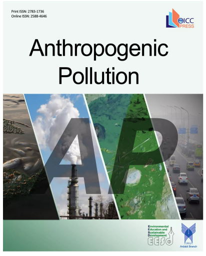

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A review on toxicity of metal oxide nanoparticles: impacts on reproductive system and respiratory tissues

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Abstract:
A nanoparticle is a small particle that ranges between 1 to 100 nanometers in size. Undetectable by the human eye, nanoparticles can exhibit significantly different physical and chemical properties to their larger material counterparts. Metal oxide nanoparticles pollution has become a major environmental concern due to its widespread production and usage. The potential toxic effects of nanoparticles on human and animal health have been investigated, but their impact on urban animals remains poorly understood. This study provides evidence that exposure to metal oxide nanoparticles leads to significant toxicity in the ovarian and respiratory tissues of urban animals. These findings highlight the importance of monitoring and controlling the release of nanoparticles into the environment to protect the health of animals and humans. Thus, the effects of metal oxide nanoparticles on urban animals provides valuable insights into the potential risks and environmental safety concerns. Continued research in this field is crucial for sustainable development and protection of both human and animal health.

Keywords: Nanoparticles; Tissues; Ovarian; Reproductive system; Animals

1. Introduction

The impact of nanoparticles on biological systems has emerged as a subject of immense concern in recent years, captivating the attention of researchers and scientists alike. Specifically, the ramifications of nanoparticles on the reproductive system and respiratory tissues of urban animals have garnered noteworthy scrutiny. The comprehension of the potential perils associated with the exposure to metal oxide nanoparticles assumes paramount importance in evaluating the environmental safety of these minuscule entities (Exbrayat et al. 2015; Brohi et al. 2017). The increasing prevalence of nanoparticle utilization across diverse industries has further accentuated the urgency of understanding their implications. These diminutive particles boast an array of distinctive properties that render them exceptionally versatile and invaluable in an expansive spectrum of applications. However, as the utilization of nanoparticles continues to surge, apprehensions have been duly raised regarding their potential repercussions on the environment and the living organisms inhabiting it, including animals. Particularly, the profound impact of copper oxide nanoparticles (CuO NPs) on the reproductive system of animals has elicited significant attention from the scientific community (Anreddy 2018; De Jong et al. 2019).

2. Understanding nanoparticles

Nanoparticles, which are meticulously crafted substances, exhibit unique and discernible characteristics in comparison to their larger-scale equivalents. These minute entities can be classified into diverse categories, encompassing metal-based nanoparticles like gold and platinum, carbon-based nanoparticles such as carbon nanotubes, and metal oxide nanoparticles like titanium oxide. What distinguishes these nanoparticles is their ability to infiltrate the human body through a range of diverse entry points, including intravenous injection, inhalation, or ingestion (Sims et al. 2017; Santacruz-Márquez et al. 2021a).

2.1 Transplacental penetration

One aspect that warrants attention is the phenomenon of transplacental penetration of nanoparticles, denoting the capacity of nanoparticles to traverse the placental barrier and attain the nascent fetus. Empirical investigations have demonstrated that specific nanoparticles, including gold nanoparticles and carbon nanotubes, exhibit the ability to cross the placental barrier and amass in the tissues of the developing fetus. This observation gives rise to apprehensions regarding plausible developmental complications and genetic irregularities in the subsequent progeny. Consequently, the transplacental migration of nanoparticles emerges as a significant area of concern warranting further exploration and investigation (Braydich-Stolle et al. 2010; Ema et al. 2017; Araújo et al. 2020).

2.2 Mechanisms of nanoparticle toxicity

The toxicity associated with nanoparticles, such as CuO NPs, can be attributed to a multitude of underlying mechanisms. Among these mechanisms, the primary one involves the generation of reactive oxygen species (ROS) and subsequent induction of oxidative stress. CuO NPs have the capability to incite the production of ROS within cells, which in turn can lead to detrimental cellular damage and impair various physiological processes. The heightened levels of ROS induced by CuO NPs can disrupt the delicate balance of antioxidant defense mechanisms, thereby instigating oxidative stress and resulting in tissue damage (He et al. 2023). In addition to their ability to induce oxidative stress, CuO NPs have also been observed to elicit genotoxic effects through the infliction of DNA damage. The interaction between CuO NPs and DNA molecules can trigger the occurrence of DNA strand breaks and chromosomal aberrations, thus contributing to genotoxicity. It is worth noting that this genotoxicity can potentially give rise to long-term consequences, including the development of cancerous cells. Furthermore, the direct interaction between CuO NPs and cellular membranes can be deemed a crucial aspect in understanding their toxicity, as it leads to membrane disruption and subsequent compromise of cell integrity. This interaction can result in membrane damage, disturbances in ion balance, as well as alterations in various cell signaling pathways. Ultimately, these disturbances have the potential to culminate in cell death or dysfunction (Braydich-Stolle et al. 2010; Buchman et al. 2019).

