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Cerium oxide nanoparticles: antioxidant properties in silicosis treatment and biomedical application prospects—a dialectical consideration

Ge Ban^{a,1}, Yuanjie Chen^{a,b,1}, Ran Zhao^a, Yingbing Liang^c, Simo Chen^d, Jingjing Jia^a, Chaoke Li^a, Jinwen Sima^b, Dan Ding^a, Xiaona Wang^a, Zhengkai Zhu^e and Yumin Han^a

^aSchool of Intelligent Medical Engineering, North Henan Medical University, Xinxiang, China; ^bClinical School, North Henan Medical University, Xinxiang, China; ^cApeloa (Shanghai) Pharma Solutions Co., Ltd., Shanghai Brilliant City, Shanghai, China; ^dDepartment of Cardiac and Thoracic Surgery, Xinyang Central Hospital, Xinyang, China; ^eShanghai Clinical Center for Blood Diseases, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China

ABSTRACT

Silicosis is a progressive fibrotic lung disease precipitated by chronic inhalation of crystalline silica. Uptake of silica particles by alveolar macrophages initiates a cascade of persistent inflammation and oxidative stress, in which reactive oxygen species (ROS) are key mediators of cellular injury and fibroproliferative remodeling. This review synthesizes the current knowledge of ROS species and signaling in silicosis and evaluates nanomaterial-based antioxidant strategies with an emphasis on cerium oxide nanoparticles (CeO₂NPs). We examine the mechanistic attributes of CeO₂NPs – including reversible Ce³⁺/Ce⁴⁺ redox cycling and enzyme-mimetic superoxide dismutase/catalase-like activities – that underpin ROS scavenging, and appraise their therapeutic potential, delivery considerations, and constraints. In parallel, we highlight opportunities and challenges associated with alternative platforms such as gold, silver, and iron-oxide nanoparticles for mitigating silica-induced oxidative injury. Among these modalities, unresolved issues include the standardization of characterization, dose–response relationships, long-term biodistribution and clearance, immunotoxicity, interference with physiological redox signaling, and optimization of drug loading for combination therapies. Addressing these biosafety and payload questions through rigorous *in vitro* and *in vivo* studies will be essential to advance nanomaterial-enabled interventions for silicosis and related pulmonary diseases toward clinical translation.

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Cerium oxide nanoparticles (CeO₂NPs); antioxidant; nanozyme; silicosis; reactive oxygen species (ROS)

1. Introduction

Silicosis is a serious occupational lung disease and a subtype of pneumoconiosis, distinguished by the formation of silica nodules and extensive pulmonary fibrosis. This condition results from the prolonged inhalation of significant quantities of free silica (SiO₂) dust particles (Greenberg et al. 2007; Leung et al. 2012). A vast number of workers are exposed to silica worldwide, with over 230 million people in total, and this population faces a significantly elevated risk of developing pneumoconiosis (Sherekar et al. 2025). The pathogenesis of silicosis is intricately linked to a sequence of biochemical reactions that follow the phagocytosis of silica dust by macrophages (Götze et al. 2021; Zhang et al. 2021). Upon the ingestion of silica dust by macrophages, the stability of the lysosomal membrane within these cells is disrupted. This disruption results in the release of hydrolases, leading to cell lysis and subsequent cell death. Consequently, silica dust is repeatedly engulfed and released, thereby generating a significant amount of reactive oxygen species (ROS) (Fubini and Hubbard 2003; Rimal et al. 2005; Pollard 2016; Lee et al. 2017; Kumari et al. 2023). ROS play a crucial role in biological systems by regulating critical physiological processes. However, excessive ROS levels can induce cellular damage and apoptosis (Schieber and Chandel 2014;

CONTACT Ge Ban  bange119@qq.com  School of Intelligent Medical Engineering, North Henan Medical University, Xinxiang 453003, China

¹Ge Ban and Yuanjie Chen contributed equally and are co-first authors.

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Hameister et al. 2020). Under oxidative stress, macrophages and alveolar epithelial cells release large amounts of inflammatory factors, leading to the sustained amplification of inflammatory signaling pathways (Sun et al. 2025; Ma et al. 2025). As these signals intensify, the death and lysis of pulmonary cells increase progressively, initiating a cycle of injury and repair in lung tissue. This eventually drives the lung tissue into a fibrotic phase (Wang et al. 2025). During this process, fibroblast activation and myofibroblast differentiation occur, accompanied by excessive deposition of collagen and other extracellular matrix components. Consequently, the lung parenchyma is disrupted, further driving the progression of pulmonary fibrosis (Wan et al. 2023, 2024; Chen et al. 2025). Ultimately, the synergistic effects of inflammatory propagation and fibrotic deposition lead to the destruction of pulmonary structures and the development of diffuse fibrosis. These pathological alterations collectively characterize silicosis as a progressive and irreversible disease process (Yang et al. 2025).

Based on this, nanomaterials are promising candidates for the search for antioxidants with excellent antioxidant properties and high bioavailability. Compared with small-molecule enzyme antioxidants, nanozymes exhibit greater antioxidant capacity and additional advantages. For example, synthetic enzymes can mimic the function of natural enzymes and are not affected by environmental conditions, making them potentially valuable for antioxidant applications. Cerium oxide nanoparticles (CeO_2NPs) are also called as Ceria Nanoparticles (Song et al. 2014), represent an important class of inorganic materials, and have extensive applications across diverse fields. Owing to their remarkably high oxygen storage capacity, CeO_2NPs are commonly employed in catalysis (Nyoka et al. 2020; Pan et al. 2024). Specifically, it functions as a highly effective catalyst for the purification of automobile exhaust, thereby significantly diminishing the emissions of noxious gases (Abdulwahab et al. 2023). CeO_2NPs have broad applications in biomedicine and have been proposed as highly promising nanomedicines in human medicine.

Regarding the material's characteristics, the $\text{Ce}^{3+}/\text{Ce}^{4+}$ ratio endows CeO_2NPs containing rare-earth elements with unique functions in scavenging free radicals and preventing oxidative damage.

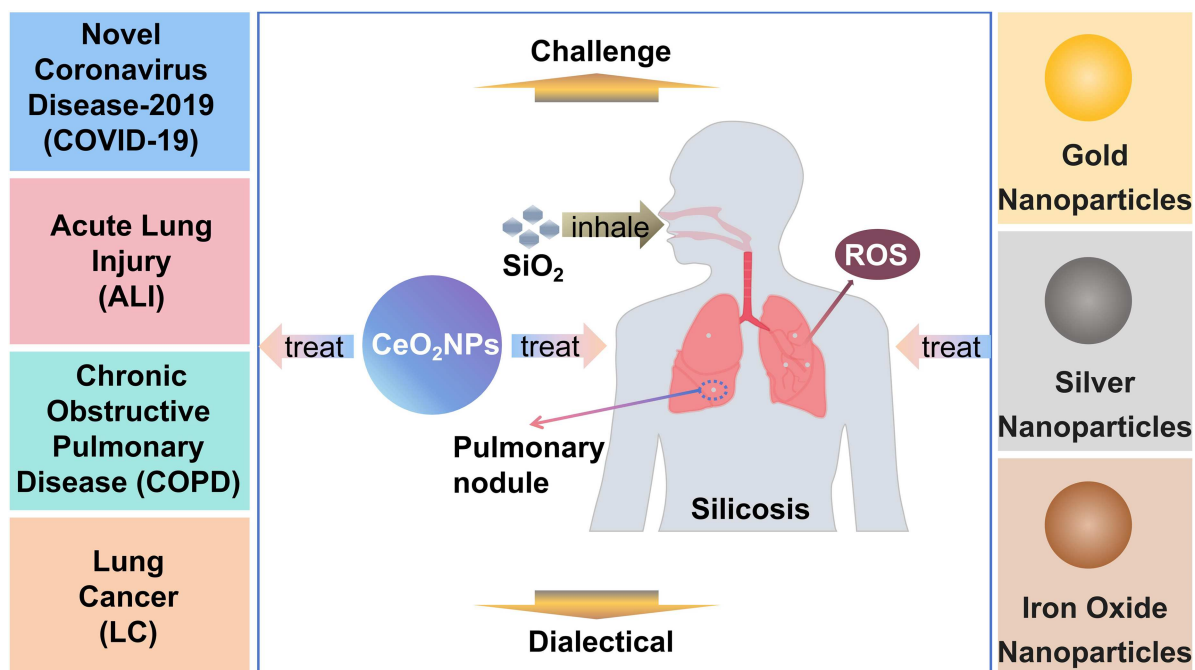
Based on this feature, CeO_2NPs can be considered for removing free radicals in silicosis to slow the progression of silicosis (Qin et al. 2019; Zhong et al. 2020). Currently, the issue of the biological toxicity of CeO_2NPs remains a subject of ongoing controversy. While some studies have indicated that, at a specific concentration, CeO_2NPs can induce adverse effects in cells, such as oxidative stress, other studies suggest that their biological toxicity is relatively low. Typically, the toxicity of CeO_2NPs is linked to several factors, such as particle size, concentration, and exposure routes. Given these circumstances, conducting in-depth investigations into the role of nanomaterials, with particular emphasis on CeO_2NPs , is essential for addressing the ROS problem in silicosis. This paper discusses the enzymatic antioxidant properties of CeO_2NPs and examines their potential for treating lung diseases and nanoparticles. In parallel with other works, dialectical consideration of the nature of nanomaterials is crucial. The pursuit of leveraging their potential to provide direction and inspiration for future nanomaterial-based diagnosis and treatment necessitates awareness of associated risks. Through such dialectical contemplation, the potential for incalculable harm can be better avoided, ensuring optimal utilization of nanomaterials to benefit humanity and society (Figure 1).

2. Role of ROS in silicosis

2.1. The species of ROS and their applications in biomedicine

ROS, oxygen-containing, chemically reactive species generated during diverse biochemical reactions within organelles, are pivotal in modulating various physiological functions in organisms. ROS serve as essential mediators of organismal growth, adaptation to diverse conditions, and aging. Interestingly, they are also significantly associated with nearly all diseases (Yang et al. 2019; Chianese and Pierantoni 2021; Jafari et al. 2022; Ren et al. 2022; Sahoo et al. 2022). The incomplete reduction of oxygen leads to the generation of a series of molecules termed ROS, which include hydrogen peroxide (H_2O_2), hypochlorous acid/hypochlorite (HOCl/ClO^-), hydroxyl radicals ($\cdot\text{OH}$), superoxide anion radical ($\text{O}_2^{\cdot-}$), and singlet oxygen ($^1\text{O}_2$) (Wu et al. 2019; Kwon et al. 2021; Chaudhary et al. 2024).

ROS play important roles in cell biology, including signal transduction, the regulation of nitric oxide production, oxidative bursts for phagocytic function, oxygen level sensing, and cell apoptosis, which are



Figures 1. The treatment and challenges of CeO_2NPs for silicosis and the prospects of nanomaterials in other lung diseases (Author-created).

crucial in human life (Figure 2) (Rani and Chawla 2018). Low levels of ROS are beneficial; however, when exogenous stimuli prompt the body to generate excessive ROS, adverse effects may occur. ROS can cause the oxidation of DNA, proteins, or lipids, leading to cell death (Prasad et al. 2017; Rendra et al. 2019; Sies and Jones 2020). From a biological perspective, the cytotoxicity of ROS is dual in disease. In treating cancer, it can be either a tumor inhibitor or a tumor promoter. ROS facilitate cancer cell invasion and metastasis in the later stages of tumor progression by activating the nuclear factor- κB (NF- κB) and mitogen-activated protein kinase (MAPK) pathways.

Nevertheless, when ROS exceed a specific threshold, they promote cell-cycle arrest and induce apoptosis in cancer cells. Because an abnormal increase in ROS levels can induce apoptosis through intrinsic and extrinsic pathways, ROS are considered tumor inhibitors in clinical treatment (Sahoo et al. 2022). Most chemotherapeutic agents are used to induce ROS production, thereby leading to cell death (Du et al. 2021; ArulJothi et al. 2022; Verma et al. 2023). ROS play a crucial role in kidney disease as key contributors to kidney damage (Ishimoto et al. 2018). Because ROS also regulate the formation of venous thrombosis, antioxidants can be employed to modulate several key processes in venous thrombosis (Gutmann et al. 2020).

Additionally, oxidative stress is widely acknowledged as a significant participant in the pathophysiology of numerous brain diseases, particularly neurodegenerative disorders such as Alzheimer's disease and Parkinson's disease (Koga et al. 2016). Excessive production of ROS can lead to lipid peroxidation, DNA damage, enzyme inhibition, mitochondrial damage, and, ultimately, neuronal death. Simultaneously, it provides a new target for disease-modifying therapy. In biomedical applications, antioxidants have been proposed and evaluated for the treatment of epilepsy (Shekh-Ahmad et al. 2019). During clinical treatment, the poor permeability of the central nervous system and the rapid depletion of oxidants pose obstacles to antioxidant therapy. Hence, the development of a drug with high antioxidant activity to address diseases induced by oxidative stress is essential, underscoring the importance of identifying a suitable antioxidant drug for oxidative stress treatment. This antioxidant drug must first possess adequate antioxidant capacity. Secondly, it should have a sustained antioxidant effect. For this purpose, CeO_2NPs with high oxidation resistance have been explored. In this work, the enzyme-like oxidation resistance of CeO_2NPs and the challenges they face in application are discussed in detail.

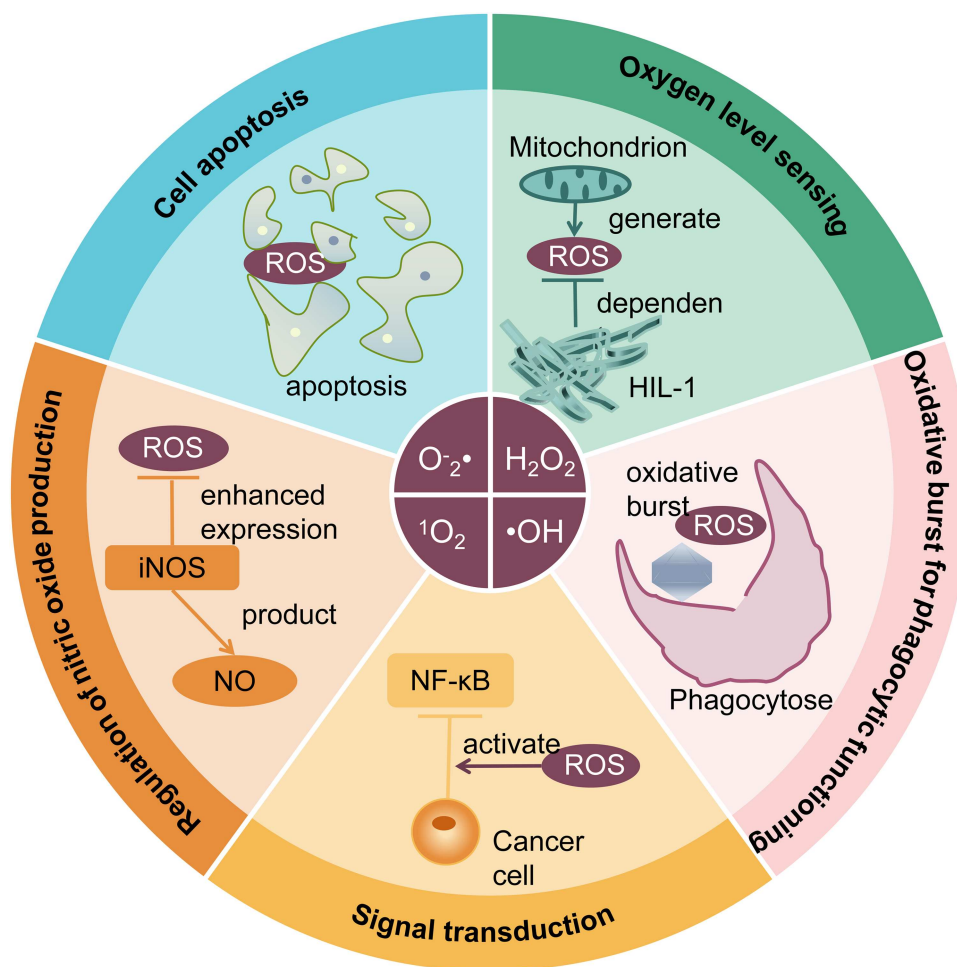


Figure 2. The role of ROS in living organisms (Author-created).

Simultaneously, ROS, which play a favorable role in disease and can therefore be utilized for periodontal therapy and root canal disinfection, have been widely reported to be effective in antibacterial photodynamic therapy (Komine et al. 2022). Antimalarial drugs kill *Plasmodium* parasites by inducing ROS-mediated damage (Egwu et al. 2021). Therefore, the role of ROS in the body cannot be generalized and should be considered dialectically. In subsequent applications, further research is needed to better understand the complex mechanisms by which ROS affect diverse biological processes and to develop targeted therapies that modulate ROS levels for therapeutic benefit.

2.2. Application of ROS in the diagnosis and treatment of silicosis

When the lungs are healthy, the production and clearance of ROS are balanced. In silicosis, a large amount of silica accumulates in the lung without being cleared, thereby inducing excessive ROS production. This disrupts the balance of intracellular fluid components, leading to oxidative stress. Upon the onset of oxidative stress in the pulmonary parenchyma, excess ROS induce pulmonary cells to undergo apoptosis, leading to parenchymal damage. To repair the damaged lung tissue, the organism recruits cells, including macrophages and fibroblasts, to the injury site, thereby leading to irreversible pulmonary fibrosis (Noubade et al. 2014; Kapoor et al. 2019; Halliwell 2022). Notably, there is a diverse range of ROS. The specific ROS implicated in silicosis must be identified to enable more effective clinical assessment and treatment of this condition. In the experiment on quartz free radicals, H_2O_2 , $\bullet HO$, $O_2^{\bullet-}$, and 1O_2 are subsequently generated in the quartz suspension (Figure 3) (Konecny et al. 2001). Based on the above conclusion, the influence of HClO/CIO should not be considered in the treatment of silicosis. Although ROS oxidize and readily induce inflammation, these properties can paradoxically be harnessed to inhibit fibroblast growth.

