properties:** Copper and copper oxide nanoparticles have excellent antibacterial and antimicrobial characteristics, which have been scientifically shown. They can destroy bacteria and other microbes by rupturing their cell membranes. These nanoparticles could be utilised to create cutting-edge antimicrobial medicines that treat illnesses and stop the spread of bacteria that are resistant to antibiotics. [37]
- 8. Wound Healing:** Copper is known to aid in the healing of wounds and the regeneration of tissues. To encourage quicker and more efficient wound healing, copper and copper oxide nanoparticles could be added to wound dressings or ointments. Additionally, they might aid in lowering the danger of infection in exposed wounds. [38]
- 9. Cancer Treatment:** Studies have looked into the possibility of copper and copper oxide nanoparticles in the treatment of cancer. These nanoparticles might be designed to target cancer cells specifically and transport therapeutic medicines right to the tumour location, causing the least amount of harm to healthy tissues. Additionally, they might be combined with other therapies including radiation therapy and chemotherapy. [39]
- 10. Drug Delivery:** Targeted medication delivery is made possible by nanoparticles, such as copper and copper oxide nanoparticles. They can transport medications and other therapeutic agents to particular cells or tissues because of their small size and distinctive surface characteristics. This might lessen negative effects while improving therapeutic effectiveness.[40]
- 11. Disorders of Copper Metabolism:** Copper is essential for the functioning of the central nervous system, and disorders of copper metabolism have been connected to neurodegenerative diseases including Alzheimer's and Parkinson's. The delivery of therapeutic medicines that alter the amounts of copper in the brain via copper nanoparticles holds the promise of delaying the course of various illnesses. [41]
- 12. Diagnostic Imaging:** Nanoparticles can also be employed in MRI and CT scans, two types of medical imaging. The contrast of pictures could be improved by copper and copper oxide nanoparticles, increasing the diagnostic precision. [42]
- 13. Biocompatibility and Safety:** Securing the biocompatibility and safety of nanoparticles is one of the difficulties associated with using them in medicine. Understanding the possible harmful effects of copper and copper oxide nanoparticles, particularly with chronic exposure, requires further research. Additionally, techniques for regulating their distribution within the body and getting rid of them once their therapeutic purpose has been achieved are required. [43]
- 14. Regulatory Approval:** Prior to receiving regulatory approval for usage in humans, copper and copper oxide nanoparticles would need to undergo extensive testing and evaluation to guarantee their safety and efficacy. The FDA (in the United States) and other regulatory organisations are crucial in determining the advantages and disadvantages of such advances. [44]



MECHANISM OF COLLOIDAL COPPER/ COPPER OXIDE NANOPARTICLES MEDIATED  
BACTERICIDAL ACTIVITY AND ITS MULTI-DIMENSIONAL OUTLOOK IN FUTURE

Overall, copper and copper oxide nanoparticles' prospects for use in human medicinal applications seem positive, but further study, development, and clinical trials are needed to fully grasp their potential and handle any issues that might occur.