2.3 Reproductive toxicity of copper oxide nanoparticles

The impact of exposure to CuO NPs on the reproductive system of urban animals, such as zebrafish, can be profound, as evidenced by a study conducted by Guizhu (Lue et al. 2023). In this study, female and male zebrafish were subjected to low concentrations of CuO NPs for a duration of 20 days. The researchers observed that the structure of the zebrafish ovary and testis suffered impairments, highlighting the vulnerability of these vital reproductive organs to the toxic effects of CuO NPs. Moreover, the levels of 17β-estradiol (E2), a key female sex hormone, showed an increase in both females and males, while the levels of testosterone (T), a crucial male sex hormone, experienced a decrease. This perturbation in sex hormone levels signifies the disruption inflicted by CuO NPs on the delicate balance of the zebrafish reproductive system (Lue et al. 2023).
To gain a deeper understanding of the toxic mechanisms at play, the researchers delved into the examination of gene expression along the hypothalamic pituitary-gonad (HPG) axis, a critical pathway involved in reproductive function. In female zebrafish, the levels of erα/er2β and cyp19a were found to be up-regulated, suggesting an increased activity of estrogen receptors and aromatase, an enzyme involved in estrogen synthesis. Similarly, in male zebrafish, the expression of erα/er2β, lhr, hmgra/hmgrb, 3β hsd, and 17β hsd was up-regulated, indicating an elevated activity of estrogen receptors, luteinizing hormone receptor, and key enzymes involved in testosterone synthesis. In contrast, the level of αr, an androgen receptor, was down-regulated in both female and male zebrafish. These differential gene expression patterns further reinforce the detrimental impact of long-term exposure to low doses of CuO NPs on the endocrine system, gonad development, and the intricate network of genes within the HPG axis. The study conducted by Guizhu (Lue et al. 2023) significantly contributes to the existing body of toxicological data pertaining to the effects of nanoparticles on aquatic vertebrates. By shedding light on the reproductive toxicity caused by CuO NPs in urban animals, this study offers invaluable insights into the potential risks associated with exposure to these nanoparticles. An understanding of these effects is crucial for accurately assessing the environmental safety of nanoparticles, as it allows for informed decision-making and the implementation of appropriate measures to mitigate any potential harm caused by these emerging contaminants. In conclusion, the research conducted by Guizhu (Lue et al. 2023) brings forth a wealth of knowledge on the adverse effects of CuO NPs on the reproductive system of zebrafish, underscoring the importance of continued investigation into the potential hazards posed by nanoparticles in our urban ecosystems (Sherins and Hodgen 1976; McAuliffe and Perry 2007; Abou-ElNaga et al. 2017; Lue et al. 2023).

3. Impact on respiratory tissues

Apart from concerns surrounding reproductive toxicity, there is also a growing apprehension regarding the impact of Copper Oxide nanoparticles (CuO NPs) on the respiratory tissues of urban animals. In order to explore this matter further, a study conducted by aimed to investigate the effects of CuO NPs on the respiratory tissues in a specific animal model (Hou et al. 2017). To accomplish this, the researchers exposed the animal model to varying concentrations of CuO NPs and subsequently assessed the changes that occurred in the structure and function of the lung tissue. It is well-established that inhalation exposure to copper nanoparticles can result in severe respiratory and cardiovascular diseases (Yazdi et al. 2023).
This is primarily due to the toxic nature of the particles, which can be attributed to their ultrafine size, chemical reactivity, and extended residence time in the atmosphere. As the particles decrease in size, their ability to penetrate deep into the lungs is enhanced. Consequently, owing to their ultrafine size and prolonged retention time, nanoparticles have the capacity to diffuse and accumulate in the alveolar region.(Fahmy and Cormier 2009) Moreover, some of these nanoparticles are capable of passing through the alveolar epithelium and capillary endothelial cells, thereby gaining access to the cardiovascular system and other internal organs. The outcomes of the aforementioned study demonstrated

that exposure to CuO NPs resulted in significant alterations within the respiratory tissues of the animal model under investigation. Specifically, the lung tissue exhibited signs of inflammation and oxidative stress, which were characterized by heightened levels of pro-inflammatory cytokines and reactive oxygen species (ROS) (Sims et al. 2017); (Elbakary et al. 2018). Furthermore, the researchers also observed instances of damage to the alveolar epithelial cells, as well as fibrosis within the lung tissue. These findings indicate that CuO NPs possess the potential to induce respiratory toxicity within urban animals. Furthermore, the inflammation and oxidative stress that occur within the respiratory tissues have the capacity to compromise lung function and overall respiratory health. Therefore, it is imperative that further studies be conducted in order to gain a comprehensive understanding of the mechanisms that underlie the respiratory effects of CuO NPs (Hou et al. 2017).

4. Effects of NPs on ovarian tissues

Numerous investigations have demonstrated the deleterious impacts that nanoparticles (NPs) have on the ovarian tissues of animals (Santacruz-Márquez et al. 2021b). Multiple research studies have underscored the potential toxicity that NPs possess on the reproductive system, specifically on the growth and operation of the ovaries. For example, experiments conducted on rodents have proven that exposure to specific types of NPs, such as silver nanoparticles (Ag-NPs) and titanium dioxide nanoparticles (TiO_2-NPs), can disturb the normal physiological mechanisms of the ovaries, resulting in reproductive abnormalities and diminished fertility (Rollerova et al. 2015; Steuber et al. 2016). In a study involving mice, it was ascertained that exposure to Ag-NPs measuring 25, 40, or 80 nm triggered oxidative stress in the ovaries, which was characterized by the presence of reactive oxygen species (ROS), DNA damage, and cell apoptosis. These effects were more pronounced with smaller-sized NPs, thus indicating that the size of NPs plays a substantive role in their toxicity. Similarly, TiO_2-NPs have been proven to provoke DNA damage and apoptosis in the ovaries of mice, consequently impeding their reproductive capacities. Furthermore, investigations conducted on fish species, such as zebrafish and trout, have furnished additional evidence pertaining to the harmful effects of NPs on ovarian tissues. Experiments carried out on zebrafish embryos that were exposed to Ag-NPs revealed developmental anomalies in the ovaries, including malformations and impaired functionality. Similarly, trout that were subjected to TiO_2-NPs exhibited pathologies in the ovaries, such as edema and thickening of the gill lamellae, as well as alterations in reproductive gene expression. These findings unequivocally indicate that NPs have the capability to disrupt the normal functioning of ovarian tissues, thereby precipitating reproductive dysfunctions and a decline in fertility among urban animals (Steuber et al. 2016; Santacruz-Márquez et al. 2021b).

5. Impact on embryo and offspring

Exposure to nanoparticles during the gestational period of pregnancy can have deleterious consequences on the developing embryo and subsequent offspring. Scientific investigations have demonstrated that specific types of nanoparticles, such as gold nanoparticles and silica-coated magnetite nanoparticles, possess the capability to induce skeletal abnormalities and phenotypic flaws in the offspring (Ma et al. 2018; Teng et al. 2021; Geng et al. 2023). Additionally, other research studies have reported an augmented mortality rate during the lactation phase and reduced growth of offspring that have been exposed to nanoparticles. Furthermore, it has been observed that nanoparticles have the capacity to disrupt the expression of genes that are crucial for embryonic development. This disruption can ultimately result in abnormal development and potential birth defects in the offspring. Although the precise mechanisms underlying these effects are still undergoing investigation, it is evident that nanoparticles can have severe implications for the health and overall well-being of the offspring (Sadrieh et al. 2010; Shahin and Mohamed 2017; Wu et al. 2022).