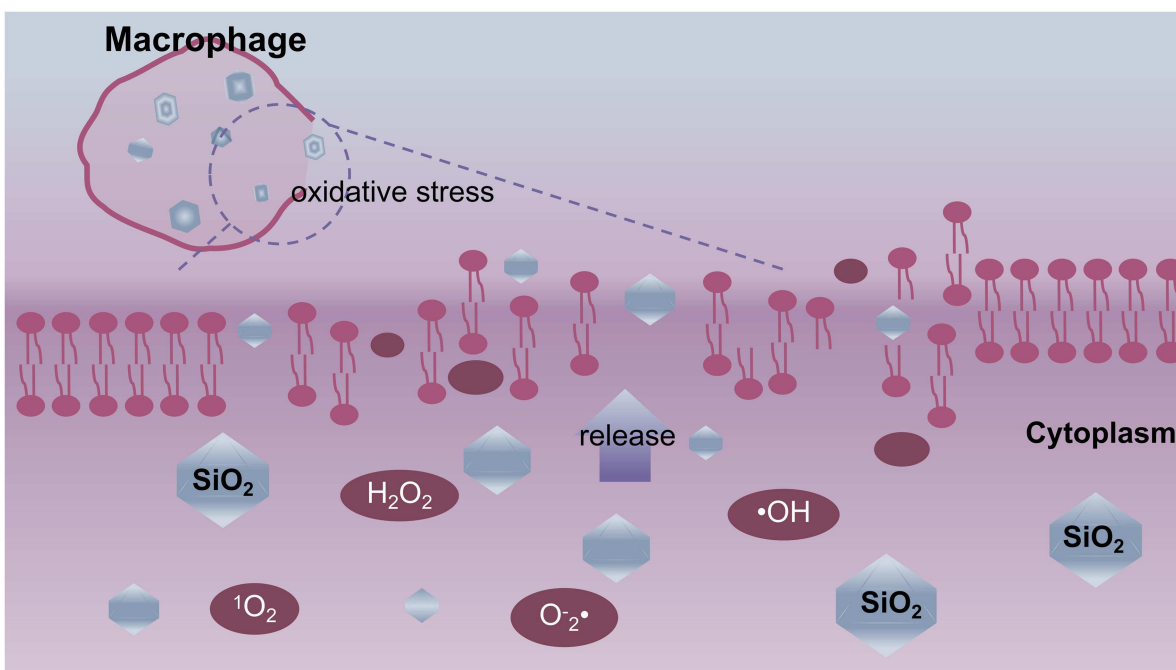


Figure 3. Macrophages are induced to lyse while releasing ROS after phagocytosing SiO₂ particles (Author-created).

This approach can slow or prevent fibrosis progression in the later stages of silicosis (Bai et al. 2024). Therefore, the effects of different substances on the organism change during disease. ROS can be regarded as therapeutic targets throughout the pathogenesis of silicosis. In the early stage of disease, leveraging the antioxidant property of CeO₂NPs to inhibit ROS is considered a treatment approach. As the disease progresses to a later stage, when damaged lung tissue undergoes fibrosis, targeting free radicals to disrupt fibrotic cell growth and impede silicosis progression can achieve specific therapeutic effects. Importantly, during fibroblast inhibition, the ROS dose and delivery route are of paramount importance. CeO₂NPs can be employed for drug targeting in the late-stage treatment of silicosis to prevent damage to other cells. Neither the properties of CeO₂NPs nor the capabilities of ROS should be considered from a single perspective. Instead, a dialectical view of these two substances is required. A dialectical consideration of the properties of these substances is crucial for advancing relevant research or treatment.

Although ROS exhibit dual roles in silicosis, most silicosis treatments target lung oxidative stress. In experiments conducted by Yunzhe et al., nebulized inhalation of linear poly (beta-amino ester) (LPAE)-HDAC10 nanocomplexes was used to treat silicosis (Tian et al. 2023). This approach has been used to increase histone deacetylase 10 (HDAC10) expression, reduce oxidative stress, and ultimately diminish oxidative stress, inflammation, and pulmonary fibrosis in silicosis.

In summary, drugs with high antioxidant activity should be sought when addressing ROS in silicosis. The drug's bioavailability must be considered during clinical application or scientific research. Hence, with the aim of alleviating the pain of silicosis patients and retarding the aggravation of this disease, the exploration of a novel type of nanomaterial that can substitute for antioxidant drugs to prevent the oxidation of ROS has become a significant research focus. The impetus for this pursuit stems from the discovery of CeO₂NPs, which exhibit remarkable antioxidant properties. Owing to their unique physicochemical characteristics, these nanoparticles can mimic the catalytic action of enzymes, enabling them to effectively scavenge and quench ROS during the treatment process.

3. The antioxidant properties of nanomaterials have been used to deal with ROS in silicosis

Nanomaterials represent one of the most promising frontiers in advancing antioxidant research (Sherekar et al. 2024). Nano-antioxidants, which possess long-term stability relative to small molecules, are less rapidly

cleared by metabolism and can target specific sites (Morry et al. 2017). Some nanomaterials display inherent redox activity, which is typically associated with free radical capture and enzyme-like activity, for example, activities similar to superoxide dismutases (SOD) and catalases (CAT) (Valgimigli et al. 2018). By mimicking enzymatic properties, it shows the same antioxidant activity and performs well in experiments. These materials are often referred to as nanozymes, i.e. nanomaterials with enzyme-like features (Yang et al. 2024). Generally, enzyme-catalyzed reactions must occur under specific conditions. Researchers have recently focused on enzymes and are considering replacing natural enzymes with synthetic ones to avoid being constrained by particular application conditions.

In contrast to natural enzymes, nanozymes are composed of bare nanoparticles or their functionalized derivatives. Nanozymes can overcome the high sensitivity of natural enzymes to environmental conditions such as pH, temperature, and other related factors (Yang et al. 2024; Jacob et al. 2024). Nanozymes are enzyme-like nanomaterials that resemble natural enzymes in size, shape, and surface charge (Qiu et al. 2021). They are the primary defense against ROS such as superoxide and peroxide free radicals (D'Autr  aux and Toledano 2007).

The data show that most nanomaterials have both SOD and CAT activities. SOD, which is essential for defending cells against oxygen exposure, helps break down O_2^- into O_2 and H_2O_2 (Ighodaro and Akinloye 2018). Meanwhile, CAT protects cells from damage caused by ROS by converting H_2O_2 into H_2O and O_2 (Peng et al. 2023). The two enzymes exhibit complementary functions (Vincent et al. 2021). CAT can rapidly eliminate the toxic intermediate H_2O_2 produced by SOD. In the context of biological antioxidant defense mechanisms, the combined action of SOD and CAT has long been demonstrated to be effective in removing superoxides (Xu et al. 2022; Bardi et al. 2023). When employed in silicosis, it can effectively suppress and eliminate a significant quantity of ROS. Consequently, it mitigates the detrimental effects of ROS on lung cells and prevents oxidative stress in the lungs.

The biological effects of nanomaterials require a dialectical perspective. On the one hand, CeO_2 NPs possess enzyme-like antioxidant properties, allowing them to function as artificial nanozyme substitutes. Their stability and catalytic efficiency surpass those of natural enzymes, an advantage that should be fully utilized. Equally important is a focused investigation into their interactions with complex biological systems (Saifi et al. 2021). CeO_2 NPs have been demonstrated to effectively scavenge and inhibit excessive ROS in silicosis. The ability of CeO_2 NPs to interact with endogenous antioxidant enzymes contributes to combating specific pulmonary lesions and inflammation caused by biomolecular damage resulting from elevated ROS levels in the body (Reuter et al. 2010). This is primarily achieved through reversible redox cycling between Ce^{3+} and Ce^{4+} . CeO_2 NPs can directly mimic the cascade catalytic functions of SOD and CAT (Korsvik et al. 2007; Pirmohamed et al. 2010). A key factor influencing the antioxidant activity of CeO_2 NPs is the surface Ce^{3+}/Ce^{4+} ratio, which directly determines which enzyme activity they simulate (Heckert et al. 2008). In the early stages of silicosis, acute oxidative stress is the main pathological manifestation and is characterized by a sudden surge in ROS production. Endogenous antioxidant enzymes are often rapidly depleted. In contrast, the catalytic capability of CeO_2 NPs is less affected by environmental factors and can sustain its effect over time, providing immediate protection suited to the defensive needs of this phase (Heckert et al. 2008; Saifi et al. 2021).

Furthermore, CeO_2 NPs also play another role in protecting the endogenous antioxidant system. Excessive ROS, such as superoxide anions and H_2O_2 , are key drivers of oxidative damage in silicosis. By directly scavenging these molecules, CeO_2 NPs reduce the overall oxidative pressure in the lung tissue environment. This alleviates the prolonged high-load state of endogenous SOD and CAT, helping prevent damage to and inactivation of enzyme proteins due to overload (Lemos 2021). Given the persistent nature of chronic oxidative damage in silicosis, maintaining the homeostasis and functional reserve of the body's own antioxidant defense system is essential, a need that is fulfilled by the protective effects of CeO_2 NPs (Belhadj et al. 2018).

The dual mechanisms of action of CeO_2 NPs address multiple aspects of pathological progression. Firstly, they interrupt the explosive sources of ROS, effectively protecting pulmonary epithelial cells. Secondly, they help preserve the function of endogenous antioxidant enzymes. Additionally, they inhibit fibroblast activation and abnormal collagen deposition induced by oxidative stress. By intervening in the vicious cycle in which oxidative stress triggers inflammation and ultimately leads to fibrosis (Miao et al. 2025), CeO_2 NPs offer a novel nanotherapeutic approach for alleviating progressive pulmonary fibrosis in silicosis.

4. Preparation and characteristics of CeO₂NPs in silicosis treatment

The use of nanoparticles in medicine is on the rise (De Jong 2008; Ahmad et al. 2024; He et al. 2024). Drug-carrying nanoparticles are increasingly used because they can transport drugs to various body parts and exert effects (Saraiva et al. 2016; Sourì et al. 2023). Biosynthesis, owing to its unique attributes, such as rapid synthesis, low cost, and pollution-free operation, is extensively used in nature because it efficiently utilizes plant components. Compared to physical and chemical synthesis methods, biosynthesis has a lower price and fewer drawbacks. The biocompatibility of biosynthetic nanoparticles is relatively high, making it safer for use in organisms (Ahmed and Ikram 2016). In biomedical applications, particularly for the treatment of pulmonary diseases such as silicosis, comprehensive physicochemical characterization of the prepared CeO₂NPs is crucial to ensure reproducibility, therapeutic efficacy, and biosafety. X-ray diffraction (XRD) is a commonly used technique for structural characterization that can verify the crystal structure and phase purity of CeO₂NPs, features closely associated with their redox stability and catalytic behavior (Ziegler-Borowska et al. 2019; Xin et al. 2021). Transmission electron microscopy (TEM) and scanning electron microscopy (SEM) are widely employed to determine particle size, morphology, and dispersibility, as the size of CeO₂NPs significantly influences their lung deposition efficiency and cellular uptake processes (McBride et al. 2013; Thomas et al. 2022). Additionally, analysis of surface-related properties, such as the specific surface area (BET) and zeta potential, provides critical insights into the colloidal stability of nanoparticles and their interactions with cells under physiological conditions (Quispe Cohaila et al. 2025).

Cerium dioxide (CeO₂) is the most abundant rare earth element. It possesses unique properties and a high oxygen storage capacity (OSC). Owing to its ability to provide local oxygen 'storage,' material is frequently utilized as a catalyst, catalyst carrier, or cocatalyst (Montini et al. 2016; Porsin et al. 2016; Kropp et al. 2017). In materials development, doping CeO₂ with other metals is a common practice that can enhance its catalytic performance (Mukherjee et al. 2017). The preparation methods for CeO₂NPs are highly diverse. In terms of chemical processes, there are hydrofluoride-mediated method (Tumkur et al. 2021), hydrothermal process (Rudayni et al. 2022), sol-gel method (Fudala et al. 2022), microemulsion method (Hadi and Yaacob 2007), and precipitation method (Domingues et al. 2023). The ball milling method (Li et al. 2004; Lu and Fang 2006; Yadav and Srivastava 2012; He 2015) and flame spray pyrolysis method (Vassie et al. 2018) are physical. In addition, several approaches to green synthesis exist. For instance, plant-mediated synthesis methods can be employed. Extracts from goldilocks, cacti, and even aloe plant leaves can be used for the green synthesis of CeO₂NPs (Kannan and Sundrarajan 2014; Arumugam et al. 2015; N et al. 2021). Through nutrition-mediated synthesis, egg white protein and honey can be used for the green synthesis of CeO₂NPs (Darroudi et al. 2014; Kargar et al. 2015). The high oxygen storage capacity of CeO₂NPs can be attributed to the generation of many oxygen vacancies within the lattice structure of CeO₂ during the transition between the Ce³⁺ and the Ce⁴⁺ valence states. The antioxidant activity of CeO₂NPs is mediated through surface oxygen vacancies (Korsvik et al. 2007). These results indicate that CeO₂NPs form more oxygen vacancies as the particle size decreases (Deshpande et al. 2005). The smaller the CeO₂NPs particles are, the stronger their antioxidant capacity becomes. CeO₂NPs are regarded as effective free radical scavengers because of their strong redox ability. In the preparation of nanoparticles, the higher the ratio of Ce³⁺/Ce⁴⁺, the higher the oxygen and electron vacancies. Consequently, its antioxidant capacity is more substantial, and its free radical scavenging ability is also more potent (Deshpande et al. 2005; Wu et al. 2020). The participation of the surface groups of CeO₂NPs in redox reactions and their ability to readily transport hydrogen and oxygen via their dynamic structure make them highly likely to be used in monotherapy. Experiments on mice have demonstrated that nanoparticles such as CeO₂ can be used as potential therapeutic agents for various oxidative stress diseases and conditions (Celardo et al. 2011; Narayanan and Park 2013; Walkey et al. 2015; Kwon et al. 2016). Notably, CeO₂NPS has become the most prevalent inorganic nanomaterial in antioxidant therapy (Yang et al. 2019; Nikitchenko et al. 2023).

4.1. Oxidation resistance of CeO₂NPS as a nanozyme

CeO₂NPS has also been applied in the biomedical field. CeO₂NPS can be used as a simulation of SOD, CAT, some oxidase (OXD), oxidoreductase, and phosphatase and can participate in the neutralization of active nitrogen (Cai et al. 2025). According to the properties of materials, CeO₂NPS can be used to scavenge free

radicals and reduce the levels of ROS, such as $O_2^{\cdot-}$, H_2O_2 , and $\cdot OH$ (Figure 4) (Khan et al. 2014; Basina et al. 2020). This effect is used to treat silicosis by inhibiting and removing ROS accumulation in the lung and reducing the inflammation caused by ROS-induced oxidative stress; it can regulate the local characteristics of silicosis, slow disease progression, and improve patient outcomes.

Through the redox cycle coupling between Ce^{3+} and Ce^{4+} , CeO_2 NPs are used as a SOD mimic to remove superoxide free radicals (Das et al. 2013). Previous studies have shown that the fraction of Ce^{3+} determines the SOD simulation activity of CeO_2 NPs on the particle surface (Celardo et al. 2011; Wei and Wang 2013). In vitro studies have reported that smaller particles (5 nm) with a higher Ce^{3+} content primarily remove superoxides, whereas those with a higher Ce^{4+} content primarily remove peroxides (Korsvik et al. 2007; Pirmohamed et al. 2010). In experiments by Cassandra Korsvik et al., CeO_2 NPs exhibited SOD enzyme activity. It can generate oxygen and Ce^{3+} through the reactions of Ce^{4+} and $O_2^{\cdot-}$, thus reducing the damage caused by $O_2^{\cdot-}$ to the lungs. The generated oxygen can ease the burden on the lungs (Korsvik et al. 2007). Zhimin Tian et al. reported that CeO_2 NPs also possessed the characteristics of CAT (Tian et al. 2015).