## REFERENCE

- [1] Shenmar, R., Norsten, V.B., Rotello, V.M.: Polymer-mediated nanoparticle assembly: structural control and applications. *Adv. Mater.* 6, 657–669 (2005)
- [2] Balzani, V., Credi, A., Venturi, M.: The bottom-up approach to molecular-level devices and machines. *Chem. A Eur. J.* 24, 5524–5532 (2002)
- [3] Lambert, S., Cellier, C., Gaigneaux, E.M., Pirard, J.P., Heinrichs, B.: Ag/SiO<sub>2</sub>, Cu/SiO<sub>2</sub> and Pd/SiO<sub>2</sub> cogelled xerogel catalysts for benzene combustion: relationships between operating synthesis variables and catalytic activity. *Catal. Commun.* 8, 1244–1248 (2007)
- [4] Zhang, H., Zhu, Q., Zhang, Y., Wang, Y., Zhao, L., Yu, B.: One-pot synthesis and hierarchical assembly of hollow Cu<sub>2</sub>O microspheres with nanocrystals-composed porous multishell and their gas-sensing properties. *Adv. Funct. Mater.* 17, 2766–2771 (2007)
- [5] Liu, Z., Bando, Y.: A novel method for preparing copper nanorods and nanowires. *Adv. Mater.* 15, 303–305 (2003)
- [6] Oritz, J.R., Ogura, T., Medina-Valtierra, J., Acosta-Ortiz, S.E., Bosh, P., De las Reyes, J.A., Lara, V.H.: A catalytic application of Cu<sub>2</sub>O and CuO films deposited over fiberglass. *Appl. Surf. Sci.* 174, 177–184 (2001)
- [7] Anzlovar, A., Orel, Z.C., Zigon, M.: Copper (I) oxide and metallic copper particles formed in 1, 2-propane diol. *Eur. Ceram. Soc.* 27, 987–991 (2007)
- [8] Kuo, C.H., Chen, C.H., Huang, M.H.: Seed-mediated synthesis of monodispersed Cu<sub>2</sub>O nanocubes with five different size ranges from 40 to 420 nm. *Nano Today* 5, 106–3780 (2010)
- [9] Jeong, S., Woo, K., Kim, D., Lim, S., Kim, J.S., Shin, H., Xia, Y., Moon, J.: Controlling the thickness of the surface oxide layer on Cu nanoparticles for the fabrication of conductive structures by ink-jet printing. *J. Adv. Funct. Mater.* 18, 679–686 (2008)
- [10] Ayesha Khan, Audil Rashid, Rafia Younas & Ren Chong: A chemical reduction approach to the synthesis of copper nanoparticles. Published: 09 November 2015, 6, 21–26 (2016)
- [11] Ibrahim Khan a, Khalid Saeed b, Idrees Khan c : Nanoparticles: Properties, applications and toxicities. November 2019, Pages 908–931
- [12] Hanna L Karlsson I, Pontus Cronholm, Yolanda Hedberg, Malin Tornberg, Laura De Battice, Sofia Svedhem, Inger Odnevall Wallinder : Cell membrane damage and protein interaction induced by copper containing nanoparticles--importance of the metal release process. PMID: 23891735 DOI: 10.1016/j.tox.2013.07.012
- [13] M. Ahamed, M.A. Siddiqui, M.J. Akhtar, I. Ahmad, A.B. Pant, H.A. Alhadlaq Genotoxic potential of copper oxide nanoparticles in human lung epithelial cells *Biochem. Biophys. Res. Commun.*, 396 (2010), pp. 578–583
- [14] Andreyev A. Y., Kushnareva Y. E., Starkov A. A. Mitochondrial metabolism of reactive oxygen species. *Biochemistry (Moscow)* 2005;70:200–214.
- [15] Turrens J. F. Mitochondrial formation of reactive oxygen species. *J. Physiol.* 2003;552:335–344.
- [16] Balaban R. S., Nemoto S., Finkel T. Mitochondria, oxidants, and aging. *Cell.* 2005;120:483–495.
- [17] Chance B., Sies H., Boveris A. Hydroperoxide metabolism in mammalian organs. *Physiol. Rev.* 1979;59:527–605.
- [18] Cadenas E., Davies K. J. Mitochondrial free radical generation, oxidative stress, and aging. *Free Radical Biol. Med.* 2000;29:222–230.
- [19] Raha S., Robinson B. H. Mitochondria, oxygen free radicals, disease and ageing. *Trends Biochem.* 2000;25:502–508.
- [20] Adam-Vizi V., Chinopoulos C. Bioenergetics and the formation of mitochondrial reactive oxygen species. *Trends Pharmacol. Sci.* 2006;27:639–645.
- [21] Muller F. The nature and mechanism of superoxide production by the electron transport chain. *J. Am. Aging Assoc.* 2000;23:227–253.
- [22] Mechanism of antibacterial activity of copper nanoparticles Arijit Kumar Chatterjee, Ruchira Chakraborty and Tarakdas Basu Department of Biochemistry and Biophysics, University of Kalyani, Kalyani-741 235, West Bengal, India

MECHANISM OF COLLOIDAL COPPER/ COPPER OXIDE NANOPARTICLES MEDIATED  
BACTERICIDAL ACTIVITY AND ITS MULTI-DIMENSIONAL OUTLOOK IN FUTURE