6. Environmental safety concerns

The employment of nanoparticles, including CuO NPs, on a widespread scale raises apprehensions regarding their environmental safety. The release of nanoparticles into the environment, whether it be through industrial processes or through consumer products, has the potential to result in their accumulation within aquatic ecosystems and urban areas. It is of utmost importance to meticulously evaluate the potential toxic effects of these nanoparticles on urban wildlife and their associated ecosystems in order to ensure their environmental safety. In order to ascertain the long-term effects of nanoparticles on different organisms and ecosystems, it is essential to conduct comprehensive studies, such as the ones that have been discussed in this particular article. These studies provide invaluable insights into the potential risks that are associated with exposure to nanoparticles. Furthermore, these studies contribute to the formulation of guidelines and regulations that serve to mitigate the environmental impact of nanoparticles (Kim et al. 2006; Nohynek et al. 2007; Schug et al. 2013; Mohammadi-Aloucheh et al. 2018; Ighalo et al. 2021).

6.1 Understanding the reproductive toxicity of CuO NPs

Researchers have undertaken studies to investigate the reproductive toxicity that is caused by CuO NPs in animals. Female and male zebrafish were selected as model organisms to assess the effects of CuO NPs on their reproductive system. These zebrafish were subjected to low concentrations of CuO NPs (10, 50, and 100 μg/L) for a duration of 20 days. Upon the completion of the exposure period, it was observed that the structure of the zebrafish ovaries and testes had been compromised. Furthermore, there was an increase in the levels of 17β-estradiol (E2) in both female and male zebrafish, while the levels of testosterone (T) were found to be diminished. These findings suggest that an imbalance in sex hormones is induced by CuO NPs. In addition, an analysis of the expression of genes along the hypothalamic pituitary-gonad (HPG) axis, which plays a pivotal role in reproductive function, was conducted. The study revealed that several genes involved in the HPG axis

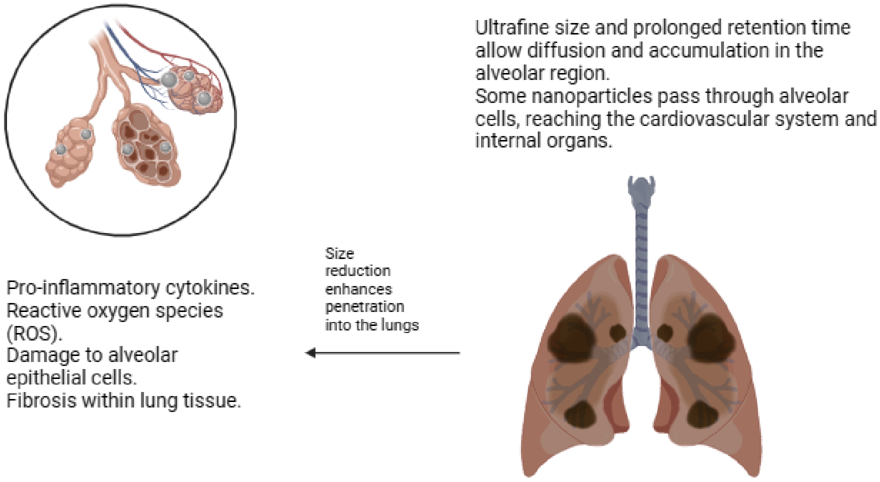

Figure 1. CuO NPs have the potential to induce respiratory toxicity in animals. Inflammation and oxidative stress may compromise lung function and overall respiratory health.

were up-regulated in both female and male zebrafish, while others were down-regulated. These results provide evidence that prolonged exposure to low doses of CuO NPs can lead to endocrine disorders, hindered development of gonads, and alterations in the expression of genes within the HPG axis(Mavon et al. 2006; McAuliffe and Perry 2007; Gallo et al. 2018)Mohammadi-Aloucheh et al,. 2021) .

6.2 Implications for environmental safety

The results obtained from this scientific investigation yield significant and valuable perspectives into the toxicological ramifications of nanoparticles on aquatic vertebrates, thus making a substantial contribution towards the evaluation and determination of environmental safety (Kumah et al. 2023). It is worth noting that copper oxide nanoparticles are extensively employed across a diverse range of industries, thus warranting careful scrutiny and deliberation with regards to their potential impact on the reproductive system of animals, thereby arousing concerns and raising questions pertaining to their broader environmental implications. Therefore, it is of utmost importance to comprehend and grasp the underlying mechanisms by which CuO NPs may influence reproductive function, as this knowledge is indispensable for the formulation and development of effective strategies aimed at mitigating any potential negative effects that may arise as a result of their usage and presence in the environment (Kiss 2009; Suarasan et al. 2018; Yusefi-Tanha et al. 2020; Martin et al. 2023)Mohammadi-Aloucheh et al,. 2021).

7. The role of nanotechnology in agriculture

The continuously increasing global human population presents a significant challenge in terms of ensuring food security for this expanding population. It is imperative to find innovative approaches to address this challenge and reduce food wastage, which amounts to approximately 1.3 billion tons of edible food materials wasted on an annual basis. In this regard, nanotechnology has emerged as a promising solution that offers various strategies to overcome the obstacles associated with food and agricultural loss (Singh et al. 2023; Philbrook et al. 2011; Neme et al. 2021) Rashidian et al., 2021).

One of the key applications of nanotechnology in agriculture is the development of novel nanoantimicrobials, which have the potential to revolutionize the field. Metal nanoparticles, such as copper nanoparticles (CuNPs), have demonstrated remarkable antimicrobial properties that can be effectively utilized for managing plant diseases. The utilization of CuNPs as a tool for combating plant pathogens, including bacteria, fungi, and viruses, has proven to be highly effective (Rajeshkumar et al. 2019; Phan et al. 2020; Rojas et al. 2021) .

The use of nanotechnology in agriculture holds great promise in addressing the challenges faced by the global food industry. By harnessing the potential of nanomaterials, it is possible to enhance food production and reduce wastage significantly. Nanotechnology offers a wide range of innovative approaches, including the development of nanoantimicrobials, to combat plant diseases and ensure the health and productivity of crops (Hotessa Halake, Muda Haro, et al. 2022).