In the experiment, CeO_2 NPs were compared with the natural enzyme horseradish peroxidase (HPR) to determine the H_2O_2 concentration required for maximal enzyme activity. The concentration of hydrogen peroxide needed to maximize the activity of CeO_2 NPs is much higher than that needed for HPR. Therefore, CeO_2 NPs are presumed to have multiple functions, such as CAT and SOD, which consume additional H_2O_2 (Tian et al. 2015). In their experiments, Laura Rubio and colleagues employed the human bronchial epithelial cell line BEAS-2B as a pulmonary-like cell model. They utilized potassium bromate ($KBrO_3$), a well-defined oxidative stress-inducing agent, to investigate the antioxidant properties of CeO_2 NPs. They reported that after 24 h of pretreatment with CeO_2 NP, the level of intracellular ROS production induced by $KBrO_3$ was significantly reduced, with this reduction being statistically significant across all the tested concentrations (2.5, 5, and 7.5 $\mu g/mL$). Furthermore, in experiments evaluating oxidative DNA damage, pretreatment with CeO_2 NPs mitigated $KBrO_3$ -induced oxidative DNA damage, with the most pronounced protective effect observed at a concentration of 2.5 $\mu g/mL$. Concomitantly, pretreatment with CeO_2 NP at 2.5 $\mu g/mL$ also led to a significant reduction in cell mortality induced by $KBrO_3$. Additionally, researchers have demonstrated that CeO_2 NP can downregulate the expression of oxidative stress-related genes such as *Ho1* and *Sod2*, which are induced by $KBrO_3$, thereby providing further evidence to substantiate the antioxidant activity of CeO_2 NP (Rubio et al. 2016). This study demonstrated that CeO_2 NPs exhibit

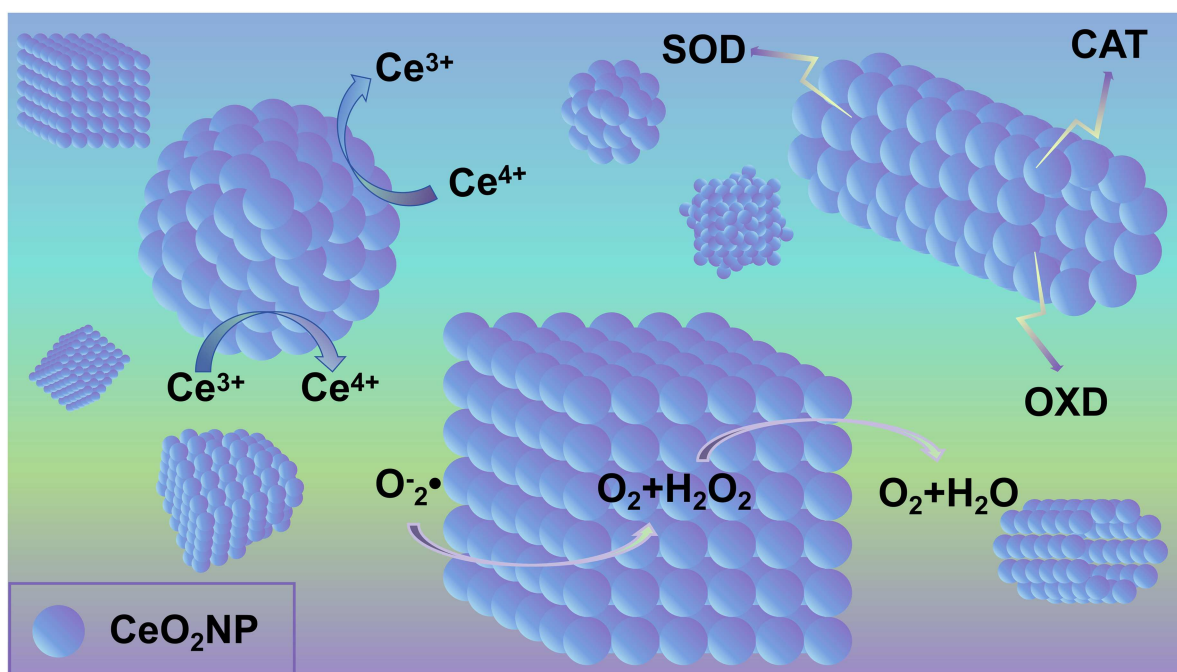


Figure 4. CeO_2 NPs are used as mimics of SOD and CAT to remove ROS (Author-created).

antioxidant activity through multiple mechanisms, as evidenced by their ability to scavenge ROS, reduce oxidative DNA damage, improve cell viability, and regulate gene expression in oxidative stress pathways. However, in the experimental studies, smaller particle sizes and lower doses of CeO₂NP exhibited more pronounced effects. Specifically, in studies of 2 and 10 nm CeO₂NP, researchers have reported that 2 nm CeO₂NP exhibit superior antioxidant performance, whereas their 10 nm counterparts show weaker activity or are inert (Nikitchenko et al. 2023). Specifically, at a concentration of 50 µg/mL, CeO₂NP did not induce ROS production. However, at concentrations of 100, 200, and 400 µg/mL, CeO₂NP triggered ROS generation, with the induced ROS levels increasing progressively with increasing concentration (Akhtar et al. 2021). These findings indicate that the biological effects of cerium oxide nanoparticles are critically dependent on both particle size and dosage. At low doses and small sizes, they predominantly exhibit antioxidant activity, whereas at higher doses, they are likely to induce oxidative stress and toxicity (Colino et al. 2020). Notably, when the concentration of CeO₂NP reached 400 µg/mL, cytotoxicity was no longer observed (Ghorbani et al. 2025). Additionally, other physicochemical parameters, such as particle shape, can also influence their biological activity of a material (Melnikova et al. 2023). This finding highlights the double-edged sword nature of CeO₂NPs. While it has the potential to treat conditions associated with excessive ROS, its cytotoxic effects must be carefully considered and mitigated. After co-culturing CeO₂NPs at a particle concentration of 0.33–660 nm with bronchial epithelial cells for 24 h, a dose-dependent decrease in intracellular ROS and cell loss was observed. Although this is sufficient to demonstrate the capacity of CeO₂NPs to remove ROS, it simultaneously poses specific harm to cells, which undoubtedly warrants our attention. This finding highlights the double-edged sword nature of CeO₂NPs. While it has the potential to treat conditions related to excessive ROS, its cytotoxic effects should be carefully considered and mitigated (Li et al. 2015). Further research is required to determine the optimal concentration and exposure conditions to maximize its beneficial effects while minimizing cell harm.

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In the experiment conducted by Suzanne M. Hirst et al., the DCFH-DA fluorescent probe method and enzyme activity assay were employed. CeO₂NPs with a size of 3–5 nm and a concentration range of 1 nM–10 µM effectively scavenged O₂^{•−}, H₂O₂, and other free radicals. This finding demonstrates the antioxidant properties of CeO₂NPs, with a more pronounced antioxidant effect observed at higher concentrations (Hirst et al. 2009). This finding further supports the potential of CeO₂NPs as antioxidants. Reducing intracellular ROS at the molecular level may have therapeutic applications in conditions involving excessive ROS production, such as various diseases and oxidative stress-related conditions. For practical application, further studies are needed to elucidate the mechanisms underlying this reduction and to assess the long-term safety and efficacy of CeO₂NPs. The production of O₂^{•−} was inhibited to a certain extent. These findings indicate that CeO₂NPs reduce existing intracellular ROS and inhibit the production of O₂^{•−}. On the one hand, this dual action further enhances their potential as therapeutic agents for conditions related to oxidative stress. On the other hand, although this is a promising finding, further research is needed to determine the optimal dose, route of administration, and potential side effects of using CeO₂NPs to inhibit O₂^{•−} production.

Furthermore, in the experiment conducted by Vellaisanmy Selvaraj and others, 0.5 mg/kg of CeO₂NPs not only exerted enzyme-mimetic effects but also induced a reduction in cytokine release (such as TNF-α, IL-1b, IL-1β, etc.), thereby lowering the level of cellular ROS. In parallel, NF-κB transcriptional activity in activated B cells decreases, and silicosis-related inflammation is inhibited, thereby promoting silicosis recovery (Selvaraj et al. 2015). In addition, during X-ray irradiation, in the preconditioning experiment involving the intraperitoneal injection of CeO₂NPs in mice, the number of caspase-3-positive cells in the colonic crypts decreased. In experiments, a significant increase in SOD₂ protein expression was also observed, indicating that CeO₂NPs can protect the gastrointestinal epithelium from radiation-induced damage via an antioxidant mechanism (Colon et al. 2010). A substantial body of data suggests that cellular nitric oxide may combine with superoxides to generate highly reactive and toxic species that can damage lung tissue (Iova et al. 2023). It has been reported that higher concentrations of Ce⁴⁺ promote the removal of nitric oxide free radicals and may play a specific role in regulating lung tissue damage.

CeO₂NPs smaller than 5 nm exhibit ROS scavenging activity in a recyclable manner. This is achieved through the reversible binding of oxygen atoms and shuttling between the surface's Ce³⁺ (reduction) and

Ce⁴⁺ (oxidation) states. They have been successfully applied to protect cells from superoxide and H₂O₂. In the adjuvant treatment of silicosis, their application can protect lung cells from ROS damage, reduce lung inflammation, and inhibit lung fibrosis (Hirst et al. 2009; Karakoti et al. 2012; Kwon et al. 2016).

4.2. CeO₂NPs are used to treat silicosis challenges

In the experiment conducted by Yuanyuan Li and others, when the size of CeO₂NPs is 5.1 ± 0.4 nm, the ratio of Ce³⁺/Ce⁴⁺ can be neglected. Notably, under ambient temperature and aerobic conditions, without the stabilization of oxygen vacancies through surface ligand coating, CeO₂NPs larger than 3 nm in size cannot maintain a significantly higher Ce³⁺/Ce⁴⁺ ratio under environmental conditions, and even CeO₂NPs smaller than 5 nm in size lose their inherent SOD-mimetic activity due to the oxidation of Ce³⁺ (Equations (1)–(2)), with the regeneration of such activity typically requiring a period ranging from several days to several weeks (Heckert et al. 2008; Li et al. 2015). In the experiments of Vellaisamy Selvaraj et al., dose–response toxicity assays using the MTT method indicated that CeO₂NPs at doses exceeding 1 µg/ml were cytotoxic (Selvaraj et al. 2015). In experiments conducted by Sheau-Fung Thai et al., CeO₂NPs not only induce the production of ROS and reactive nitrogen species (RNS) but also cause DNA damage (Thai et al. 2019). This finding demonstrates the size dependence of nanomaterials and the experimental uncertainty regarding their cytotoxicity.



According to experimental inference, Ce³⁺ reacts with O₂^{•−} and hydrogen ions to produce a certain amount of H₂O₂. This is suspected to be a continuous reaction (Korsvik et al. 2007). Based on this inference, it can be concluded that certain limitations exist when materials are utilized to remove ROS in the treatment of silicosis. In the case of application within living organisms, the activity of CeO₂NPs, whether they act as an antioxidant to protect mammalian cells from death or inhibiting microbial growth, is regulated by a specific environment. Whether the lung's environment is suitable remains a matter worthy of consideration (Matter et al. 2019). Notably, Yang Li and others found that CeO₂NPs generate O₂^{•−} under ultraviolet light when the mechanism of ROS generation by various oxidizing compounds is studied. In the treatment of silicosis, materials should avoid excessive exposure to ultraviolet light to prevent the generation of excessive O₂^{•−}, as this would aggravate the degree of inflammation (Li et al. 2012). Some reports suggest that Ce³⁺ increases toxicity. In this context, it is necessary to examine the in vitro physicochemical properties more carefully (Peng et al. 2014; Pulido-Reyes et al. 2015).

In recent years, extensive research has focused on modifying the redox properties of CeO₂NPs by altering the nanocrystal environment (Seal et al. 2020). Inducing different types of lattice defects alters the oxygen storage capacity. The presence of oxygen vacancies in the lattice promote the free radical scavenging capacity. The scavenging of •OH and O₂^{•−} requires more oxygen vacancies (Ce³⁺ sites) (Karakoti et al. 2010; Singh et al. 2011). This issue poses a significant challenge for the use of CeO₂NPs in the treatment of silicosis. The drug dosage must be precisely controlled to enable it to clear O₂^{•−} in silicosis while causing minimal damage to the body. Although numerous reports have focused on improving the defect concentration, synthesizing CeO₂NPs with specific sizes and tunable surface defects via a single method remains a significant challenge (Meng et al. 2013; Vinothkumar et al. 2018).

The translation of CeO₂NPs into clinical use is fundamentally challenged by their dualistic physicochemical nature and the unpredictability of their interactions within complex biological systems. Their hallmark antioxidant activity is highly dependent on the surface Ce³⁺/Ce⁴⁺ ratio and oxygen vacancy concentration. However, these critical parameters are not only difficult to control during synthesis precisely but also susceptible to alterations within the intricate physiological microenvironment in vivo. Studies have confirmed that in the acidic environment of lysosomes, the redox state of CeO₂NPs can shift, potentially transforming from an antioxidant into a pro-oxidant. This phenomenon fundamentally affects their biosafety and the controllability of their therapeutic efficacy (Das et al. 2012).

Furthermore, the size, morphology, and surface charge of nanoparticles profoundly influence their cellular uptake efficiency, in vivo biodistribution, and metabolic clearance pathways. For instance, while smaller particles possess stronger cell-penetrating capabilities, they may also cross biological barriers in unpredictable ways. Similarly, surface modification strategies aimed at improving particle dispersity and the circulation half-life can alter particle specificity toward target cells (Asati et al. 2010). Consequently, balancing biocompatibility, structural stability, and therapeutic activity remains an urgent challenge in nanomaterial design.

To effectively deliver CeO₂NPs to silicotic fibrotic lesions and preserve their bioactivity, one must overcome the lung's unique, multiple physiological barriers. In silicosis, pathological features, including disrupted mucus secretion, damaged epithelial barriers, abnormal fibrous tissue proliferation, and persistent inflammatory responses, collectively create a complex drug delivery landscape (Hu et al. 2024; Sherekar et al. 2025). Nanocarriers must sequentially evade mucociliary clearance, penetrate dense fibrotic tissue, and ultimately be efficiently internalized by activated macrophages or myofibroblasts to exert their intended therapeutic effect. Currently, active targeting tailored to the pathological microenvironment of pulmonary fibrosis is still in its early stages, with low delivery efficiency posing a critical bottleneck to therapeutic outcomes.

Significant gaps remain in our understanding of the pharmacokinetic profile and long-term fate of CeO₂NPs in the body, representing a major obstacle to assessing their clinical safety. Existing studies have yet to establish clear and consistent conclusions regarding key issues, such as retention time in the lungs after inhalation or systemic administration; biodegradation rate; metabolic byproduct composition; and clearance pathways via the lungs, liver, and kidneys. In particular, the potential for long-term accumulation of these nanoparticles in the reticuloendothelial system and the associated risk of chronic toxic effects still lack systematic and sufficient safety evaluation data (Tarnuzzer et al. 2005).

Given the preceding viewpoints, the application methods and safety of CeO₂NPs in the human body remain important. When CeO₂NPs are used in biomedicine, they can be loaded into a material or coated with a biocompatible polymer. Chitosan and polyethylene glycol were initially considered. These two substances can enhance the biosafety of CeO₂NPs without affecting the material's inherent properties. Meanwhile, they can enhance the bioavailability of a material. Secondly, combination with albumin improved the antioxidant performance of CeO₂NPs. Moreover, albumin itself exerts an immunomodulatory effect on damaged tissues. The application of specific auxiliary materials warrants further exploration. When aiming to enhance biosafety, hydrogels are a viable option. If the goal is to improve biodegradability, chitosan can be selected. If specific gene alterations are detected or genes for treatment are discovered in the research, DNA/RNA should be chosen. If methods for utilizing CeO₂NPs in the biomedical field are identified, loading them onto metal–organic frameworks (MOFs) can be a viable approach. This not only facilitates imaging and detection but also provides adjuvant treatment. By harnessing the antioxidant activity of CeO₂NPs and the properties of auxiliary materials, various free radicals in the lungs of patients with silicosis can be inhibited and scavenged, thereby alleviating silicosis.

4.3. Approaches to mitigate the toxic side effects of CeO₂NPs

The toxic side effects of CeO₂NPs are a significant concern. Researchers have found that these effects vary to some extent depending on the size, shape and charge of CeO₂NPs. In an inhalation toxicity study of CeO₂NPs, researchers exposed mice to four variants with distinct sizes, shapes, and surface charges. The results showed that spherical nanoparticles exhibited the lowest toxicity, whereas polygonal nanoparticles induced the most substantial adverse effects. Larger nanoparticles also demonstrated greater toxicity compared to smaller ones. Interestingly, the toxic responses differed between rats and mice, with rats exhibiting more pronounced adverse effects (Dekkers et al. 2018). Although the CeO₂NPs in this experiment also differed in surface charge, the study did not address the influence of this parameter on toxicity (Dekkers et al. 2018). However, other studies have shown that positively charged nanoparticles exhibit significantly higher cellular uptake compared to negatively charged or neutral nanoparticles, which is attributed to their enhanced ability to adsorb plasma proteins. Nonetheless, they may also induce hemolysis and platelet aggregation, leading to systemic toxicity (Goodman et al. 2004). Additionally, in normal saline, direct interaction between positively charged CeO₂NPs and the cell wall destabilize the

membrane, leading to increased ROS production and reduced cell viability. In contrast, although exposure to PBS still induces membrane destabilization and elevated ROS levels, no detectable cytotoxicity is observed under these conditions (He et al. 2012).

Larger CeO₂NPs may exhibit higher toxicity toward eukaryotic cells, potentially attributed to the tendency of smaller CeO₂NPs to agglomerate, which diminishes their toxic effects (Schubert et al. 2006; Kumar et al. 2014). The aggregation of CeO₂NPs is influenced by pH, natural organic matter, and ionic strength. Increases in pH and ionic strength promote their aggregation. Under low-pH conditions, natural organic matter exhibits a high adsorption affinity for CeO₂NPs, thereby significantly reducing their toxicity by inhibiting interactions between nanoparticles and target cells (Van Hoecke et al. 2011). In contrast, high concentrations of aggregated CeO₂NPs exhibit toxic effects (Röhder et al. 2014). In *in vitro* studies, researchers have found that CeO₂NPs are toxic to alveolar epithelial cells (Gasser et al. 2009; Mittal et al. 2014). It is hypothesized that the toxic mechanism may be related to nanoparticle aggregation induced by respiratory mucus, and that this aggregation could contribute to enhanced toxicity (Frieke Kuper et al. 2015).

Regarding the morphology of CeO₂NPs, studies have shown that spherical nanoparticles exhibit lower toxicity. This is attributed to the fact that spherical nanoparticles are more readily and rapidly endocytosed than their rod-shaped or fibrous counterparts. In contrast, non-spherical nanomaterials tend to translocate through capillaries, thereby triggering additional biological consequences (Champion and Mitragotri 2006; Lee et al. 2007; Kim et al. 2012). The varying toxicity of CeO₂NPs arising from different shapes may also be associated with their aspect ratio (the ratio of length to width); a higher aspect ratio generally correlates with stronger toxicity of CeO₂NPs (Mortazavi Milani et al. 2017). Specifically, when the length is ≥ 200 nm and the aspect ratio is ≥ 22 , CeO₂ nanorods induce persistent pro-inflammatory effects and cytotoxicity (Booth et al. 2015).