- [23] Gonealez Lison D, Krisch-Volders M. Gneotoxicity of engineered nanomaterials: a critical review. *Nanotoxicology*. 2008;2:252–273.
- [24] Landsiedel R, Kapp MD, Schulz M, Wiench K, Oesch F. Genotoxicity investigation on nanomaterials: methods, preparation and characterization of test material, potential artifacts and limitations-many questions, some answers. *Mutat. Res*. 2009;681:541–528.
- [25] C Boitard, A Michel, C Ménager, N Griffete : Protein Denaturation Through the Use of Magnetic Molecularly Imprinted Polymer Nanoparticles .*Molecules*, 2021•mdpi.com
- [26] Charlotte Boitard, Aude Michel, Christine Ménager,\* and Nébéwia Griffete\*Interactions of nanomaterials with ion channels and related mechanisms
- [27] Yang-yang Niu, Ying-ying Zhang, Zhi Zhu, Xiao-qin Zhang, Xi Liu, Sai-ya Zhu, Ye Song, Xian Jin, Bengt Lindholm, and Chen YuElevated intracellular copper contributes a unique role to kidney fibrosis by lysyl oxidase mediated matrix crosslinking
- [28] One-Step Fabrication of Copper Electrode by Laser-Induced Direct Local Reduction and Agglomeration of Copper Oxide Nanoparticle Bongchul Kang, Seungyong Han, Jongsu Kim, Seunghwan Ko, and Minyang Yang\*
- [29] Zhao, Xiaoxuan Su, Yiyu Wang, Xiangyu Yang, Mohan Bi, Qiang He, Yi Chen: Copper oxide nanoparticles inhibited denitrifying enzymes and electron transport system activities to influence soil denitrification and N2O emission
- [30] M. Studer, Ludwig K. Limbach, Luu Van Duc, Frank Krumeich, Evagelos K. Athanassiou, Lukas C. Gerber, Holger Moch, Wendelin J. Stark: Nanoparticle cytotoxicity depends on intracellular solubility: Comparison of stabilized copper metal and degradable copper oxide nanoparticles.
- [31] Fang Liu, Yi Xiao, Xing-Lai Ji, Ke-Qin Zhang & Cheng-Gang Zou: The cAMP-PKA pathway-mediated fat mobilization is required for cold tolerance in *C. elegans*. Published: 04 April 2017
- [32] panelJie Xue, Jizhong Song, Yuhui Dong, Leimeng Xu, Jianhai Li, Haibo Zeng :Nanowire-based transparent conductors for flexible electronics and optoelectronics
- [33] **Hany A. Elazab**, *Missouri University of Science and Technology*: The Catalytic Activity of Copper Oxide Nanoparticles Towards Carbon Monoxide Oxidation Catalysis: Microwave – Assisted Synthesis Approach.
- [34] Dipanwita Majumdar a, Srabanti Ghosh b 1: Recent advancements of copper oxide based nanomaterials for supercapacitor applications. February 2021, 101995
- [35] Joshua, O. Ighalo, Patience, A. Sagboye , Great Umenweke , Oluwaseun J. Ajala , Fredrick, O. Omoarukhe , Comfort A. Adeyanju , Samuel Ogunniyi , Adewale G. Adeniyi: CuO nanoparticles (CuO NPs) for water treatment: A review of recent advances. May 2021, 100443
- [36] Sunday Adewale Akintelu , Aderonke Similoluwa Folorunso , Femi Adekunle Folorunso, Abel Kolawole Oyebamiji: Green synthesis of copper oxide nanoparticles for biomedical application and environmental remediation. *Heliyon* 6 (2020) e04508.
- [37] S. Anita, T. Ramachandran, [...], and M. Mahalakshmi, A study of the antimicrobial property of encapsulated copper oxide nanoparticles on cotton fabric. April 8, 2011.
- [38] A. A. Rakhmetova, T. P. Alekseeva, O. A. Bogoslovskaya, I. O. Leipunskii, I. P. Ol'khovskaya, A. N. Zhigach & N. N. Glushchenko : Wound-healing properties of copper nanoparticles as a function of physicochemical parameters .271–276 (2010)
- [39] Torki A. Zughaibi, Ahmed A. Mirza, Mohd Suhail, Nasimudeen R. Jabir, Syed Kashif Zaidi, Samina Wasi, Ayat Zawawi, and Shams Tabrez, Evaluation of Anticancer Potential of Biogenic Copper Oxide Nanoparticles (CuO NPs) against Breast Cancer. 11 Apr 2022
- [40] Yashar Ahmadian, Asghar Bakravi, Hamed Hashemi & Hassan Namazi : Synthesis of polyvinyl alcohol/CuO nanocomposite hydrogel and its application as drug delivery agent. 1967–1983 (2019).
- [41] Valentín Ceña and Pablo Játiva: Nanoparticle crossing of blood–brain barrier: a road to new therapeutic approaches to central nervous system diseases. 12 Jul 2018.
- [42] Xiangjun Han, Ke Xu, Olena Taratula, and Khashayar Farsad: Applications of Nanoparticles in Biomedical Imaging.
- [43] S.M. Gowtham, R. Dhivya, L. Muthulakshmi, S. Sureshkumar, M. Ashraf, M. Pandi, J. Mayandi, J. Annaraj, Suresh Sagadevan: Environmentally benign and biocompatible CuO@Si core-shell nanoparticles: As electrochemical l-cysteine sensor, antibacterial and anti-lung cancer agents. 15 March 2023, Pages 10023-10031
- [44] Puja Kumari, Pritam Kumar Panda, Ealisha Jha, Khushboo Kumari, Kumari Nisha, M. Anwar Mallick & Suresh K. Verma :Mechanistic insight to ROS and Apoptosis regulated cytotoxicity inferred by Green synthesized CuO nanoparticles from *Calotropis gigantea* to Embryonic Zebrafish. 24 November 2017, Article number: 16284 (2017)