Nanoantimicrobials, such as CuNPs, have been extensively studied and have shown great potential in managing plant diseases. The unique properties of CuNPs, such as their small size and high surface area-to-volume ratio, enable them to interact with pathogens at a molecular level and inhibit their growth. This antimicrobial activity of CuNPs has been observed against a wide range of plant pathogens, making them a versatile and effective tool in the field of agriculture (El-Saadony et al. 2022).

In addition to their antimicrobial properties, nanomaterials have the potential to revolutionize other aspects of agriculture as well. For example, the use of nanosensors can enable real-time monitoring of plant health and environmental conditions, allowing for precise and targeted application of resources such as water and fertilizers. Nanocarriers can also be utilized to deliver nutrients and pesticides directly to plants, minimizing wastage and enhancing their efficacy (Hotessa Halake, Muda Haro, et al. 2022).

Furthermore, nanotechnology can also play a crucial role in improving the nutritional quality of crops. Nanoparticles can be used to fortify crops with essential nutrients, such as iron and zinc, to address micronutrient deficiencies in certain regions. This approach holds great potential in tackling malnutrition and improving the overall health and well-being of populations (Neme et al. 2021; Hotessa Halake, Muda Haro, et al. 2022).

In conclusion, the growing global human population presents a significant challenge in terms of ensuring food security. However, nanotechnology offers innovative solutions to overcome these challenges and reduce food wastage. The development of nanoantimicrobials, such as CuNPs, holds great promise in managing plant diseases and enhancing crop productivity. Furthermore, the use of nanosensors, nanocarriers, and nanoparticle fortification can revolutionize various aspects of agriculture, including resource management and crop nutrition. By harnessing the potential of nanotechnology, it is possible to address the challenges of food security and pave the way for a sustainable and prosperous future (Singh et al. 2023).

7.1 Utilizing CuNPs for food preservation

Food preservation is an extremely crucial component in the realm of ensuring the safety of consumable goods and minimizing the detrimental effects of food spoilage. A notable area that has been explored in the quest for achieving this objective is the utilization of CuNPs, or copper nanoparticles, which possess promising potential in inhibiting the proliferation of microorganisms responsible for food spoilage. In order to harness the inhibitory effects of CuNPs against various food spoilage bacteria, researchers have dedicated their efforts towards the development of agar-based nanocomposite films that incorporate these nanoparticles. These innovative films have exhibited remarkable efficacy in preventing the growth of food spoilage microorganisms, thereby proving their value as packaging materials that can tangibly extend the shelf life of diverse food products (Arfat et al. 2017; Mohammadi-Aloucheh et al. 2018).

Moreover, the antimicrobial activity of CuNPs has been found to be particularly noteworthy in the context of combating the prevalence of common food-borne pathogens, such as Salmonella enterica and Campylobacter jejuni. The application of CuNPs in the realm of food preservation not only contributes towards diminishing the risk of foodborne illnesses, but also serves as a formidable instrument in bolstering the overall safety of food products. By incorporating CuNPs into food preservation practices, it becomes possible to enhance the protection against the aforementioned pathogens, which can inflict severe harm upon human health. This pioneering approach, therefore, deserves significant recognition due to its ability to revolutionize the realm of food safety and safeguard the well-being of consumers. Consequently, it is imperative to further explore and exploit the immense potential that CuNPs possess in order to optimize their effectiveness and foster the continued advancement of food preservation practices (Sportelli et al. 2019; Mamman et al. 2023).

In conclusion, the integration of CuNPs into the domain of food preservation presents a compelling avenue towards ensuring the safety of food products and mitigating the adverse effects of food spoilage. The development of agar-based nanocomposite films containing CuNPs has showcased their inhibitory effects against a wide range of food spoilage bacteria, thereby making them invaluable as packaging materials that can effectively hinder microbial growth and extend the shelf life of consumable goods. Additionally, the remarkable antimicrobial activity of CuNPs against common food-borne pathogens further emphasizes their potential in reducing the risk of foodborne illnesses and elevating the overall safety of food products. The utilization of CuNPs in food preservation practices, therefore, warrants comprehensive exploration and exploitation to maximize their efficacy and propel the continuous progress in the field of food safety (Arfat et al. 2017).

7.2 CuNPs as plant nutrients

Plants necessitate a variety of nutrients to facilitate their growth and development. Among these nutrients, copper holds a paramount importance as an indispensable micronutrient for plants. Its role in fundamental processes such as chlorophyll synthesis, protein and carbohydrate metabolism, and overall plant growth cannot be undermined (Rai et al. 2018; Bahrulolum et al. 2021). In light of this, researchers have delved into exploring the potential of CuNPs as plant nutrients. These nanoparticles possess the unique ability to offer plants with a form of copper that is readily available and easily absorbed. Research has demonstrated that CuNPs can exert a positive influence on seed germination as well as root growth in various crops, including soybean and chickpea. Furthermore, the application of CuNPs has been found to contribute to enhanced plant growth and increased crop yield in wheat. Nonetheless, it is imperative to acknowledge that the concentration of CuNPs must be carefully regulated, as excessive amounts can have detrimental effects on plant growth. This underscores the significance of establishing appropriate dosage and application methods to ensure optimal outcomes (Song et al. 2016; Saran et al. 2018; Bakshi and Kumar 2021).

7.3 CuNPs for insect pest and disease management

In addition to their crucial role as vital nutrients for plants, copper nanoparticles (CuNPs) have exhibited tremendous potential in the management of pests and diseases in the field of agriculture. For many years, copper has been employed as a potent fungicidal agent to safeguard crops against devastating fungal diseases. However, the unique properties of CuNPs have further augmented their antimicrobial efficacy, enabling them to effectively combat an extensive array of plant pathogens, including both fungi and bacteria (Dassanayake et al. 2021).