Based on the analysis of the aforementioned toxicity-influencing factors, it is advisable to preferentially select spherical, small-sized, and negatively charged CeO₂NPs for subsequent applications to mitigate their potential adverse effects. Moreover, to mitigate the toxic effects of CeO₂NPs, surface-coating modifications can be employed. This approach enhances nanoparticle stability and inhibits the release of toxic ions, thereby reducing or eliminating associated adverse reactions (Kirchner et al. 2005). To this end, surface modifications of NPs employing hydrophilic and flexible polyethylene glycol (e.g. pegylation) and other surfactant copolymers (e.g. poloxamers and polyethylene) have been widely used since the beginning of this advanced field of nanotechnology to stabilize nanoparticulate systems in biological milieus (Gatoo et al. 2014). Inhalable or aerosolized formulations of CeO₂NPs can be developed to enable precise pulmonary delivery at low doses. This approach is grounded in the principle that particles 1–5 μ m in size effectively deposit in alveolar regions, while those smaller than 100 nm are also capable of efficient lung targeting (Gholap et al. 2025). Compared with systemic administration, such localized delivery can achieve therapeutic effects at lower dosages. The incorporation of CeO₂NPs into pulmonary delivery carriers, such as polymeric nanoparticles, lipid nanoparticles, liposomes, solid lipid nanoparticles or inhalable microspheres, enables better control of the local concentration and release kinetics within the pulmonary microenvironment, enhances local bioavailability, reduces the required dose, and thereby mitigates pro-inflammatory responses (Chan et al. 2023). In addition, materials possessing inherent anti-oxidant and anti-inflammatory properties can also be selected as delivery carriers. Alternatively, CeO₂NPs can be integrated into hydrogels to create ROS- or inflammatory factor-responsive systems, enabling targeted release in specific pathological microenvironments and thereby achieving precise therapeutic outcomes (Pu et al. 2024).

5. Biomedical application prospects

5.1. Prospect of CeO₂NPs in the treatment of pulmonary diseases

5.1.1. CeO₂NPs in the treatment of COVID-19

Novel Coronavirus Disease-2019 (COVID-19), caused by infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is characterized by pulmonary lesions, with diffuse alveolar damage as its core pathological feature. Following viral invasion of the body, the pathogen specifically targets lung tissue,

triggering an inflammatory response and subsequently leading to pulmonary cell injury (Ricard et al. 2021). All these processes are associated with the development of oxidative stress, which makes an essential contribution to the pathogenesis of viral infections (Chernyak et al. 2020).

SARS-CoV-2 first binds to the angiotensin-converting enzyme 2 (ACE2) receptor via its spike (S) protein, facilitating membrane fusion. The RNA genome is subsequently released and translated; the resulting structural and non-structural proteins then interact with mitochondrial components, disrupting mitochondrial function. This cascade drives elevated reactive oxygen species (ROS) production, which in turn triggers oxidative stress and inflammatory responses (Noonong et al. 2023).

In relevant studies, researchers have shown that 3 nm CeO₂NPs can target the 5 nm cavity within the spike protein trimer that forms upon SARS-CoV-2 binding to the ACE2 receptor on the host cell surface. These nanoparticles bind tightly to the receptor-binding domain (RBD), thereby blocking subsequent viral–cell interactions and functioning as highly efficient antiviral agents (Zhang et al. 2024). This mechanism can effectively inhibit viral replication and mitigate mitochondrial damage, thereby reducing ROS production and ultimately exerting antioxidative, anti-inflammatory, and antiviral effects.

5.1.2. CeO₂NPs in the treatment of LC

ROS exert distinct roles at different stages of lung cancer progression. During the precancerous phase, ROS can induce oxidative stress that damages tumor suppressor genes, thereby promoting the initiation and progression of lung cancer. At later stages of tumor progression, they facilitate cancer cell invasion and metastasis by activating the NF- κ B and MAPK pathways. However, at advanced stages, when ROS exceed the threshold, they promote cell-cycle arrest and induce apoptosis in cancer cells (ArulJothi et al. 2022). Therefore, the antioxidative effect of CeO₂NPs is mainly applicable to the early and middle stages of lung cancer, but not to the advanced stage.

CeO₂NPs can mitigate oxidative damage via Ce³⁺/Ce⁴⁺ redox cycles and scavenge superoxide anions and hydrogen peroxide through their nanozyme-mimetic activity (Corsi et al. 2023). Consequently, they can protect tumor suppressor genes from ROS-induced damage during the pre-cancerous stage. Furthermore, at advanced stages of cancer, CeO₂NPs can alleviate the inflammatory response and delay further cancer progression by reducing ROS production and inhibiting the MAPK-NF- κ B signaling pathway (Li et al. 2024).

5.1.3. CeO₂NPs in the treatment of COPD

Chronic obstructive pulmonary disease (COPD) includes chronic bronchitis and emphysema. Oxidant–antioxidant imbalance is recognized as a significant factor in COPD pathogenesis (Bialas et al. 2016). It is believed that oxidative stress is increased in patients with COPD due to chronic exposure to cigarette smoke, a primary risk factor that involves high concentrations of oxidants and ROS (Boukhenouna et al. 2018). Extrinsic ROS can induce oxidative stress and thereby activate immune cells. In turn, activated immune cells further release endogenous ROS. This positive feedback loop contributes to the persistent progression of COPD even in the absence of extrinsic ROS stimulation (Hobbins et al. 2017; Boukhenouna et al. 2018).

Analysis of the pathogenic mechanisms of COPD reveals that both extrinsic and intrinsic factors are closely associated with ROS. These findings indicate that mitigating oxidative stress with antioxidants or enhancing the function of the endogenous antioxidant system is an effective therapeutic strategy for targeting potential pathogenic mechanisms of COPD (Barnes 2020). CeO₂NPs exert antioxidant effects by scavenging free radicals and inhibiting the autooxidation of phosphatidylcholine. One of the core pathological features of COPD is an imbalance between the oxidative and antioxidant systems, and the prooxidant properties of CeO₂NPs contribute to this dysregulation, ultimately helping to restore the prooxidant/antioxidant balance to physiological homeostasis (Nikitchenko et al. 2023).

5.1.4. CeO₂NPs in the treatment of ALI

The pathogenesis of acute lung injury (ALI) is widely recognized to involve pulmonary or systemic inflammatory responses. Inflammatory cytokines can activate inflammasomes and induce oxidative stress, which in turn promotes cell apoptosis and mitochondrial damage. Mitochondrial dysfunction further amplifies inflammation and oxidative stress, ultimately disrupting the pulmonary barrier (Liu et al. 2025).

In one study, researchers utilized cerium oxide nanoparticles to load probes, thereby achieving both therapeutic and diagnostic effects on ALI. Meanwhile, leveraging the SOD-mimetic and CAT-mimetic activities inherent to CeO_2NPs , the system exerted a synergistic effect that suppressed oxidative stress, downregulated proinflammatory cytokines, ameliorated pulmonary edema, and repolarized proinflammatory macrophages (Li et al. 2024). These effects demonstrate the therapeutic potential of cerium dioxide nanoparticles for ALI, as they can effectively mitigate oxidative stress and alleviate inflammatory responses associated with this condition.

Lung diseases share similarities in their pathogenesis, and oxidative stress plays a crucial role in the pathogenic mechanisms of various pulmonary conditions, including COVID-19, LC, COPD, and ALI (Paola Rosanna and Salvatore 2012; Han et al. 2016; Gautam et al. 2017; Suhail et al. 2020; Nordberg and Arnér). Therefore, antioxidant therapy represents a promising approach for the treatment of these diseases (Taniguchi et al. 2021; Sul et al. 2023). As discussed in this paper, CeO_2NPs with excellent nanozyme properties hold great potential for treating such conditions. By leveraging their nanozyme activities, CeO_2NPs can inhibit and scavenge excess ROS generated in these diseases, thereby slowing disease progression and alleviating clinical symptoms (Yuan et al. 2022). Consistent with these findings, ROS inhibition mitigates disease progression, and nanozyme-active CeO_2NPs may serve as effective therapeutic agents by targeting excessive ROS and halting disease progression (Figure 5).

5.2. Therapeutic delivery prospects of CeO_2NPs in pulmonary therapy

The application of CeO_2NPs in lung diseases warrants further exploration. Nevertheless, the currently commonly used drugs in clinical practice have shortcomings, such as being unable to target diseases precisely, resulting in a large amount of drug waste. To this end, CeO_2NPs can be magnetized. By doing so, targeted drug delivery can be achieved using the currently advanced clinical treatment technology of magnetic resonance navigation. This approach can help avoid the waste of CeO_2NPs drugs. The use of innovative technology has significantly enhanced the accuracy and convenience of current treatment methods. The antioxidation properties of CeO_2NPs alone are relatively simplistic. Hence, loading drugs on the surface of CeO_2NPs can achieve the effect of doubling antioxidation.

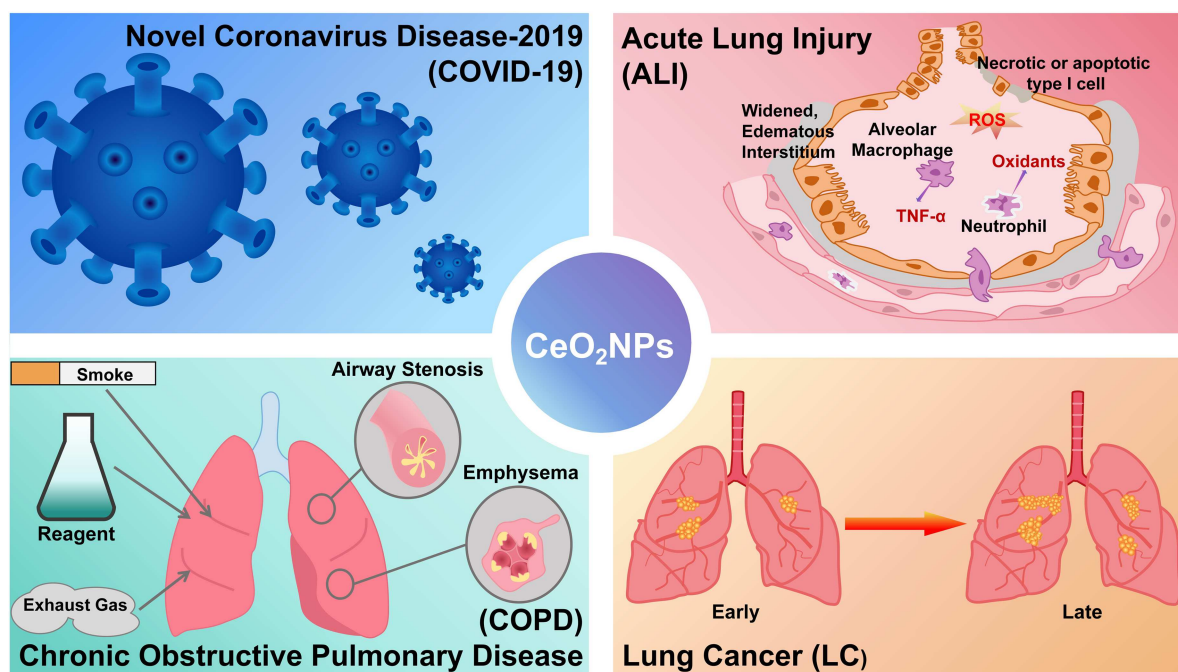


Figure 5. CeO_2NPs can be used to address other diseases related to oxidative stress (Author-created).

For drug selection, intelligent molecular docking can be used for screening. Firstly, the treatment target proteins of silicosis, such as NLRP3, must be identified. Then, determine the drugs that can be used for docking, such as GDC-2394, costunolide, etc. Finally, docking software for drug-target docking should be utilized (McBride et al. 2022; Xu et al. 2023). Among the currently popular NLRP3 inhibitors, GDC-2394 exhibits the greatest adaptability. Drugs with greater target matching can achieve better therapeutic outcomes and reduce the waste of experimental time and resources.

With respect to drug loading, electrostatic adsorption technology can reduce the formation of certain unknown chemical constituents and reduce their impact on experimental results compared with chemical–physical adsorption. The drawback of direct loading of drugs, i.e. insufficient binding of drugs, cannot be ignored. Thus, suitable biosafe polymers can be selected to encapsulate drugs and CeO₂NPs. Alternatively, the drug can be incorporated into a polymer, and CeO₂NPs can then be combined with or coated onto the polymer. The use of polymers enhances nanoparticle biosecurity and reduces the risk of drug loss during targeting, offering significant advantages for clinical treatment. Notably, not only is the cost increase still under consideration, but the selection of polymers also warrants attention. It is necessary to avoid situations where the drug is not easy to dissolve or diffuse and prevent the bioavailability of drugs from being reduced. The efficacy of commonly used polymers, such as polyethylene glycol, and hydrogels must be verified experimentally. Notably, when polymers are selected, the limitations of CeO₂NPs in treatment should be considered. It is necessary to determine whether a polymer can overcome the limitations of CeO₂NPs while enabling drug coating. An essential consideration is that, in subsequent studies, drugs, polymers, and CeO₂NPs must be sterilized to prevent bacterial contamination from affecting experimental results. In subsequent clinical use, preventing bacteria attached to nanomedicine from causing additional harm to patients and avoiding iatrogenic infection are essential.

5.3. Additional application prospects of CeO₂NPs in silicosis

The pathogenic factors of silicosis are not limited to ROS, and numerous factors are involved. Meanwhile, the therapeutic effect of CeO₂NPs in silicosis is not limited to their antioxidant properties. Lipopolysaccharide was used to stimulate macrophages in cell experiments, and control experiments were conducted simultaneously. CeO₂NPs blocked inflammatory signaling pathways (such as the NF- κ B and MAPK pathways). As a result, the release of pro-inflammatory cytokines (such as TNF- α , IL-6, and IL-1 β) is reduced, and the inflammatory level of cells is decreased (Figure 6) (Selvaraj et al. 2015). If applied to the treatment of silicosis, it could reduce damage to lung cells and slow disease progression (Hirst et al. 2009). Although the fate of macrophages has not been reported in the literature, the experimental results indicate that macrophage lysis can be inhibited. This inhibition, which reduces the release of inflammatory mediators from macrophages, significantly minimizes the adverse effects on the surrounding lung parenchyma. Owing to silicosis patients' diminished immunity and the concomitant presence of diverse bacteria on silica particles, silicosis patients frequently experience concurrent bacterial infections (Howlett et al. 2025). In experiments, CeO₂NPs exhibited anti-inflammatory effects and the potential to prevent and alleviate bacterial infections. As documented in the present study, during sepsis, lymphocyte percentages decreased while granulocyte percentages increased at both the 6 and 24 h time points. However, nanoparticle treatment reversed these alterations specifically at the 6 h mark (Selvaraj et al. 2015). This demonstrates its anti-inflammatory effect, as it can reduce inflammation in damaged tissues and mitigate the impact of inflammatory cells on the organism. An analysis of experiments conducted by Srinivasulu Chigurupati et al. indicated that CeO₂NPs can promote wound healing and angiogenesis (Chigurupati et al. 2013). Damaged lung tissues can accelerate tissue repair. Although tissue healing involves fibroblast aggregation, continuous release of inflammatory factors from damaged tissues that remain unhealed can harm nearby cells and tissues. The resulting lung damage is increased, potentially leading to further deterioration of silicosis. Therefore, timely healing is beneficial for patient recovery. Given the impact of fibroblast formation on patients, the use of stem cells for treatment may be considered later. In treating diseases, the first consideration should be disease control; subsequent improvement can then be achieved gradually.

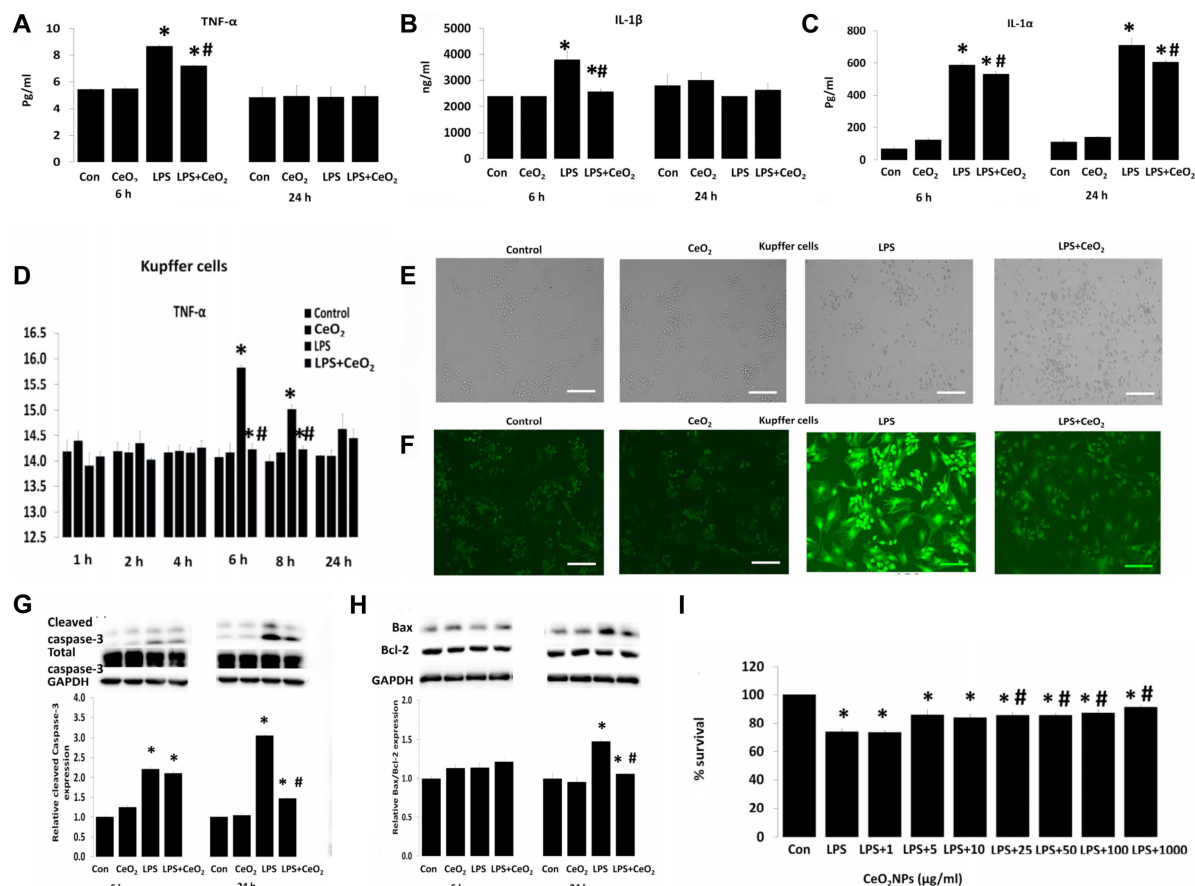


Figure 6. CeO₂NPs exert anti-inflammatory, antioxidant, and anti-apoptotic effects in LPS-challenged Kupffer cells. (A–C) CeO₂NPs significantly reduced the LPS-induced secretion of TNF-α, IL-1β, and IL-1α at 6 h, and attenuated IL-1α release at 24 h. (D) Time-course analysis showed that CeO₂NPs suppressed LPS-driven TNF-α expression in Kupffer cells. (E) Morphological assessment revealed that CeO₂NPs preserved normal cell morphology compared with that of LPS-treated cells. (F) Fluorescence imaging indicated that CeO₂NPs alleviated LPS-induced ROS accumulation. (G) Western blot analysis demonstrated that CeO₂NPs inhibited the LPS-triggered cleavage of caspase-3. (H) CeO₂NPs decreased the Bax/Bcl-2 ratio, suggesting attenuation of apoptotic signaling. (I) Cell viability assays confirmed that CeO₂NPs improved Kupffer cell survival in a dose-dependent manner. Data are adapted from Selvaraj et al., *Biomaterials* 59, 160–171 (2015) (Selvaraj et al. 2015).