Numerous researchers have conducted studies to showcase the remarkable effectiveness of CuNPs in controlling a wide range of diseases such as downy mildew, blight, and rust in diverse crops such as tea, banana, cocoa, citrus, and coffee. Furthermore, the utilization of CuNPs in the realm

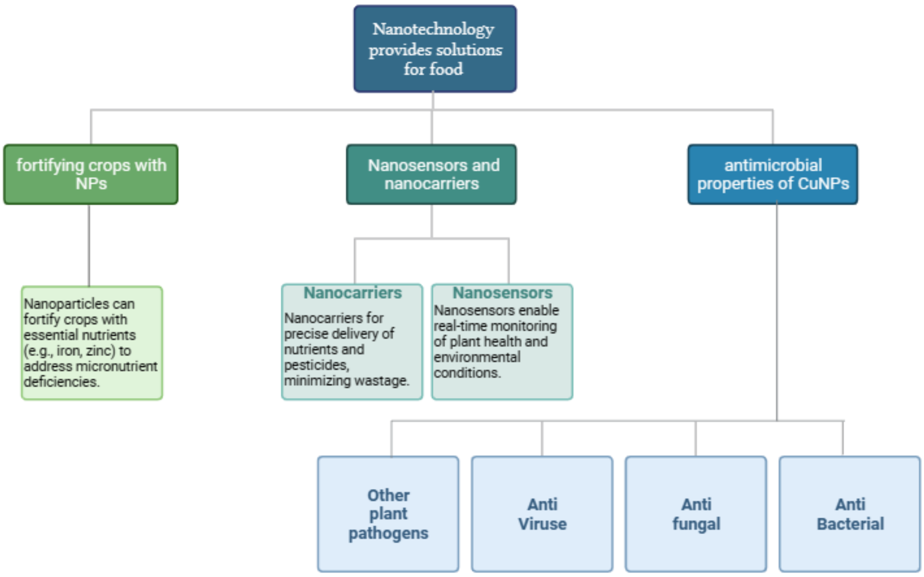

Figure 2. Nanotechnology provides solutions for food security challenges through the development of nanoantimicrobials and innovative applications, implying that nanotechnology can revolutionize agriculture, offering sustainable solutions for the future.

of organic farming as a plant protectant has also been explored, thereby offering a sustainable approach to disease management. Nevertheless, it is crucial to note that there is still a requirement for additional research endeavors in order to optimize the application methods of CuNPs and simultaneously minimize their potential environmental impact, ensuring a balance between effective pest and disease management and ecological sustainability (Headrick 2021).

8. Mechanisms of action of CuNPs against microbes

The antimicrobial action of CuNPs is ascribed to several mechanisms that have been extensively studied and documented in scientific literature. When CuNPs come into contact with microbial cells, they exhibit a remarkable ability to release copper ions, which subsequently interact with the cell wall, thereby initiating a cascade of events that ultimately culminate in the generation of reactive oxygen species (ROS) and membrane damage. This intricate process has been found to disrupt various cellular metabolic pathways, leading to oxidative stress and interfering with protein synthesis and DNA structure. Consequently, the cumulative effect of these multifaceted actions results in the inevitable demise of the microbial cell (Rong-Mullins et al. 2017; Phan et al. 2020; Salah et al. 2021; Ma et al. 2022). It is worth noting that the size of CuNPs, along with their electrostatic properties, collectively contribute to the overall susceptibility of microbes to the antimicrobial activity of CuNPs. Moreover, the specific composition of microbial cell walls and membranes also plays a pivotal role in determining the extent to which these organisms are affected by the presence of CuNPs. For instance, certain microbes possess cell walls and membranes that possess intrinsic characteristics rendering them more resistant to the antimicrobial action of CuNPs, thereby necessitating a comprehensive understanding of these intricate mechanisms in order to devise effective and targeted nano-based antimicrobial strategies (Essa and Khallaf 2016; Rong-Mullins et al. 2017; Mohammadi-Aloucheh et al. 2018; Ermini and Voliani 2021; Rojas et al. 2021)

9. Concerns and future perspectives

However, despite the numerous benefits associated with the use of CuNPs in agriculture and food sectors, it is imperative to consider the potential risks and environmental implications that may arise from their application. It is incumbent upon researchers and scientists to delve deeper into the accumulation, biomagnification, and biotransformation of nanoparticles in food crops, as further investigation is necessary to ensure the safe and sustainable implementation of these nanoparticles in these crucial sectors. By conducting rigorous studies and assessing the potential long-term effects of CuNPs on the environment and living organisms, we can gain valuable insights into the optimal dosage and application methods of CuNPs, with the ultimate goal of minimizing any negative repercussions that may arise (Pandit et al. 2017).
Moreover, it is imperative to explore alternative materials and approaches that can be employed in order to reduce the over-reliance on CuNPs, thereby mitigating any potential harm to the environment. By diversifying our range of antimicrobial agents and developing more environmentally friendly solutions for agriculture and food production, we can contribute to a more sustainable and resilient future. Therefore, it is imperative that future research endeavors focus on expanding our knowledge base in this field, as this will undoubtedly pave the way for the development of safer and more effective strategies that can be employed in various sectors. In conclusion, the antimicrobial action of CuNPs is indeed a fascinating field that holds immense po-

tential for the betterment of society, and it is our responsibility to ensure that this potential is harnessed in the most prudent and sustainable manner possible (Longmire et al. 2008; Pandit et al. 2017).

10. Conclusion

The effects of nanoparticles, specifically copper oxide nanoparticles, on the reproductive system and respiratory tissues of urban animals are of great concern. Studies have shown that exposure to CuO NPs can lead to reproductive toxicity, disrupting the endocrine system and impairing gonad development. Furthermore, CuO NPs can induce respiratory toxicity, causing inflammation, oxidative stress, and tissue damage in the lungs. Understanding the mechanisms underlying nanoparticle toxicity is essential for evaluating the environmental safety of nanoparticles. The generation of reactive oxygen species, genotoxicity, and membrane interactions are among the key mechanisms by which nanoparticles exert their toxic effects. To ensure environmental safety, further research is needed to assess the long-term effects of nanoparticles on urban animals and their ecosystems. This research will contribute to the development of strategies and regulations to minimize the potential risks associated with nanoparticle exposure. In conclusion, the study of the effects of nanoparticles on urban animals provides valuable insights into the potential risks and environmental safety concerns. Continued research in this area is crucial for sustainable development and the protection of both human and animal health. The use of nanoparticles, particularly copper oxide nanoparticles, in agriculture and food sectors has the potential to revolutionize these industries. CuNPs offer unique properties that can be harnessed for plant protection, food preservation, and improved crop yield. However, it is essential to consider the potential environmental and health impacts of CuNPs and develop sustainable and responsible approaches for their use. Further research is needed to fully understand the mechanisms of action of CuNPs and optimize their application in agriculture and food systems.

Conflict of interest statement
The authors declare that they have no conflict of interest.

References

Abou-ElNaga A, Mutawa G, El-Sherbiny IM, Abd-ElGhaffar H, Allam AA, Ajarem J, Mousa SA (2017) Novel nano-therapeutic approach actively targets human ovarian cancer stem cells after xenograft into nude mice. *International Journal of Molecular Sciences* 18 (4): 813. https://doi.org/10.3390/ijms18040813

Anreddy RNR (2018) Copper oxide nanoparticles induces oxidative stress and liver toxicity in rats following oral exposure. *Toxicology Reports* 5:903–904. https://doi.org/10.1016/j.toxrep.2018.08.022

Araújo TE de, Milián ICB, Souza G de, Silva RJ da, Rosini AM, Guirelli PM, Franco PS, Barbosa BF, Ferro EAV, Costa IN da (2020) Experimental models of maternal–fetal interface and their potential use for nanotechnology applications. *Cell Biology International* 44 (1): 36–50.

Arfat YA, Ahmed J, Jacob H (2017) Preparation and characterization of agar-based nanocomposite films reinforced with bimetallic (Ag-Cu) alloy nanoparticles. *Carbohydrate Polymers* 155:382–390.

Bahrulolum H, Nooraei S, Javanshir N, Tarrahimofrad H, Mirbagheri VS, Easton AJ, Ahmadian G (2021) Green synthesis of metal nanoparticles using microorganisms and their application in the agrifood sector. *Journal of Nanobiotechnology* 19 (1): 1–26. https://doi.org/10.1186/s12951-021-00834-3

Bakshi M, Kumar A (2021) Copper-based nanoparticles in the soil-plant environment: Assessing their applications, interactions, fate and toxicity. *Chemosphere* 281:130940. https://doi.org/10.1016/j.chemosphere.2021.130940

Braydich-Stolle LK, Lucas B, Schrand A, Murdock RC, Lee T, Schlager JJ, Hussain SM, Hofmann M-C (2010) Silver nanoparticles disrupt GDNF/Fyn kinase signaling in spermatogonial stem cells. *Toxicological sciences* 116 (2): 577–589. https://doi.org/10.1093/toxsci/kfq148

Brohi RD, Wang L, Talpur HS, Wu D, Khan FA, Bhattarai D, Rehman Z-U, Farmanullah F, Huo L-J (2017) Toxicity of nanoparticles on the reproductive system in animal models: a review. *Frontiers in Pharmacology,* 606. https://www.frontiersin.org/articles/10.3389/fphar.2017.00606

Buchman JT, Hudson-Smith NV, Landy KM, Haynes CL (2019) Understanding nanoparticle toxicity mechanisms to inform redesign strategies to reduce environmental impact. *Accounts of Chemical Research* 52 (6): 1632–1642.

Dassanayake MK, Chong CH, Khoo T-J, Figiel A, Szumny A, Choo CM (2021) Synergistic field crop pest management properties of plant-derived essential oils in combination with synthetic pesticides and bioactive molecules: A review. *Foods* 10 (9): 2016.

De Jong WH, De Rijk E, Bonetto A, Wohlleben W, Stone V, Brunelli A, Badetti E, Marcomini A, Gosens I, Cassee FR (2019) Toxicity of copper oxide and basic copper carbonate nanoparticles after short-term oral exposure in rats. *Nanotoxicology* 13 (1): 50–72. https://doi.org/10.1080/17435390.2018.1530390

El-Saadony MT, Saad AM, Soliman SM, Salem HM, Desoky El-M, Babalghith AO, El-Tahan AM, Ibrahim OM, Ebrahim AAM, El-Mageed ABD, et al. (2022) Role of nanoparticles in enhancing crop tolerance to abiotic stress: A comprehensive review. *Frontiers in Plant Science* 13:946717.

Elbakary RH, Okasha EF, Ragab AMH, Ragab MH (2018) Histological effects of gold nanoparticles on the lung tissue of adult male albino rats. *Journal of Microscopy and Ultrastructure* 6 (2): 116. https://doi.org/10.4103/JMAU.JMAU_25_18

Ema M, Okuda H, Gamo M, Honda K (2017) A review of reproductive and developmental toxicity of silver nanoparticles in laboratory animals. *Reproductive Toxicology* 67:149–164. https://doi.org/10.1016/j.reprotox.2017.01.005

Ermini ML, Voliani V (2021) Antimicrobial nano-agents: The copper age. *ACS Nano* 15 (4): 6008–6029. https://doi.org/10.1021/acsnano.0c10756

Essa AMM, Khallaf MK (2016) Antimicrobial potential of consolidation polymers loaded with biological copper nanoparticles. *BMC Microbiology* 16 (1): 1–8. https://doi.org/10.1186/s12866-016-0766-8

Exbrayat J-M, Moudilou EN, Lapied E, et al. (2015) Harmful effects of nanoparticles on animals. *Journal of Nanotechnology* 2015

Fahmy B, Cormier SA (2009) Copper oxide nanoparticles induce oxidative stress and cytotoxicity in airway epithelial cells. *Toxicology in Vitro* 23 (7): 1365–1371. https://doi.org/10.1016/j.tiv.2009.08.005

Gallo A, Manfra L, Boni R, Rotini A, Migliore L, Tosti E (2018) Cytotoxicity and genotoxicity of CuO nanoparticles in sea urchin spermatozoa through oxidative stress. *Environment International* 118:325–333.

Geng Y, Liu Z, Hu R, Huang Y, Li F, Ma W, Wu X, Dong H, Song K, Xu X, et al. (2023) Toxicity of microplastics and nanoplastics: invisible killers of female fertility and offspring health. *Frontiers in Physiology* 14 https://www.frontiersin.org/articles/10.3389/fphys.2023.1254886

He F, Liu R, Tian G, Qi Y, Wang T (2023) Ecotoxicological evaluation of oxidative stress-mediated neurotoxic effects, genetic toxicity, behavioral disorders, and the corresponding mechanisms induced by fluorene-contaminated soil targeted to earthworm (Eisenia fetida) brain. *Science of The Total Environment* 871:162014.

Headrick D (2021) The future of organic insect pest management: be a better entomologist or pay for someone who is. *Insects* 12 (2): 140.