Because silica particles in the lungs are too small to be readily excreted, CeO₂NPs can be used to facilitate the expulsion of these particles by adsorbing SiO₂. The aggregated particles are more likely to be expelled from the lungs through respiration and coughing. Here, two adsorption methods are discussed. First, the two can be adsorbed via hydrogen bonding. The hydroxyl groups (–OH) on the surface of CeO₂NPs serve as hydrogen-bond donors, providing hydrogen atoms (Plakhova et al. 2019). The oxygen atoms on the surface of SiO₂ (or the oxygen in the hydroxyl group) act as hydrogen-bond acceptors, accepting hydrogen atoms (Zhuravlev 2000). Through the action of hydrogen bonds, stable connections are formed between the surfaces of CeO₂NPs and SiO₂ (Meot-Ner (Mautner), M., 2005; Buckingham et al. 2008). Secondly, electrostatic attraction between positive and negative charges can also be considered, in addition to hydrogen bonds. Silicon dioxide exhibits a negative charge in the body's environment. This occurred because silanol groups (Si–OH) are formed on the surface of SiO₂ in an aqueous solution. When pH > 2, the silanol groups undergo deprotonation, generating a net negative charge on the surface of SiO₂ (Sulpizi et al. 2012). Moreover, CeO₂NPs can carry a positive charge during preparation (Parimi et al. 2019). Consequently, they can adsorb negatively charged SiO₂ upon application. In theory, both methods described above can use CeO₂NPs to adsorb small SiO₂ particles in the lungs. This facilitates the expulsion of the aggregated SiO₂ and reduces the continuous damage to lung tissues caused by a large amount of non-excretable SiO₂.

6. Conclusion and discussion

Silicosis is a severe form of pneumoconiosis caused by the long-term inhalation of a large quantity of free silica dust particles. The formation of silicotic nodules and extensive pulmonary fibrosis characterize it. ROS play a crucial role in the development of silicosis. When silica enters the lungs, the normal balance between ROS production and clearance can be disrupted. The pathogenesis of silicosis involves macrophages that undergo a series of reactions after exposure to silica dust. This leads to the production of ROS. In turn, these ROS cause lung inflammation, oxidative stress, and damage to cells and tissues. Eventually, this may progress to respiratory failure and heart failure. The antioxidant properties of these nanomaterials provide hope for the treatment of silicosis. Nano-antioxidants have the advantages of high stability and can target specific sites. Nanozymes can overcome the limitations of natural enzymes, which are sensitive to environmental conditions.

CeO₂NPs possess unique properties and a high oxygen storage capacity. Surface oxygen vacancies mediate their antioxidant activity. The smaller the particle size and the higher the Ce³⁺/Ce⁴⁺ ratio, the greater the antioxidant and free-radical scavenging capacity. In the treatment of silicosis, it can be used to simulate various enzymes to clear ROS, reduce inflammation, regulate silicosis-related characteristics, and slow disease progression. However, CeO₂NPs have non-negligible limitations in the treatment of silicosis. For example, at specific sizes, it has low simulated SOD activity. This material is susceptible to light exposure; it can absorb both visible light and ultraviolet radiation, thus enhancing its catalytic performance. The possible increased toxicity of Ce³⁺ is also a concern. Additionally, accurately controlling the dosage of drugs is difficult.

CeO₂NPs hold great potential in the treatment of lung diseases. In various lung diseases, ROS accumulation promotes disease progression. The nanozyme properties of CeO₂NPs can be utilized to inhibit and clear ROS, slow disease progression, and alleviate symptoms. To improve therapeutic efficacy, magnetized CeO₂NPs can be used for targeted guidance. They can also be loaded with drugs or coated with polymers to enhance their antioxidant properties. However, issues such as polymer selection, cost, and sterilization treatment warrant attention. In addition, gold, silver, and iron oxide nanoparticles also possess antioxidant properties and can be used to treat silicosis. Importantly, the biosafety and drug payload of nanomaterials remain under investigation. In clinical use, the uniqueness of nanoparticles should be fully understood to ensure the effectiveness and safety of treatment.

In this work, the enzyme-like antioxidant properties of CeO₂NPs were explored. However, in terms of the material itself, it has not been thoroughly researched. If CeO₂NPs are to be used in laboratory or clinical settings, their shape and size are essential considerations. It should be tested whether the properties of nanoparticles with different shapes are identical and whether the capabilities of nanoparticles of various sizes are the same. The antioxidant activity of these compounds should be critically considered in future discussions of lung disease and nanoparticles. Among the situations that require attention, nanoparticle biosafety is of paramount importance. In clinical use, the material being addressed is not a simple substance. Instead, a physical entity with a unique structure and properties, akin to a miniature reactor, is considered. In treatment, the therapeutic effect of nanoparticles is not solely determined by the particles themselves. Instead, nanoparticles can be combined with modern science and technology to achieve better therapeutic effects.

7. Future directions

7.1. Long-term prospects of nanoparticle therapy in silicosis

In addition to the antioxidation effects of the CeO₂NPs discussed in this paper, standard gold and silver nanoparticles also possess similar antioxidant properties in daily life. Owing to their excellent biocompatibility, low toxicity, and tunable stability, gold nanoparticles have been widely used in detection, biosensing, bioimaging, medical diagnosis, and therapy (Jain et al. 2006; Zeng et al. 2011). According to experiments, gold nanoparticles possess peroxidase activity, SOD activity, and CAT activity (Lin et al. 2014). In rat experiments by Saba Safari et al., silver nanoparticles had the same antioxidant capacity and could be used to treat oxidative stress caused by excessive ROS accumulation (Safari et al. 2023). In the current literature, gold and silver nanoparticles are widely used in biomedicine. These nanoparticles possess unique properties that make them valuable for various applications. Gold and silver nanoparticles, such as

CeO₂NPs, exhibit similar nanozyme properties and can be used to treat silicosis by removing and inhibiting excessive ROS accumulation. In biomedical applications, mercaptan polyethylene glycol (PEG-SH) is often used as a surface ligand for gold nanoparticles (Dreaden et al. 2009). After identifying the appropriate ligand, the efficiency of the experiment improved significantly.

In addition to the two standard nanoparticles used in medicine (gold and silver), oxide nanoparticles should also be considered for the treatment of silicosis. Iron oxide nanoparticles serve as excellent antioxidants. Unlike CeO₂NPs, iron oxide nanoparticles possess magnetic properties and thus do not require magnetization of the material when employed in nuclear magnetic resonance navigation (Fahmy 2020). Interestingly, compared with that of chemically synthesized iron oxide nanoparticles, the antioxidant activity of biologically derived iron oxide nanoparticles is increased by two-fold (Neupane et al. 2019). In this context, magnetic iron oxide nanoparticles can inhibit oxidative stress-induced damage caused by ROS in silicosis. Iron oxide nanoparticles can be synthesized via a green chemical method. Since nanoparticles synthesized from natural products can enhance bioavailability, the targeted controlled-release properties of natural drugs, and their therapeutic value, they provide a solid basis for the future use of iron oxide nanomaterials in the treatment of silicosis (Barras et al. 2009; Sherekar et al. 2024).

Nanoparticles are highly diverse in type, and this article primarily focuses on three representative nanomaterials: gold, silver, and iron oxide, with the remaining content addressed in the table (Table 1). This selection is based on the fact that gold and silver are two other common noble metals. Iron oxide, a common oxide encountered in daily life, is also highly representative. In the search for silicosis treatment materials, in addition to considering the antioxidant properties of the materials themselves, attention should also be given to the antibacterial properties of the materials. The biosafety and drug-loading capacity of nanomaterials require further investigation for practical applications. In the treatment of silicosis, unstable materials should be avoided. This prevents material instability from causing harm to the body during treatment. When selecting the shape of nanomaterials, spherical nanoparticles should be

Table 1. Antioxidant properties of nanoparticles.

Nanoparticles	Synthetic materials	Antioxidant application	References
Copper nanoparticles	<i>Cissus amotiana</i>	The mechanism behind the antioxidant property is attributed to the inhibition of chain reactions, decomposition of peroxides, binding of transition metal ion catalysts, radical scavenging activity and inhibition of continued hydrogen abstraction. Among the radical scavenging property of the copper nanoparticles, the highest percentage of inhibition is observed at 40 µg/ml.	Rajeshkumar et al. (2019)
Platinum nanoparticles	<i>Tragia involucrata</i>	The synthesized Ti-PtNPs exhibited the highest DPPH free radical scavenging activity ($64 \pm 0.43\%$) at a concentration of 1 mg/ml, with a concentration-dependent activity profile. Meanwhile, the reducing capacity of Ti-PtNPs was proportional to their concentration, showing activities ranging from $13.45 \pm 0.23\%$ to $58 \pm 0.27\%$ across the Ti-PtNPs concentration range of 0.2–1 mg/ml. Additionally, the total antioxidant capacity of Ti-PtNPs ranged from $15.85 \pm 0.22\%$ to $59.37 \pm 0.14\%$ within the concentration range of 0.2–1 mg/ml.	Selvi et al. (2020)
Aluminum oxide nanoparticles	<i>Clerodendrum phlomidis</i>	The aluminum oxide nanoparticles exhibit in vitro DPPH free radical scavenging activity in a dose-dependent manner, with concentrations tested at 100, 200, 300, 400, and 500 µg/ml, and they demonstrate significant antioxidant activity at the concentration of 500 µg/ml.	Thanaraj et al. (2024)
Magnesium oxide nanoparticles	<i>Alstonia scholaris</i>	At concentrations of 0.05, 0.125, 0.25, and 0.5 mg/mL, the scavenging rates of biosynthesized magnesium oxide nanoparticles were 22.34%, 42.55%, 62.76%, and 69.14% respectively, whereas the scavenging rates of standard ascorbic acid at the same concentrations were 12.77%, 28.94%, 36.49%, and 46.70% respectively. The scavenging rate of the biosynthesized magnesium oxide nanoparticles was higher than that of standard ascorbic acid. Compared with standard ascorbic acid, the prepared magnesium oxide nanoparticles exhibit higher antioxidant potential.	Shahid et al. (2022)
Manganese dioxide nanoparticles	Green tomato	Whether at high or low intake levels of manganese dioxide nanoparticles, the activities of SOD, glutathione, and glutathione peroxidase were all elevated, with higher intake levels inducing stronger enzyme activities than lower levels of manganese oxide. Furthermore, the impact on glutathione S-transferase activity was not significant.	Helbawi et al. (2024)

chosen. Compared with spherical nanoparticles, sharp-edged nanoparticles have the potential to generate free radicals and cause mechanical damage to cells (Karakoti et al. 2012; Das et al. 2013).

The materials mentioned above represent an extension of the CeO₂NPs discussed in this article and offer prospects for future nanoparticle applications. The reason for choosing CeO₂NPs in this study is that, in terms of their antioxidant properties, CeO₂NPs possess more substantial antioxidant capabilities. Silver nanoparticles are primarily used for antibacterial applications in biomedical settings. This is because silver nanoparticles also generate ROS, thereby exerting antibacterial effects (Park et al. 2009). Compared with CeO₂NPs, gold nanoparticles exhibit weaker antioxidant properties. They function mainly by loading antioxidant drugs to achieve antioxidant effects (Sharpe et al. 2011; Das et al. 2013). The antioxidant capacity of iron oxide nanoparticles is also rather normal. More importantly, iron oxide nanoparticles are highly cytotoxic, making them difficult to control when used in the treatment of silicosis or even in biomedical engineering (Liu et al. 2013).

Meanwhile, gold nanoparticles are more frequently applied in drug delivery, while iron oxide nanoparticles are more commonly used in tissue engineering. Therefore, we selected CeO₂NPs because of their high antioxidant capacity and biosafety; no lung damage was observed in lung experiments (Hirst et al. 2009). Moreover, compared with gold and silver nanoparticles, CeO₂NPs are less costly, imposing a relatively lighter burden on patients. During patient care, physicians should comprehensively evaluate the treatment plan from multiple perspectives, and humanistic care is indispensable.

7.2. Looking ahead: CeO₂NPs in biomedicine

In the biomedical applications of nanoparticles, the efficacy of nanoparticles is by no means limited to the inherent properties of the particles themselves. In future experiments and clinical applications, nanoparticles should be integrated with advanced intelligent medical technologies. For instance, well-developed nano-drug delivery technology can be utilized. This technology can overcome drug hydrophobicity and enhance their bioavailability. Moreover, it can maintain the antioxidant state of drugs, thereby continuously inhibiting and scavenging ROS, enabling effective and sustained treatment of silicosis. By leveraging this technology to treat silicosis and other pulmonary diseases, CeO₂NPs can be precisely delivered to diseased sites. This not only improves treatment efficacy but also reduces damage to healthy tissues, minimizes drug waste, and lowers treatment costs for patients.

It is worth pondering whether combining the properties of nanomaterials with drug effects can enhance drug efficacy. The specific outcome needs to be verified by subsequent experiments. However, every issue requires a dialectical approach. While leveraging the antioxidant properties of nanomaterials, the dosage of these materials should also be considered. When antioxidant activity is too strong, it is uncertain whether drawbacks will arise and, if so, what they might be.

CeO₂NPs can also be used in combination with high-resolution imaging techniques. Monitoring the distribution, action, and circulation process of nanoparticles in the body provides a basis for improving treatment plans. Additionally, with gene-editing technology, nanoparticles can be functionally modified to receive signals from specific genes, enabling more precise treatment. Moreover, when combined with fluorescence imaging technology, this method can enhance contrast, supporting the detection of minute lesions in the body.

When CeO₂NPs are used in medicine, they are expected to play a crucial role in the treatment of nervous system diseases. Oxidative stress plays a significant role in the pathogenesis of neurodegenerative diseases such as Alzheimer's disease and Parkinson's disease. Owing to their excellent antioxidant properties and tiny particle size, CeO₂NPs are highly likely to cross the blood–brain barrier and reach disease-affected sites. They can then scavenge excess ROS within nerve cells, mitigate oxidative damage, and slow the apoptotic process. In the treatment of cardiovascular diseases, CeO₂NPs can prevent the formation and progression of atherosclerosis by inhibiting the inflammatory response and enhancing vascular endothelial cell function. CeO₂NPs perform regenerative tasks in medical applications and are used to regenerate skin, muscles, etc. (Ren et al. 2022; Allu et al. 2023). Based on this property, it is feasible to consider the application of CeO₂NPs for the treatment of cardiovascular diseases (Guerra-Ojeda et al. 2022). They can repair damaged blood vessels and the heart, thereby enhancing survival rates among patients with cardiovascular and cerebrovascular

diseases. CeO₂NPs prevent the formation and development of atherosclerosis by suppressing the inflammatory response and improving the function of vascular endothelial cells. Meanwhile, given its antioxidant capacity, it can also be considered for use in plastic surgery. It can promote the recovery of surgical tissues and has the effects of beauty enhancement and anti-aging.

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Author contributions

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Data availability statement

Figures 1–5 are original creations by the authors. Figure 6 incorporates data from external sources, for which the necessary copyright permissions have been obtained. All the aforementioned materials will be made available upon reasonable request.