Hotessa Halake N, Muda Haro J, et al. (2022) Role of Nanobiotechnology Towards Agri-Food System. *Journal of Nanotechnology* 2022 https://doi.org/10.1155/2022/6108610

Hou J, Wang X, Hayat T, Wang X (2017) Ecotoxicological effects and mechanism of CuO nanoparticles to individual organisms. *Environmental Pollution* 221:209–217.

Ighalo JO, Sagboye PA, Umenweke G, Ajala OJ, Omoarukhe FO, Adeyanju CA, Ogunniyi S, Adeniyi AG (2021) CuO nanoparticles (CuO NPs) for water treatment: A review of recent advances. *Environmental Nanotechnology, Monitoring & Management* 15:100443.

Kim JS, Yoon T-J, Yu KN, Kim BG, Park SJ, Kim HW, Lee KH, Park SB, Lee J-K, Cho MH (2006) Toxicity and tissue distribution of magnetic nanoparticles in mice. *Toxicological Sciences* 89 (1): 338–347. https://doi.org/10.1093/toxsci/kfj027

Kiss B (2009) Investigation of micronized titanium dioxide penetration in human skin xenografts and its effect on cellular functions. PhD diss. https://doi.org/10.1111/j.1600-0625.2007.00683.x

Kumah EA, Fopa RD, Harati S, Boadu P, Zohoori FV, Pak T (2023) Human and environmental impacts of nanoparticles: a scoping review of the current literature. *BMC Public Health* 23 (1): 1–28. https://doi.org/10.1186/s12889-023-15958-4

Longmire M, Choyke PL, Kobayashi H (2008) Clearance properties of nano-sized particles and molecules as imaging agents: considerations and caveats. https://doi.org/10.2217/17435889.3.5.703

Lue H-C, Wu M-H, Wang J-K, Lin M-T, Lu C-W, Chiu S-N, Chen C-A, Wu E-T, Wang C-C, Fu C-M, et al. (2023) Normal ECG standards and percentile charts for infants, children and adolescents. *Pediatrics & Neonatology* 64 (3): 256–273.

Ma X, Yang X, Wang Y, Liu J, Jin S, Li S, Liang X-J (2018) Gold nanoparticles cause size-dependent inhibition of embryonic development during murine pregnancy. *Nano Research* 11:3419–3433. https://doi.org/10.1007/s12274-018-1969-0

Ma X, Zhou S, Xu X, Du Q (2022) Copper-containing nanoparticles: Mechanism of antimicrobial effect and application in dentistry-a narrative review. *Frontiers in Surgery* 9:905892. https://doi.org/10.3389/fsurg.2022.905892

Mamman AJ, Myek B, Ladan Z (2023) Antimicrobial activity of green synthesized copper nanoparticles (CuNPs) using aqueous extract of Psidium Guajava on clinical bacteria isolates. https://doi.org/10.26434/chemrxiv-2023-7z7v6

Martin C, Nourian A, Babaie M, Nasr GG (2023) Environmental, health and safety assessment of nanoparticle application in drilling mud–Review. *Geoenergy Science and Engineering,* 211767. https://doi.org/10.1016/j.geoen.2023.211767

Mavon A, Miquel C, Lejeune O, Payre B, Moretto P (2006) In vitro percutaneous absorption and in vivo stratum corneum distribution of an organic and a mineral sunscreen. *Skin Pharmacology and Physiology* 20 (1): 10–20. https://doi.org/10.1159/000096167

McAuliffe ME, Perry MJ (2007) Are nanoparticles potential male reproductive toxicants? A literature review. *Nanotoxicology* 1 (3): 204–210. https://doi.org/10.1080/17435390701675914

Mohammadi-Aloucheh R, Habibi-Yangjeh A, Bayrami A, Latifi-Navid S, Asadi As (2018) Enhanced anti-bacterial activities of ZnO nanoparticles and ZnO/CuO nanocomposites synthesized using Vaccinium arctostaphylos L. fruit extract. *Artificial Cells, Nanomedicine, and Biotechnology* 46 (sup1): 1200–1209.

Neme K, Nafady A, Uddin S, Tola YB (2021) Application of nanotechnology in agriculture, postharvest loss reduction and food processing: Food security implication and challenges. *Heliyon* 7 (12) https://doi.org/10.1016/j.heliyon.2021.e08539

Nohynek GJ, Lademann J, Ribaud C, Roberts MS (2007) Grey goo on the skin? Nanotechnology, cosmetic and sunscreen safety. *Critical Reviews in Toxicology* 37 (3): 251–277. https://doi.org/10.1080/10408440601177780

Pandit R, Gaikwad S, Rai M (2017) Biogenic fabrication of CuNPs, Cu bioconjugates and in vitro assessment of antimicrobial and antioxidant activity. *IET Nanobiotechnology* 11 (5): 568–575.

Phan D-N, Dorjjugder N, Saito Y, Khan MQ, Ullah A, Bie X, Taguchi G, Kim I-S (2020) Antibacterial mechanisms of various copper species incorporated in polymeric nanofibers against bacteria. *Materials Today Communications* 25:101377. https://doi.org/10.1016/j.mtcomm.2020.101377

Philbrook NA, Winn LM, Afrooz ARMN, Saleh NB, Walker VK (2011) The effect of TiO_2 and Ag nanoparticles on reproduction and development of Drosophila melanogaster and CD-1 mice. *Toxicology and Applied Pharmacology* 257 (3): 429–436. https://doi.org/10.1016/j.taap.2011.09.027

Rai M, Ingle AP, Pandit R, Paralikar P, Shende S, Gupta I, Biswas JK, Silva SS da (2018) Copper and copper nanoparticles: Role in management of insect-pests and pathogenic microbes. *Nanotechnology Reviews* 7 (4): 303–315. https://doi.org/10.1515/ntrev-2018-0031

Rajeshkumar S, Menon S, Kumar SV, Tambuwala MM, Bakshi HA, Mehta M, Satija S, Gupta G, Chellappan DK, Thangavelu L, et al. (2019) Antibacterial and antioxidant potential of biosynthesized copper nanoparticles mediated through Cissus arnotiana plant extract. *Journal of Photochemistry and Photobiology B: Biology* 197:111531.