References

- Abdulwahab KO, Khan MM, Jennings JR. 2023. Doped ceria nanomaterials: preparation, properties, and uses. *ACS Omega*. 8:30802–30823. <https://doi.org/10.1021/acsomega.3c01199>
- Ahmad A, Haneef M, Kamal A et al. 2024. Biological synthesis of silver nanoparticles and their medical applications (Review). *World Acad Sci J*. 6:22. <https://doi.org/10.3892/wasj.2024.237>
- Ahmed S, Ikram S. 2016. Chitosan and gelatin based biodegradable packaging films with UV-light protection. *J Photochem Photobiol B*. 163:115–124. <https://doi.org/10.1016/j.jphotobiol.2016.08.023>
- Akhtar MJ, Ahamed M, Alhadlaq H. 2021. Anti-inflammatory CeO₂ nanoparticles prevented cytotoxicity due to exogenous nitric oxide donors via induction rather than inhibition of superoxide/nitric oxide in HUVE cells. *Molecules*. 26:5416. <https://doi.org/10.3390/molecules26175416>
- Allu I, Kumar Sahi A, Kumari P et al. 2023. A brief review on cerium oxide (CeO₂NPs)-based scaffolds: recent advances in wound healing applications. *Micromachines*. 14:865. <https://doi.org/10.3390/mi14040865>
- ArulJothi KN, Kumaran K, Senthil S et al. 2022. Implications of reactive oxygen species in lung cancer and exploiting it for therapeutic interventions. *Med Oncol*. 40:43. <https://doi.org/10.1007/s12032-022-01900-y>
- Arumugam A, Karthikeyan C, Haja Hameed AS et al. 2015. Synthesis of cerium oxide nanoparticles using gloriosa superba L. Leaf extract and their structural, optical and antibacterial properties. *Mater Sci Eng C*. 49:408–415. <https://doi.org/10.1016/j.msec.2015.01.042>
- Asati A, Santra S, Kaithanis C et al. 2010. Surface-charge-dependent cell localization and cytotoxicity of cerium oxide nanoparticles. *ACS Nano*. 4:5321–5331. <https://doi.org/10.1021/nn100816s>
- Bai Y, Liang C, Gao L et al. 2024. Celastrol pyrazine derivative alleviates silicosis progression via inducing ROS-Mediated apoptosis in activated fibroblasts. *Molecules*. 29:538. <https://doi.org/10.3390/molecules29020538>

- Bardi G, Boselli L, Pompa PP. 2023. Anti-inflammatory potential of platinum nanozymes: mechanisms and perspectives. *Nanos*. 15:14284–14300. <https://doi.org/10.1039/D3NR03016D>
- Barnes PJ. 2020. Oxidative stress-based therapeutics in COPD. *Redox Biol*. 33:101544. <https://doi.org/10.1016/j.redox.2020.101544>
- Barras A, Mezzetti A, Richard A et al. 2009. Formulation and characterization of polyphenol-loaded lipid nanocapsules. *Int J Pharm*. 379:270–277. <https://doi.org/10.1016/j.ijpharm.2009.05.054>
- Basina G, Polychronopoulou K, Zedan AF et al. 2020. Ultrasmall metal-doped CeO₂ nanoparticles for low-temperature CO oxidation. *ACS Appl Nano Mater*. 3:10805–10813. <https://doi.org/10.1021/acsanm.0c02090>
- Belhadj S, Hentati O, Hamdaoui G et al. 2018. Beneficial effect of jojoba seed extracts on hyperglycemia-induced oxidative stress in RINm5f beta cells. *Nutrients*. 10:384. <https://doi.org/10.3390/nu10030384>
- Białas AJ, Sitarek P, Miłkowska-Dymanowska J et al. 2016. The role of mitochondria and Oxidative/Antioxidative imbalance in pathobiology of chronic obstructive pulmonary disease. *Oxid Med Cell Longev*. 2016:7808576. <https://doi.org/10.1155/2016/7808576>
- Booth A, Størseth T, Altin D et al. 2015. Freshwater dispersion stability of PAA-stabilised cerium oxide nanoparticles and toxicity towards pseudokirchneriella subcapitata. *Sci Total Environ*. 505:596–605. <https://doi.org/10.1016/j.scitotenv.2014.10.010>
- Boukhenouna S, Wilson MA, Bahmed K et al. 2018. Reactive oxygen species in chronic obstructive pulmonary disease. *Oxid Med Cell Longev*. 2018:5730395.
- Buckingham AD, Del Bene JE, McDowell SAC. 2008. The hydrogen bond. *Chem Phys Lett*. 463:1–10. <https://doi.org/10.1016/j.cplett.2008.06.060>
- Celardo I, Pedersen JZ, Traversa E et al. 2011. Pharmacological potential of cerium oxide nanoparticles. *Nanos*. 3:1411. <https://doi.org/10.1039/c0nr00875c>
- Celardo I, De Nicola M, Mandoli C et al. 2011. Ce³⁺ ions determine redox-dependent anti-apoptotic effect of cerium oxide nanoparticles. *ACS Nano*. 5:4537–4549. <https://doi.org/10.1021/nn200126a>
- Cai Y, Ren W, Du C et al. 2025. Cerium Oxide Nanozymes: Exploring Synthesis, Catalytic Activity, and Biomedical Potential. *Small*. 21:2504436. <https://doi.org/10.1002/smll.202504436>
- Champion JA, Mitravotri S. 2006. Role of target geometry in phagocytosis. *Proc Natl Acad Sci*. 103:4930–4934. <https://doi.org/10.1073/pnas.0600997103>
- Chan HW, Chow S, Zhang X et al. 2023. Inhalable nanoparticle-based dry powder formulations for respiratory diseases: challenges and strategies for translational research. *AAPS PharmSciTech*. 24:98. <https://doi.org/10.1208/s12249-023-02559-y>
- Chaudhary P, Janmeda P, Setzer WN et al. 2024. Breaking free from free radicals: harnessing the power of natural antioxidants for health and disease prevention. *Chem Pap*. 78:2061–2077. <https://doi.org/10.1007/s11696-023-03197-1>
- Chen L, Zhang K, Xu J. 2025. Shared pathogenic mechanisms linking obesity and idiopathic pulmonary fibrosis revealed by bioinformatics and in vivo validation. *Sci Rep*. 15:25896. <https://doi.org/10.1038/s41598-025-12046-y>
- Chernyak BV, Popova EN, Prikhodko AS et al. 2020. COVID-19 and oxidative stress. *Biochem Mosc*. 85:1543–1553. <https://doi.org/10.1134/S0006297920120068>
- Chianese R, Pierantoni R. 2021. Mitochondrial reactive oxygen species (ROS) production alters sperm quality. *Antioxidants*. 10:92. <https://doi.org/10.3390/antiox10010092>
- Chigurupati S, Mughal MR, Okun E et al. 2013. Effects of cerium oxide nanoparticles on the growth of keratinocytes, fibroblasts and vascular endothelial cells in cutaneous wound healing. *Biomaterials*. 34:2194–2201. <https://doi.org/10.1016/j.biomaterials.2012.11.061>
- Colino CI, Lanao JM, Gutierrez-Millan C. 2020. Targeting of hepatic macrophages by therapeutic nanoparticles. *Front Immunol*. 11:218. <https://doi.org/10.3389/fimmu.2020.00218>
- Colon J, Hsieh N, Ferguson A et al. 2010. Cerium oxide nanoparticles protect gastrointestinal epithelium from radiation-induced damage by reduction of reactive oxygen species and upregulation of superoxide dismutase 2. *Nanomed Nanotechnol Biol Med*. 6:698–705. <https://doi.org/10.1016/j.nano.2010.01.010>
- Corsi F, Tarquini GD, Urbani M et al. 2023. The impressive anti-inflammatory activity of cerium oxide nanoparticles: more than redox? *Nanomater*. Basel Switz. 13:2803. <https://doi.org/10.3389/fimmu.2020.00218>
- D'Autréaux B, Toledano MB. 2007. ROS as signalling molecules: mechanisms that generate specificity in ROS homeostasis. *Nat Rev Mol Cell Biol*. 8:813–824. <https://doi.org/10.1038/nrm2256>
- Darroudi M, Hoseini SJ, Kazemi Oskuee R et al. 2014. Food-directed synthesis of cerium oxide nanoparticles and their neurotoxicity effects. *Ceram Int*. 40:7425–7430. <https://doi.org/10.1016/j.ceramint.2013.12.089>
- Das S, Dowding JM, Klump KE et al. 2013. Cerium oxide nanoparticles: applications and prospects in nanomedicine. *Nanomed*. 8:1483–1508. <https://doi.org/10.2217/nnm.13.133>
- Das S, Singh S, Dowding JM et al. 2012. The induction of angiogenesis by cerium oxide nanoparticles through the modulation of oxygen in intracellular environments. *Biomaterials*. 33:7746–7755. <https://doi.org/10.1016/j.biomaterials.2012.07.019>
- De Jong. 2008. Drug delivery and nanoparticles: applications and hazards. *Int J Nanomed*. 133. <https://doi.org/10.2147/IJN.S596>
- Dekkers S, Ma-Hock L, Lynch I et al. 2018. Differences in the toxicity of cerium dioxide nanomaterials after inhalation can be explained by lung deposition, animal species and nanoforms. *Inhal Toxicol*. 30:273–286. <https://doi.org/10.1080/08958378.2018.1516834>

- Deshpande S, Patil S, Kuchibhatla SV et al. 2005. Size dependency variation in lattice parameter and valency states in nanocrystalline cerium oxide. *Appl Phys Lett*. 87:133113. <https://doi.org/10.1063/1.2061873>
- Domingues JM, Miranda CS, Homem NC et al. 2023. Nanoparticle synthesis and their integration into polymer-based fibers for biomedical applications. *Biomedicines*. 11:1862. <https://doi.org/10.3390/biomedicines11071862>
- Dreaden EC, Mwakwari SC, Sodji QH et al. 2009. Tamoxifen–Poly(ethylene glycol)–Thiol gold nanoparticle conjugates: enhanced potency and selective delivery for breast cancer treatment. *Bioconjug Chem*. 20:2247–2253. <https://doi.org/10.1021/bc9002212>
- Du J, Jiang F, Xu S et al. 2021. Tephrosin induces apoptosis of human pancreatic cancer cells through the generation of reactive oxygen species. *J Cancer*. 12:270–280. <https://doi.org/10.7150/jca.50360>
- Egwu CO, Augereau J-M, Reybier K et al. 2021. Reactive oxygen species as the brainbox in malaria treatment. *Antioxidants*. 10:1872. <https://doi.org/10.3390/antiox10121872>
- Fahmy HM. 2020. Oxidative impact of carob leaf extract–synthesized iron oxide magnetic nanoparticles on the kidney, liver, testis, and spleen of wistar rats. *Bionanoscience*. 10:54–61. <https://doi.org/10.1007/s12668-019-00704-1>
- Frieke Kuper C, Gröllers-Mulderij M, Maarschalkerweerd T et al. 2015. Toxicity assessment of aggregated/agglomerated cerium oxide nanoparticles in an in vitro 3D airway model: the influence of mucociliary clearance. *Toxicol In Vitro*. 29:389–397. <https://doi.org/10.1016/j.tiv.2014.10.017>
- Fubini B, Hubbard A. 2003. Reactive oxygen species (ROS) and reactive nitrogen species (RNS) generation by silica in inflammation and fibrosis. *Free Radic Biol Med*. 34:1507–1516. [https://doi.org/10.1016/S0891-5849\(03\)00149-7](https://doi.org/10.1016/S0891-5849(03)00149-7)
- Fudala AS, Salih WM, Alkazaz FF. 2022. Synthesis different sizes of cerium oxide CeO₂ nanoparticles by using different concentrations of precursor via sol–gel method. *Mater Today Proc*. 49:2786–2792. <https://doi.org/10.1016/j.matpr.2021.09.452>
- Gasser M, Riediker M, Mueller L et al. 2009. Toxic effects of brake wear particles on epithelial lung cells in vitro. *Part Fibre Toxicol*. 6:30. <https://doi.org/10.1186/1743-8977-6-30>
- Gatoo MA, Naseem S, Arfat MY et al. 2014. Physicochemical properties of nanomaterials: implication in associated toxic manifestations. *BioMed Res Int*. 2014:1–8. <https://doi.org/10.1155/2014/498420>
- Gautam J, Ku J, Regmi SC et al. 2017. Dual inhibition of NOX₂ and receptor tyrosine kinase by BJ-1301 enhances anticancer therapy efficacy via suppression of autocrine-stimulatory factors in lung cancer. *Mol Cancer Ther*. 16:2144–2156. <https://doi.org/10.1158/1535-7163.MCT-16-0915>
- Gholap A, Pardeshi S, Giram P et al. 2025. Breathing new life nanomedicines for pulmonary drug delivery: targeting approaches, experimental models, and regulatory aspects. *Beni-Suef Univ J Basic Appl Sci*. 14:65. <https://doi.org/10.1186/s43088-025-00646-6>
- Ghorbani M, Sepahdoost N, Vaezi Z et al. 2025. Antioxidant effects of silver-ceria nanoparticles on the reduction of melanin in amelanotic melanoma cell biology. *Sci Rep*. 15:11177. <https://doi.org/10.1038/s41598-025-96366-z>
- Goodman CM, McCusker CD, Yilmaz T et al. 2004. Toxicity of gold nanoparticles functionalized with cationic and anionic side chains. *Bioconjug Chem*. 15:897–900. <https://doi.org/10.1021/bc049951i>
- Götze J, Pan Y, Müller A. 2021. Mineralogy and mineral chemistry of quartz: a review. *Mineral Mag*. 85:639–664. <https://doi.org/10.1180/mgm.2021.72>
- Greenberg MI, Waksman J, Curtis J. 2007. Silicosis: a review. *Dis Mon*. 53:394–416. <https://doi.org/10.1016/j.disamonth.2007.09.020>
- Guerra-Ojeda S, Marchio P, Rueda C et al. 2022. Cerium dioxide nanoparticles modulate antioxidant defences and change vascular response in the human saphenous vein. *Free Radic Biol Med*. 193:694–701. <https://doi.org/10.1016/j.freeradbiomed.2022.11.012>
- Gutmann C, Siow R, Gwozdz AM et al. 2020. Reactive oxygen species in venous thrombosis. *Int J Mol Sci*. 21:1918. <https://doi.org/10.3390/ijms21061918>
- Hadi A, Yaacob IL. 2007. Novel synthesis of nanocrystalline CeO₂ by mechanochemical and water-in-oil microemulsion methods. *Mater Lett*. 61:93–96. <https://doi.org/10.1016/j.matlet.2006.04.013>
- Halliwell B. 2022. Reactive oxygen species (ROS), oxygen radicals and antioxidants: where are we now, where is the field going and where should we go? *Biochem Biophys Res Commun*. 633:17–19. <https://doi.org/10.1016/j.bbrc.2022.08.098>
- Hameister R, Kaur C, Dheen ST et al. 2020. Reactive oxygen/nitrogen species (ROS/RNS) and oxidative stress in arthroplasty. *J Biomed Mater Res B Appl Biomater*. 108:2073–2087. <https://doi.org/10.1002/jbm.b.34546>
- Han M, Zhang T, Yang L et al. 2016. Association between NADPH oxidase (NOX) and lung cancer: a systematic review and meta-analysis. *J Thorac Dis*. 8:1704–1711. <https://doi.org/10.21037/jtd.2016.06.31>
- He H. 2015. Preparation and dispersion of nanosize ceria in high electrolyte slurry by ball-milling. *Integr Ferroelectr*. 16:136–44. <https://doi.org/10.1080/10584587.2015.1035594>
- He Y, Zhang S, She Y et al. 2024. Innovative utilization of cell membrane-coated nanoparticles in precision cancer therapy. *Exploration*. 4:20230164. <https://doi.org/10.1002/EXP.20230164>
- He X, Kuang Y, Li Y et al. 2012. Changing exposure media can reverse the cytotoxicity of ceria nanoparticles for *escherichia coli*. *Nanotoxicology*. 6:233–240. <https://doi.org/10.3109/17435390.2011.569097>
- Heckert EG, Karakoti AS, Seal S et al. 2008. The role of cerium redox state in the SOD mimetic activity of nanoceria. *Biomaterials*. 29:2705–2709. <https://doi.org/10.1016/j.biomaterials.2008.03.014>

- Helbawi ES, Abd El-Latif SA, Toson MA et al. 2024. Impacts of biosynthesized manganese dioxide nanoparticles on antioxidant capacity, hematological parameters, and antioxidant protein docking in broilers. *ACS Omega*. 9:9396–9409. <https://doi.org/10.1021/acsomega.3c08775>
- Hirst SM, Karakoti AS, Tyler RD et al. 2009. Anti-inflammatory properties of cerium oxide nanoparticles. *Small*. 5:2848–2856. <https://doi.org/10.1002/sml.200901048>
- Hobbins S, Chapple I, Sapey E et al. 2017. Is periodontitis a comorbidity of COPD or can associations be explained by shared risk factors/behaviors? *Int J Chron Obstruct Pulmon Dis*. 12:1339–1349. <https://doi.org/10.2147/COPD.S127802>
- Howlett P, Said B, Mwanga E et al. 2025. Confronting the growing epidemic of silicosis and tuberculosis among small-scale miners. *Lancet Public Health*. 10:e343–e346. [https://doi.org/10.1016/S2468-2667\(25\)00014-3](https://doi.org/10.1016/S2468-2667(25)00014-3)
- Hu A, Li R, Chen G et al. 2024. Impact of respiratory dust on health: a comparison based on the toxicity of PM_{2.5}, silica, and nanosilica. *Int J Mol Sci*. 25:7654. <https://doi.org/10.3390/ijms25147654>
- Ighodaro OM, Akinloye OA. 2018. First line defence antioxidants-superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPX): their fundamental role in the entire antioxidant defence grid. *Alex J Med*. 54:287–293.
- Iova O-M, Marin G, Lazar I et al. 2023. Nitric oxide/nitric oxide synthase system in the pathogenesis of neuro-degenerative disorders—an overview. *Antioxidants*. 12:753. <https://doi.org/10.3390/antiox12030753>
- Ishimoto Y, Tanaka T, Yoshida Y. 2018. Physiological and pathophysiological role of reactive oxygen species and reactive nitrogen species in the kidney. *Clin Exp Pharmacol Physiol*. 45:1097–1105. <https://doi.org/10.1111/1440-1681.13018>
- Jacob E, Mathew D, Benny L et al. 2024. Emerging nanomaterials as versatile nanozymes: a new dimension in biomedical research. *Top Curr Chem*. 382:28. <https://doi.org/10.1007/s41061-024-00473-w>
- Jafari M, Sriram V, Premnauth G et al. 2022. Modified peroxamide-based reactive oxygen species (ROS)-responsive doxorubicin prodrugs. *Bioorganic Chem*. 127:105990. <https://doi.org/10.1016/j.bioorg.2022.105990>
- Jain PK, Lee KS, El-Sayed IH et al. 2006. Calculated absorption and scattering properties of gold nanoparticles of different size, shape, and composition: applications in biological imaging and biomedicine. *J Phys Chem B*. 110:7238–7248. <https://doi.org/10.1021/jp057170o>
- Kannan SK, Sundrarajan M. 2014. A Green approach for the synthesis of a cerium oxide nanoparticle: characterization and antibacterial activity. *Int J Nanosci*. 13:1450018. <https://doi.org/10.1142/S0219581X14500185>
- Kapoor D, Singh S, Kumar V et al. 2019. Antioxidant enzymes regulation in plants in reference to reactive oxygen species (ROS) and reactive nitrogen species (RNS). *Plant Gene*. 19:100182. <https://doi.org/10.1016/j.plgene.2019.100182>
- Karakoti A, Singh S, Dowding JM et al. 2010. Redox-active radical scavenging nanomaterials. *Chem Soc Rev*. 39:4422. <https://doi.org/10.1039/b919677n>
- Karakoti AS, Munusamy P, Hostetler K et al. 2012. Preparation and characterization challenges to understanding environmental and biological impacts of ceria nanoparticles. *Surf Interface Anal*. 44:882–889. <https://doi.org/10.1002/sia.5006>
- Kargar H, Ghazavi H, Darroudi M. 2015. Size-controlled and bio-directed synthesis of ceria nanopowders and their in vitro cytotoxicity effects. *Ceram Int*. 41:4123–4128. <https://doi.org/10.1016/j.ceramint.2014.11.108>
- Khan MM, Ansari SA, Lee J et al. 2014. Electrochemically active biofilm assisted synthesis of Ag@CeO₂ nanocomposites for antimicrobial activity, photocatalysis and photoelectrodes. *J Colloid Interface Sci*. 431:255–263. <https://doi.org/10.1016/j.jcis.2014.06.026>
- Kim ST, Chompoosor A, Yeh Y et al. 2012. Dendronized gold nanoparticles for siRNA delivery. *Small*. 8:3253–3256. <https://doi.org/10.1002/sml.201201141>
- Kirchner C, Liedl T, Kudera S et al. 2005. Cytotoxicity of colloidal CdSe and CdSe/ZnS nanoparticles. *Nano Lett*. 5:331–338. <https://doi.org/10.1021/nl047996m>
- Koga M, Serritella AV, Sawa A et al. 2016. Implications for reactive oxygen species in schizophrenia pathogenesis. *Schizophr Res*. 176:52–71. <https://doi.org/10.1016/j.schres.2015.06.022>
- Komine C, Uchibori S, Tsudukibashi O et al. 2022. Application of reactive oxygen species in dental treatment. *J Pers Med*. 12:1531. <https://doi.org/10.3390/jpm12091531>
- Konecny R, Leonard S, Shi X et al. 2001. Reactivity of free radicals on hydroxylated quartz surface and its implications for pathogenicity of silicas: experimental and quantum mechanical study. *J Environ Pathol Toxicol Oncol*. 20:14. <https://doi.org/10.1615/JEnvironPatholToxicolOncol.v20.iSuppl.1.110>
- Korsvik C, Patil S, Seal S et al. 2007. Superoxide dismutase mimetic properties exhibited by vacancy engineered ceria nanoparticles. *Chem Commun*. 1056. <https://doi.org/10.1039/b615134e>
- Kropp T, Paier J, Sauer J. 2017. Interactions of water with the (111) and (100) surfaces of ceria. *J Phys Chem C*. 121:21571–21578. <https://doi.org/10.1021/acs.jpcc.7b08150>
- Kumar A, Das S, Munusamy P et al. 2014. Behavior of nanoceria in biologically-relevant environments. *Env Sci Nano*. 1:516–532. <https://doi.org/10.1039/C4EN00052H>
- Kumari J, Advani M, Purohit G. 2023. Prevalence of pulmonary hypertension in chronic simple silicosis patients and its correlation with smoking history, occupation type, age and duration of silica exposure. *Monaldi Arch Chest Dis*. <https://doi.org/10.4081/monaldi.2023.2719>
- Kwon N, Kim D, Swamy KMK et al. 2021. Metal-coordinated fluorescent and luminescent probes for reactive oxygen species (ROS) and reactive nitrogen species (RNS). *Coord Chem Rev*. 427:213581. <https://doi.org/10.1016/j.ccr.2020.213581>
- Kwon HJ, Cha M, Kim D et al. 2016. Mitochondria-targeting ceria nanoparticles as antioxidants for alzheimer's disease. *ACS Nano*. 10:2860–2870. <https://doi.org/10.1021/acsnano.5b08045>

- Lee M-K, Lim S-J, Kim C-K. 2007. Preparation, characterization and in vitro cytotoxicity of paclitaxel-loaded sterically stabilized solid lipid nanoparticles. *Biomaterials*. 28:2137–2146. <https://doi.org/10.1016/j.biomaterials.2007.01.014>
- Lee S, Hayashi H, Mastuzaki H et al. 2017. Silicosis and autoimmunity. *Curr Opin Allergy Clin Immunol*. 17:78–84. <https://doi.org/10.1097/ACI.0000000000000350>
- Lemos MFL. 2021. Biomarker studies in stress biology: from the gene to population, from the organism to the application. *Biology*. 10:1340. <https://doi.org/10.3390/biology10121340>
- Leung CC, Yu ITS, Chen W. 2012. Silicosis. *Lancet*. 379:2008–2018. [https://doi.org/10.1016/S0140-6736\(12\)60235-9](https://doi.org/10.1016/S0140-6736(12)60235-9)
- Li Y, Zhang W, Niu J et al. 2012. Mechanism of photogenerated reactive oxygen species and correlation with the antibacterial properties of engineered metal-oxide nanoparticles. *ACS Nano*. 6:5164–5173. <https://doi.org/10.1021/nn300934k>
- Li X, Chang W-C, Chao YJ et al. 2004. Nanoscale structural and mechanical characterization of a natural nanocomposite material: the shell of red abalone. *Nano Lett*. 4:613–617. <https://doi.org/10.1021/nl049962k>
- Li Y, Xia X, Niu Z et al. 2024. hCeO₂@ Cu₅4O nanoparticle alleviates inflammatory responses by regulating the CTSB-NLRP3 signaling pathway. *Front Immunol*. 15:1344098. <https://doi.org/10.3389/fimmu.2024.1344098>
- Li Y, Liu D, Chen T et al. 2024. Inhaled NIR-II nanocatalysts for real-time monitoring and immunomodulatory therapy of acute lung injury. *Adv Funct Mater*. 34:2403183. <https://doi.org/10.1002/adfm.202403183>
- Li Y, He X, Yin J et al. 2015. Acquired superoxide-scavenging ability of ceria nanoparticles. *Angew Chem*. 127:1852–1855. <https://doi.org/10.1002/ange.201410398>
- Lin Y, Ren J, Qu X. 2014. Nano-gold as artificial enzymes: hidden talents. *Adv Mater*. 26:4200–4217. <https://doi.org/10.1002/adma.201400238>
- Liu G, Gao J, Ai H et al. 2013. Applications and potential toxicity of magnetic iron oxide nanoparticles. *Small*. 9:1533–1545. <https://doi.org/10.1002/sml.201201531>
- Liu H, Dong J, Xu C et al. 2025. Acute lung injury: pathogenesis and treatment. *J Transl Med*. 23:926. <https://doi.org/10.1186/s12967-025-06994-2>
- Lu J, Fang ZZ. 2006. Synthesis and characterization of nanoscaled cerium (IV) oxide via a solid-state mechanochemical method. *J Am Ceram Soc*. 89:842–847. <https://doi.org/10.1111/j.1551-2916.2005.00829.x>
- Ma C, Dai Y, Qin W et al. 2025. Simvastatin mitigates ventilator-induced lung injury in mice with acute respiratory distress syndrome via a mechanism partly dependent on neutrophil extracellular traps. *Eur J Med Res*. 30:302. <https://doi.org/10.1186/s40001-025-02544-0>
- Matter MT, Furer LA, Starsich FHL et al. 2019. Engineering the bioactivity of flame-made ceria and Ceria/Bioglass hybrid nanoparticles. *ACS Appl Mater Interfaces*. 11:2830–2839. <https://doi.org/10.1021/acsami.8b18778>
- McBride AA, Price DN, Lamoureux LR et al. 2013. Preparation and characterization of novel magnetic nano-in-microparticles for site-specific pulmonary drug delivery. *Mol Pharm*. 10:3574–3581. <https://doi.org/10.1021/mp3007264>
- McBride C, Trzoss L, Povero D et al. 2022. Overcoming preclinical safety obstacles to discover (S)- N -((1, 2, 3, 5, 6, 7-Hexahydro- s -indacen-4-yl)carbamoyl)-6-(methylamino)-6, 7-dihydro-5 H -pyrazolo[5, 1- b][1, 3]oxazine-3-sulfonamide (GDC-2394): a Potent and Selective NLRP3 Inhibitor. *J Med Chem*. 65:14721–14739. <https://doi.org/10.1021/acs.jmedchem.2c01250>
- Melnikova N, Sheferov I, Panteleev D et al. 2023. Design and study of nanoceria modified by 5-Fluorouracil for gel and polymer dermal film preparation. *Pharm Basel Switz*. 16:1082.
- Meng F, Wang L, Cui J. 2013. Controllable synthesis and optical properties of nano-CeO₂ via a facile hydrothermal route. *J Alloys Compd*. 556:102–108. <https://doi.org/10.1016/j.jallcom.2012.12.096>
- Meot-Ner (Mautner), M. 2005. The ionic hydrogen bond. *Chem Rev*. 105:213–284. <https://doi.org/10.1021/cr9411785>
- Miao X, Jiang P, Wang Z et al. 2025. Mitochondrial transplantation: a novel therapeutic approach for treating diseases. *MedComm*. 6:e70253. <https://doi.org/10.1002/mco.2.70253>
- Mittal N, Morada M, Tripathi P et al. 2014. Cryptosporidium parvum has an active hypusine biosynthesis pathway. *Mol Biochem Parasitol*. 195:14–22. <https://doi.org/10.1016/j.molbiopara.2014.05.005>
- Montini T, Melchionna M, Monai M et al. 2016. Fundamentals and catalytic applications of CeO₂ -Based materials. *Chem Rev*. 116:5987–6041. <https://doi.org/10.1021/acs.chemrev.5b00603>
- Morry J, Ngamcherdtrakul W, Yantasee W. 2017. Oxidative stress in cancer and fibrosis: opportunity for therapeutic intervention with antioxidant compounds, enzymes, and nanoparticles. *Redox Biol*. 11:240–253. <https://doi.org/10.1016/j.redox.2016.12.011>
- Mortazavi Milani Z, Charbgo F, Darroudi M. 2017. Impact of physicochemical properties of cerium oxide nanoparticles on their toxicity effects. *Ceram Int*. 43:14572–14581. <https://doi.org/10.1016/j.ceramint.2017.08.177>
- Mukherjee D, Venkataswamy P, Devaiah D et al. 2017. Crucial role of titanium dioxide support in soot oxidation catalysis of manganese doped ceria. *Catal Sci Technol*. 7:3045–3055. <https://doi.org/10.1039/C7CY01029J>
- N BR, T PGN, S PO et al. 2021. Eco-friendly synthesis of CeO₂ NPs using aloe barbadensis mill extract: its biological and photocatalytic activities for industrial dye treatment applications. *J Photochem Photobiol*. 7:100038. <https://doi.org/10.1016/j.jpap.2021.100038>
- Narayanan KB, Park HH. 2013. Pleiotropic functions of antioxidant nanoparticles for longevity and Medicine. *Adv Colloid Interface Sci*. 201–202:30–42. <https://doi.org/10.1016/j.cis.2013.10.008>
- Neupane BP, Chaudhary D, Paudel S et al. 2019. Himalayan honey loaded iron oxide nanoparticles: synthesis, characterization and study of antioxidant and antimicrobial activities. *Int J Nanomed*. 14:3533–3541. <https://doi.org/10.2147/IJN.S196671>

- Nikitchenko YV, Klochkov VK, Kavok NS et al. 2023. CeO₂ nanoparticles improve prooxidant/antioxidant balance, life quality and survival of old Male rats. *Biogerontology*. 24:47–66. <https://doi.org/10.1007/s10522-022-09987-6>
- Noonong K, Chatatikun M, Surinkaew S et al. 2023. Mitochondrial oxidative stress, mitochondrial ROS storms in long COVID pathogenesis. *Front Immunol*. 14:1275001. <https://doi.org/10.3389/fimmu.2023.1275001>
- Nordberg J, Arnér ESJ. Reactive oxygen species, antioxidants, and the mammalian thioredoxin system. *Free Radic Biol Med*. 31(11):1287–1312.
- Noubade R, Wong K, Ota N et al. 2014. NRROS negatively regulates reactive oxygen species during host defence and autoimmunity. *Nature*. 509:235–239. <https://doi.org/10.1038/nature13152>
- Nyoka M, Choonara YE, Kumar P et al. 2020. Synthesis of cerium oxide nanoparticles using various methods: implications for biomedical applications. *Nanomater Basel Switz*. 10:242. <https://doi.org/10.3390/nano10020242>
- Pan Y, Li N, Wu C et al. 2024. Unlocking the potential of metal-doping Fe₂O₃/Rice husk ash catalysts for low-temperature CO-SCR enhancement. *ACS Omega*. 9:16621–16630.
- Paola Rosanna D, Salvatore C. 2012. Reactive oxygen species, inflammation, and lung diseases. *Curr Pharm Des*. 18:3889–3900. <https://doi.org/10.2174/138161212802083716>
- Parimi D, Sundararajan V, Sadak O et al. 2019. Synthesis of positively and negatively charged CeO₂ nanoparticles: investigation of the role of surface charge on growth and development of drosophila melanogaster. *ACS Omega*. 4:104–113. <https://doi.org/10.1021/acsomega.8b02747>
- Park H-J, Kim JY, Lee J et al. 2009. Silver-ion-mediated reactive oxygen species generation affecting bactericidal activity. *Water Res*. 43:1027–1032. <https://doi.org/10.1016/j.watres.2008.12.002>
- Peng L, He X, Zhang P et al. 2014. Comparative pulmonary toxicity of two ceria nanoparticles with the same primary size. *Int J Mol Sci*. 15:6072–6085. <https://doi.org/10.3390/ijms15046072>
- Peng M, Shao M, Dong H et al. 2023. Nanodrug rescues liver fibrosis via synergistic therapy with H₂O₂ depletion and saikosaponin b1 sustained release. *Commun Biol*. 6:184. <https://doi.org/10.1038/s42003-023-04473-2>
- Pirmohamed T, Dowding JM, Singh S et al. 2010. Nanoceria exhibit redox state-dependent catalase mimetic activity. *Chem Commun*. 46:2736. <https://doi.org/10.1039/b922024k>
- Plakhova TV, Romanchuk AY, Butorin SM et al. 2019. Towards the surface hydroxyl species in CeO₂ nanoparticles. *Nanos*. 11:18142–18149. <https://doi.org/10.1039/C9NR06032D>
- Pollard KM. 2016. Silica, silicosis, and autoimmunity. *Front Immunol*. 7:97. <https://doi.org/10.3389/fimmu.2016.00097>
- Porsin AV, Alikin EA, Bukhtiyarov VI. 2016. A low-temperature method for measuring oxygen storage capacity of ceria-containing oxides. *Catal Sci Technol*. 6:5891–5898. <https://doi.org/10.1039/C6CY00283H>
- Prasad S, Gupta SC, Tyagi AK. 2017. Reactive oxygen species (ROS) and cancer: role of antioxidative nutraceuticals. *Cancer Lett*. 387:95–105. <https://doi.org/10.1016/j.canlet.2016.03.042>
- Pu M, Cao H, Zhang H et al. 2024. ROS-responsive hydrogels: from design and additive manufacturing to biomedical applications. *Mater Horiz*. 11:3721–3746. <https://doi.org/10.1039/D4MH00289J>
- Pulido-Reyes G, Rodea-Palomares I, Das S et al. 2015. Untangling the biological effects of cerium oxide nanoparticles: the role of surface valence states. *Sci Rep*. 5:15613. <https://doi.org/10.1038/srep15613>
- Qin F, Shen T, Cao H et al. 2019. CeO₂NPs relieve radiofrequency radiation, improve testosterone synthesis, and clock gene expression in leydig cells by enhancing antioxidation. *Int J Nanomed*. 14:4601–4611. <https://doi.org/10.2147/IJN.S206561>
- Qiu Y, Tan G, Fang Y et al. 2021. Biomedical applications of metal–organic framework (MOF)-based nano-enzymes. *New J Chem*. 45:20987–21000. <https://doi.org/10.1039/D1NJ04045F>
- Quispe Cohaila AB, Fora Quispe G, Cáceda Quiroz CJ et al. 2025. Biogenic ZnO nanoparticles synthesized by *B. Licheniformis*: a selective cytotoxicity against NG-108 glioblastoma cells. *Nanomater Basel Switz*. 15:1338. <https://doi.org/10.3390/nano15171338>
- Rajeshkumar S, Menon S, Venkat Kumar S et al. 2019. Antibacterial and antioxidant potential of biosynthesized copper nanoparticles mediated through *Cissus arotiana* plant extract. *J Photochem Photobiol B*. 197:111531. <https://doi.org/10.1016/j.jphotobiol.2019.111531>
- Rani S, Chawla D. 2018. Preeclampsia and reactive oxygen species. *Indian J Pediatr*. 85:333–334. <https://doi.org/10.1007/s12098-018-2657-5>
- Ren S, Zhou Y, Zheng K et al. 2022. Cerium oxide nanoparticles loaded nanofibrous membranes promote bone regeneration for periodontal tissue engineering. *Bioact Mater*. 7:242–253. <https://doi.org/10.1016/j.bioactmat.2021.05.037>
- Ren X, Liu H, Wu X et al. 2022. Reactive oxygen species (ROS)-Responsive biomaterials for the treatment of bone-related diseases. *Front Bioeng Biotechnol*. 9:820468. <https://doi.org/10.3389/fbioe.2021.820468>
- Rendra E, Riabov V, Mossel DM et al. 2019. Reactive oxygen species (ROS) in macrophage activation and function in diabetes. *Immunobiology*. 224:242–253. <https://doi.org/10.1016/j.imbio.2018.11.010>
- Reuter S, Gupta SC, Chaturvedi MM et al. 2010. Oxidative stress, inflammation, and cancer: how are they linked? *Free Radic Biol Med*. 49:1603–1616.
- Ricard N, Bailly S, Guignabert C et al. 2021. The quiescent endothelium: signalling pathways regulating organ-specific endothelial normalcy. *Nat Rev Cardiol*. 18:565–580. <https://doi.org/10.1038/s41569-021-00517-4>
- Rimal B, Greenberg AK, Rom WN. 2005. Basic pathogenetic mechanisms in silicosis: current understanding. *Curr Opin Pulm Med*. 11:169–173. <https://doi.org/10.1097/01.mcp.0000152998.11335.24>