Rojas B, Soto N, Villalba M, Bello-Toledo H, Meléndrez-Castro M, Sánchez-Sanhueza G (2021) Antibacterial activity of copper nanoparticles (Cunps) against a resistant calcium hydroxide multispecies endodontic biofilm. *Nanomaterials* 11 (9): 2254. https://doi.org/10.3390/nano11092254

Rollerova E, Jurcovicova J, Mlynarcikova A, Sadlonova I, Bilanicova D, Wsolova L, Kiss A, Kovriznych J, Kronek J, Ciampor F, et al. (2015) Delayed adverse effects of neonatal exposure to polymeric nanoparticle poly (ethylene glycol)-block-polylactide methyl ether on hypothalamic–pituitary–ovarian axis development and function in Wistar rats. *Reproductive Toxicology* 57:165–175. https://doi.org/10.1016/j.reprotox.2015.07.072

Rong-Mullins X, Winans MJ, Lee JB, Lonergan ZR, Pilolli VA, Weatherly LM, Carmenzind TW, Jiang L, Cumming JR, Oporto GS, et al. (2017) Proteomic and genetic analysis of the response of S. cerevisiae to soluble copper leads to improvement of the antimicrobial function of cellulosic copper nanoparticles. *Metallomics* 9 (9): 1304–1315.

Sadrieh N, Wokovich AM, Gopee NV, Zheng J, Haines D, Parmiter D, Siitonen PH, Cozart CR, Patri AK, McNeil SE, et al. (2010) Lack of significant dermal penetration of titanium dioxide from sunscreen formulations containing nano-and submicron-size TiO_2 particles. *Toxicological Sciences* 115 (1): 156–166. https://doi.org/10.1093/toxsci/kfq041

Salah I, Parkin IP, Allan E (2021) Copper as an antimicrobial agent: Recent advances. *RSC Advances* 11 (30): 18179–18186. https://doi.org/10.1039/D1RA02149D

Santacruz-Márquez R, Santos M Gonzalez-De los, Hernandez-Ochoa I (2021a) Ovarian toxicity of nanoparticles. *Reproductive Toxicology* 103:79–95. https://doi.org/10.1016/j.reprotox.2021.06.002

——— (2021b) Ovarian toxicity of nanoparticles. *Reproductive Toxicology* 103:79–95.

Saran M, Vyas S, Mathur M, Bagaria A (2018) Green synthesis and characterisation of CuNPs: insights into their potential bioactivity. *IET Nanobiotechnology* 12 (3): 357–364. https://doi.org/10.1049/iet-nbt.2017.0138

Schug TT, Nadadur SS, Johnson AF (2013) Nano GO Consortium—a team science approach to assess engineered nanomaterials: reliable assays and methods. *Environmental Health Perspectives* 121 (6): a514–a516. https://doi.org/10.1289/ehp.1306866

Shahin NN, Mohamed MM (2017) Nano-sized titanium dioxide toxicity in rat prostate and testis: Possible ameliorative effect of morin. *Toxicology and Applied Pharmacology* 334:129–141. https://doi.org/10.1016/j.taap.2017.08.014

Sherins RJ, Hodgen GD (1976) Testicular gamma glutamyltranspeptidase: an index of Sertoli cell function in man. *Reproduction* 48 (1): 191–193. https://doi.org/10.1530/jrf.0.0480191

Sims CM, Hanna SK, Heller DA, Horoszko CP, Johnson ME, Bustos ARM, Reipa V, Riley KR, Nelson BC (2017) Redox-active nanomaterials for nanomedicine applications. *Nanoscale* 9 (40): 15226–15251. https://doi.org/10.1039/C7NR05429G

Singh R, Dutt S, Sharma P, Sundramoorthy AK, Dubey A, Singh A, Arya S (2023) Future of nanotechnology in food industry: Challenges in processing, packaging, and food safety. *Global Challenges* 7 (4): 2200209.

Song G, Hou W, Gao Y, Wang Y, Lin L, Zhang Z, Niu Q, Ma R, Mu L, Wang H (2016) Effects of CuO nanoparticles on Lemna minor. *Botanical Studies* 57:1–8.

Sportelli MC, Izzi M, Volpe A, Lacivita V, Clemente M, Di Franco C, Conte A, Del Nobile MA, Ancona A, Cioffi N (2019) A new nanocomposite based on LASiS-generated CuNPs as a preservation system for fruit salads. *Food Packaging and Shelf Life* 22:100422. https://doi.org/10.1016/j.fpsl.2019.100422

Steuber N, Vo K, Wadhwa R, Birch J, Iacoban P, Chavez P, Elbayoumi TA (2016) Tocotrienol nanoemulsion platform of curcumin elicit elevated apoptosis and augmentation of anticancer efficacy against breast and ovarian carcinomas. *International Journal of Molecular Sciences* 17 (11): 1792. https://doi.org/10.3390/ijms17111792

Suarasan Sorina, Licarete Emilia, Astilean Simion, Craciun Ana-Maria (2018) Probing cellular uptake and tracking of differently shaped gelatin-coated gold nanoparticles inside of ovarian cancer cells by two-photon excited photoluminescence analyzed by fluorescence lifetime imaging (FLIM). PhD diss. https://doi.org/10.1016/j.colsurfb.2018.03.016

Teng C, Jiang C, Gao S, Liu X, Zhai S (2021) Fetotoxicity of nanoparticles: causes and mechanisms. *Nanomaterials* 11 (3): 791. https://doi.org/10.3390/nano11030791

Wu M, Dong Q, Lu X, Liu Y, Wang X, Qin X, Li Z (2022) Placenta-specific virulence factors involved in Listeria monocytogenes infection. *Sheng Wu Gong Cheng Xue Bao* 38 (6): 2139–2152.

Yazdi MET, Qayoomian M, Beigoli S, Boskabady MH (2023) Recent advances in nanoparticle applications in respiratory disorders: A review. *Frontiers in Pharmacology* 14 https://doi.org/10.3389/fphar.2023.1059343

Yusefi-Tanha E, Fallah S, Rostamnejadi A, Pokhrel LR (2020) Particle size and concentration dependent toxicity of copper oxide nanoparticles (CuONPs) on seed yield and antioxidant defense system in soil grown soybean (Glycine max cv. Kowsar). *Science of the Total Environment* 715:136994.