- Röhder LA, Brandt T, Sigg L et al. 2014. Influence of agglomeration of cerium oxide nanoparticles and speciation of cerium(III) on short term effects to the Green algae *Chlamydomonas reinhardtii*. *Aquat Toxicol.* 152:121–130. <https://doi.org/10.1016/j.aquatox.2014.03.027>
- Rubio L, Annangi B, Vila L et al. 2016. Antioxidant and anti-genotoxic properties of cerium oxide nanoparticles in a pulmonary-like cell system. *Arch Toxicol.* 90:269–278. <https://doi.org/10.1007/s00204-015-1468-y>
- Rudayni HA, Chaudhary AA, Abu-Taweel GM et al. 2022. Hydrothermal synthesis of CeO₂ nanoparticles and its application in electrochemical detection of nitrofurantoin antibiotics. *Europhys Lett.* 137:66005. <https://doi.org/10.1209/0295-5075/ac6065>
- Safari S, Bahramikia S, Dezfoulian O. 2023. Silver nanoparticles synthesized from *Quercus brantii* ameliorated ethanol-induced gastric ulcers in rats by decreasing oxidative stress and improving antioxidant systems. *Inflammopharmacology.* 31:2615–2630. <https://doi.org/10.1007/s10787-023-01284-z>
- Sahoo BM, Banik BK, Borah P et al. 2022. Reactive oxygen species (ROS): key components in cancer therapies. *Anticancer Agents Med Chem.* 22:215–222. <https://doi.org/10.2174/1871520621666210608095512>
- Saifi MA, Seal S, Godugu C. 2021. Nanoceria, the versatile nanoparticles: promising biomedical applications. *J Controlled Release.* 338:164–189. <https://doi.org/10.1016/j.jconrel.2021.08.033>
- Saraiva C, Praça C, Ferreira R et al. 2016. Nanoparticle-mediated brain drug delivery: overcoming blood–brain barrier to treat neurodegenerative diseases. *J Controlled Release.* 235:34–47. <https://doi.org/10.1016/j.jconrel.2016.05.044>
- Schieber M, Chandel NS. 2014. ROS function in redox signaling and oxidative stress. *Curr Biol.* 24:R453–R462. <https://doi.org/10.1016/j.cub.2014.03.034>
- Schubert D, Dargusch R, Raitano J et al. 2006. Cerium and yttrium oxide nanoparticles are neuroprotective. *Biochem Biophys Res Commun.* 342:86–91. <https://doi.org/10.1016/j.bbrc.2006.01.129>
- Seal S, Jeyaranjan A, Neal CJ et al. 2020. Engineered defects in cerium oxides: tuning chemical reactivity for biomedical, environmental, & energy applications. *Nanos.* 12:6879–6899. <https://doi.org/10.1039/D0NR01203C>
- Selvaraj V, Nepal N, Rogers S et al. 2015. Inhibition of MAP kinase/NF-κB mediated signaling and attenuation of lipopolysaccharide induced severe sepsis by cerium oxide nanoparticles. *Biomaterials.* 59:160–171. <https://doi.org/10.1016/j.biomaterials.2015.04.025>
- Selvi AM, Palanisamy S, Jeyanthi S et al. 2020. Synthesis of *Tragia involucrata* mediated platinum nanoparticles for comprehensive therapeutic applications: antioxidant, antibacterial and mitochondria-associated apoptosis in HeLa cells. *Process Biochem.* 98:21–33. <https://doi.org/10.1016/j.procbio.2020.07.008>
- Shahid S, Ejaz A, Javed M et al. 2022. The anti-inflammatory and free radical scavenging activities of bio-inspired nano magnesium oxide. *Front Mater.* 9:875163. <https://doi.org/10.3389/fmats.2022.875163>
- Sharpe E, Andreescu D, Andreescu S. 2011. Artificial nanoparticle antioxidants. In: Andreescu S, Hepel M, editors. *ACS Symp Ser. Vol. 1083*. American Chemical Society: Washington, DC. p. 235–253. <https://doi.org/10.1021/bk-2011-1083.ch008>
- Shekh-Ahmad T, Kovac S, Abramov AY et al. 2019. Reactive oxygen species in status epilepticus. *Epilepsy Behav.* 101:106410. <https://doi.org/10.1016/j.yebeh.2019.07.011>
- Sherekar P, Suke SG, Dani R et al. 2024. Nanoformulation, characterization, and in vivo pharmacokinetic studies of Diosgenin- and emodin-loaded polymeric nanoparticles. *Bionanoscience.* 14:164–174. <https://doi.org/10.1007/s12668-023-01254-3>
- Sherekar P, Suke SG, Dhok A et al. 2025. Global scenario of silica-associated diseases: a review on emerging pathophysiology of silicosis and potential therapeutic regimes. *Toxicol Rep.* 14:101941. <https://doi.org/10.1016/j.toxrep.2025.101941>
- Sherekar P, Suke SG, Dhok A et al. 2024. Nano-enabled delivery of diosgenin and emodin ameliorates respirable silica dust-induced pulmonary fibrosis silicosis in rats. *Ecotoxicol Environ Saf.* 279:116483. <https://doi.org/10.1016/j.ecoenv.2024.116483>
- Sies H, Jones DP. 2020. Reactive oxygen species (ROS) as pleiotropic physiological signalling agents. *Nat Rev Mol Cell Biol.* 21:363–383. <https://doi.org/10.1038/s41580-020-0230-3>
- Singh S, Dosani T, Karakoti AS et al. 2011. A phosphate-dependent shift in redox state of cerium oxide nanoparticles and its effects on catalytic properties. *Biomaterials.* 32:6745–6753. <https://doi.org/10.1016/j.biomaterials.2011.05.073>
- Song W, Soo Lee S, Savini M et al. 2014. Ceria nanoparticles stabilized by organic surface coatings activate the lysosome-autophagy system and enhance autophagic clearance. *ACS Nano.* 8:10328–10342. <https://doi.org/10.1021/nn505073u>
- Souri M, Kiani Shahvandi M, Chiani M et al. 2023. Stimuli-sensitive nano-drug delivery with programmable size changes to enhance accumulation of therapeutic agents in tumors. *Drug Deliv.* 30:2186312. <https://doi.org/10.1080/10717544.2023.2186312>
- Suhail S, Zajac J, Fossum C et al. 2020. Role of oxidative stress on SARS-CoV (SARS) and SARS-CoV-2 (COVID-19) infection: a review. *Protein J.* 39:644–656. <https://doi.org/10.1007/s10930-020-09935-8>
- Sul OJ, Choi HW, Oh J et al. 2023. GSPE attenuates CSE-induced lung inflammation and emphysema by regulating autophagy via the reactive oxygen species/TFEB signaling pathway. *Food Chem Toxicol.* 177:113795. <https://doi.org/10.1016/j.fct.2023.113795>
- Sulpizi M, Gageot M-P, Sprik M. 2012. The Silica–Water interface: how the silanols determine the surface acidity and modulate the water properties. *J Chem Theory Comput.* 8:1037–1047. <https://doi.org/10.1021/ct2007154>

- Sun J, Wu J, Zhao W et al. 2025. Multienzyme active melanin nanodots for antioxidant-immunomodulatory therapy of hyperoxia lung injury. *Mater. Today Bio.* 31:101609. <https://doi.org/10.1016/j.mtbio.2025.101609>
- Taniguchi A, Tsuge M, Miyahara N et al. 2021. Reactive oxygen species and antioxidative defense in chronic obstructive pulmonary disease. *Antioxidants.* 10:1537. <https://doi.org/10.3390/antiox10101537>
- Tarnuzzer RW, Colon J, Patil S et al. 2005. Vacancy engineered ceria nanostructures for protection from radiation-induced cellular damage. *Nano Lett.* 5:2573–2577. <https://doi.org/10.1021/nl052024f>
- Thai S-F, Jones CP, Nelson GB et al. 2019. Differential effects of nano TiO₂ and CeO₂ on normal human lung epithelial cells in vitro. *J Nanosci Nanotechnol.* 19:6907–6923. <https://doi.org/10.1166/jnn.2019.16737>
- Thanaraj S, Mitthun A, Geetha Sravanthy P. 2024. Green synthesis of aluminum oxide nanoparticles using clerodendrum phlomidis and their antibacterial, anti-inflammatory, and antioxidant activities. *Cureus.* 16:e52279. <https://doi.org/10.7759/cureus.52279>
- Thomas P, Lai CW, Johan MR. 2022. Facile synthesis of multifunctional C@Fe₃O₄-MoO₃-rGO ternary composite and its versatile roles as sonoadsorbent to ameliorate triphenylmethane textile dye and as potential electrode for supercapacitor applications. *Environ Res.* 212:113417. <https://doi.org/10.1016/j.envres.2022.113417>
- Tian Z, Li J, Zhang Z et al. 2015. Highly sensitive and robust peroxidase-like activity of porous nanorods of ceria and their application for breast cancer detection. *Biomaterials.* 59:116–124. <https://doi.org/10.1016/j.biomaterials.2015.04.039>
- Tian Y, Shi H, Zhang D et al. 2023. Nebulized inhalation of LPAE-HDAC10 inhibits acetylation-mediated ROS/NF- κ B pathway for silicosis treatment. *J Controlled Release.* 364:618–631. <https://doi.org/10.1016/j.jconrel.2023.10.018>
- Tumkur PP, Gunasekaran NK, Lamani BR et al. 2021. Cerium oxide nanoparticles: synthesis and characterization for biosafe applications. *Nanomanufacturing.* 1:176–189. <https://doi.org/10.3390/nanomanufacturing1030013>
- Valgimigli L, Baschieri A, Amorati R. 2018. Antioxidant activity of nanomaterials. *J Mater Chem B.* 6:2036–2051. <https://doi.org/10.1039/C8TB00107C>
- Van Hoecke K, De Schampelaere KAC, Van Der Meeren P et al. 2011. Aggregation and ecotoxicity of CeO₂ nanoparticles in synthetic and natural waters with variable pH, organic matter concentration and ionic strength. *Environ Pollut.* 159:970–976. <https://doi.org/10.1016/j.envpol.2010.12.010>
- Vassie JA, Whitelock JM, Lord MS. 2018. Targeted delivery and redox activity of folic acid-functionalized nanoceria in tumor cells. *Mol Pharm.* 15:994–1004. <https://doi.org/10.1021/acs.molpharmaceut.7b00920>
- Verma P, Rishi B, George NG et al. 2023. Recent advances and future directions in etiopathogenesis and mechanisms of reactive oxygen species in cancer treatment. *Pathol Oncol Res.* 29:1611415. <https://doi.org/10.3389/pore.2023.1611415>
- Vincent A, Thauvin M, Quévrain E et al. 2021. Evaluation of the compounds commonly known as superoxide dismutase and catalase mimics in cellular models. *J Inorg Biochem.* 219:111431. <https://doi.org/10.1016/j.jinorgbio.2021.111431>
- Vinothkumar G, Arunkumar P, Mahesh A et al. 2018. Size- and defect-controlled anti-oxidant enzyme mimetic and radical scavenging properties of cerium oxide nanoparticles. *New J Chem.* 42:18810–18823. <https://doi.org/10.1039/C8NJ04435J>
- Walkey C, Das S, Seal S et al. 2015. Catalytic properties and biomedical applications of cerium oxide nanoparticles. *Environ Sci Nano.* 2:33–53. <https://doi.org/10.1039/C4EN00138A>
- Wan R, Wang L, Duan Y et al. 2023. ADRB2 inhibition combined with antioxidant treatment alleviates lung fibrosis by attenuating TGF β /SMAD signaling in lung fibroblasts. *Cell Death Discov.* 9:407. <https://doi.org/10.1038/s41420-023-01702-9>
- Wan R, Long S, Ma S et al. 2024. NR2F2 alleviates pulmonary fibrosis by inhibition of epithelial cell senescence. *Respir Res.* 25:154. <https://doi.org/10.1186/s12931-024-02777-3>
- Wang Y, Chen S, Zhou Z et al. 2025. Tetrathiomolybdate alleviates bleomycin-induced pulmonary fibrosis by reducing copper concentration and suppressing EMT. *Eur J Med Res.* 30:394. <https://doi.org/10.1186/s40001-025-02640-1>
- Wei H, Wang E. 2013. Nanomaterials with enzyme-like characteristics (nanozymes): next-generation artificial enzymes. *Chem Soc Rev.* 42:6060. <https://doi.org/10.1039/c3cs35486e>
- Wu W-L, Ma H, Xi L et al. 2019. A novel lipid droplets-targeting ratiometric fluorescence probe for hypochlorous acid in living cells. *Talanta.* 194:308–313. <https://doi.org/10.1016/j.talanta.2018.10.006>
- Wu L, Liu G, Wang W et al. 2020. Cyclodextrin-modified CeO₂ nanoparticles as a multifunctional nanozyme for combinational therapy of psoriasis. *Int J Nanomed.* 15:2515–2527. <https://doi.org/10.2147/IJN.S246783>
- Xin W, Wei Z, Yao S et al. 2021. Co9S8@carbon nanofiber as the high-performance anode for potassium-ion storage. *RSC Adv.* 11:15416–15421. <https://doi.org/10.1039/D1RA01069G>
- Xu D, Wu L, Yao H et al. 2022. Catalase-like nanozymes: classification, catalytic mechanisms, and their applications. *Small.* 18:2203400. <https://doi.org/10.1002/smll.202203400>
- Xu H, Chen J, Li W et al. 2023. Costunolide covalently targets NACHT domain of NLRP3 to inhibit inflammasome activation and alleviate NLRP3-driven inflammatory diseases. *Acta Pharm Sin B.* 13:678–693. <https://doi.org/10.1016/j.apsb.2022.09.014>
- Yadav TP, Srivastava ON. 2012. Synthesis of nanocrystalline cerium oxide by high energy ball milling. *Ceram Int.* 38:5783–5789. <https://doi.org/10.1016/j.ceramint.2012.04.025>
- Yang B, Chen Y, Shi J. 2019. Reactive oxygen species (ROS)-Based nanomedicine. *Chem Rev.* 119:4881–4985. <https://doi.org/10.1021/acs.chemrev.8b00626>
- Yang L, Xu X, Song Y et al. 2024. Research progress of nanozymes in colorimetric biosensing: classification, activity and application. *Chem Eng J.* 487:150612. <https://doi.org/10.1016/j.cej.2024.150612>

- Yang L, Qiao Y, Huang Z et al. 2025. Role of environmental pollutants-induced ferroptosis in pulmonary diseases. *Front Med.* 12:1542275. <https://doi.org/10.3389/fmed.2025.1542275>
- Yuan R, Li Y, Han S et al. 2022. Fe-curcumin nanozyme-mediated reactive oxygen species scavenging and anti-inflammation for acute lung injury. *ACS Cent Sci.* 8:10–21. <https://doi.org/10.1021/acscentsci.1c00866>
- Zeng S, Yong K, Roy I et al. 2011. A review on functionalized gold nanoparticles for biosensing applications. *Plasmonics.* 6:491–506. <https://doi.org/10.1007/s11468-011-9228-1>
- Zhang Z, Tian H, Liu H et al. 2021. The role of macrophage-derived TGF- β 1 on SiO₂-induced pulmonary fibrosis: a review. *Toxicol Ind Health.* 37:240–250. <https://doi.org/10.1177/0748233721989896>
- Zhang G, Wang X, Suo X et al. 2024. Nanoparticles insert a three dimensional cavity structure of proteins for function inhibition: the case of CeO₂ and SARS-CoV-2. *Nano Today.* 55:102183. <https://doi.org/10.1016/j.nantod.2024.102183>
- Zhong H, Geng Y, Chen J et al. 2020. Maternal exposure to CeO₂NPs during early pregnancy impairs pregnancy by inducing placental abnormalities. *J Hazard Mater.* 389:121830. <https://doi.org/10.1016/j.jhazmat.2019.121830>
- Zhuravlev LT. 2000. The surface chemistry of amorphous silica. Zhuravlev model. *Colloids Surf. Physicochem Eng Asp.* 173:1–38. [https://doi.org/10.1016/S0927-7757\(00\)00556-2](https://doi.org/10.1016/S0927-7757(00)00556-2)
- Ziegler-Borowska M, Mylkie K, Kozłowska M et al. 2019. Effect of geometrical structure, drying, and synthetic method on aminated chitosan-coated magnetic nanoparticles utility for HSA effective immobilization. *Mol Basel Switz.* 24:1925. <https://doi.org/10.3390/molecules24101925>