



## RESEARCH ARTICLE

## A Critical Assessment of the Harmful Effects of Nanoparticles on the Respiratory System

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ARTICLE INFO	ABSTRACT
Received: Feb 22, 2024 Accepted: May 9, 2024	The biological sciences have advanced significantly as a result of recent advancements in nanotechnology. Nonetheless, there is a growing apprehension regarding the impact of exposure to both naturally-occurring and man-made nano-sized particles on the prevalence of various human diseases. The lungs play a crucial role in the exchange of gases within the body. Owing to their distinctive location, the lungs serve as the primary pathway through which nanoparticles (NPs) can infiltrate the human system, consequently leading to toxic repercussions. Despite the widespread utilization of NPs, the precise health implications following exposure remain incompletely elucidated. In order to tackle this issue, an examination is conducted on the biophysical characteristics of both naturally-occurring and synthetic NPs, their pathological influences on the respiratory system, and the potential risks they pose to human health. The objective of this analysis is to present the current body of evidence elucidating the health outcomes associated with the exposure to these nanoparticles.
<b>Keywords</b> Nanoparticles Respiratory system Nanotechnology Biological sciences	
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### INTRODUCTION

#### 1.1. Importance of recent developments in nanotechnology within the field of biomedical sciences.

Recent developments in the field of nanotechnology have made a considerable impression on the biomedical sector, presenting extensive possibilities for a range of uses. Nevertheless, apprehensions are mounting regarding the potential negative repercussions of nanoparticle exposure on human health, specifically on the respiratory system and various organs. The primary pathway for nanoparticles to enter the body is through the lungs, rendering them vulnerable to harmful effects induced by both naturally existing and man-made nanoparticles.

Despite the widespread use of nanoparticles, there is still limited understanding of their precise effects on health following exposure. Therefore, it is crucial to examine the biophysical properties of nanoparticles and their pathological effects on the respiratory system in order to assess the potential risks they pose to human health. By understanding these processes, we can effectively prevent and treat nanoparticle-induced diseases.

Nanoparticles can induce inflammation and cause tissue injury in the respiratory system through their interaction with innate and adaptive immune responses. They can also generate reactive oxygen species, disintegrate within cells, modulate cell signaling pathways, form protein coronas, and elicit

immunogenicity mediated by poly(ethylene glycol). These mechanisms contribute to the toxicity of nanoparticles at organ, tissue, cell, and biomolecular levels.

To mitigate these risks and ensure safe applications of nanoparticles in humans, it is essential to advance our understanding of nanoparticle toxicity. This includes developing standardized regulatory frameworks based on comprehensive nanotoxicity research. By exploring nanotoxicity mechanisms and evaluating toxicity at different levels, we can gain insights into how nanoparticles interact with the body and identify strategies for safe nanoparticle use.

Furthermore, studying nano-bio interactions in the lung is critical for designing novel pulmonary drug delivery platforms and addressing environmental health and safety concerns related to particulate air pollutants. Nanomedicines hold promise for treating respiratory complications such as lung cancer, pneumonia, cystic fibrosis, tuberculosis, acute lung injury, and diabetes.

However, it is important to consider the potential toxicity of nanoparticles to pulmonary surfactant, alveolar epithelium, and the immune system. Deep insights into the origin, transportation, deposition, and toxicity of atmospheric nanoparticles are vital for understanding their impact on the respiratory system and their association with hazardous diseases in humans.

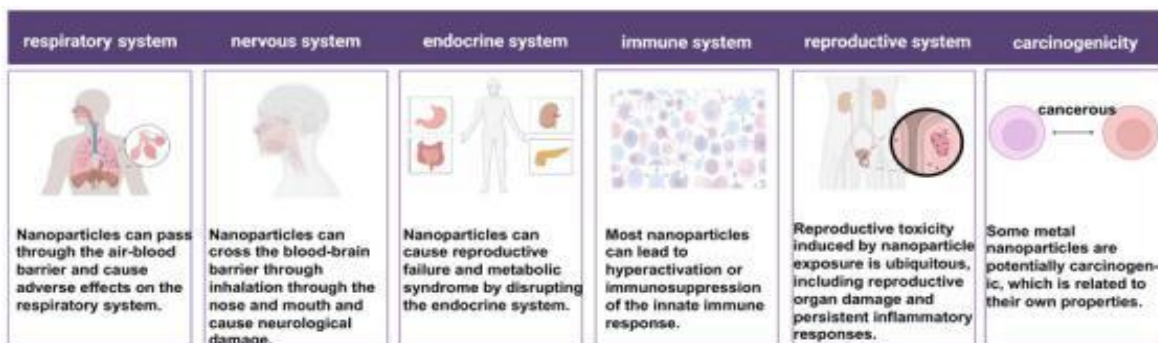
In conclusion, recent advances in nanotechnology have revolutionized biomedical sciences. However, it is crucial to address the potential adverse effects of nanoparticles on human health, particularly their impact on the respiratory system and organs. By understanding nanoparticle toxicity mechanisms and developing mitigation strategies, we can harness the full potential of nanotechnology while minimizing harm to humans. Further research is needed to comprehensively evaluate nanoparticle effects on respiratory disorders and promote public awareness of their benefits and risks. See references: [1], [2], [3], [7], [14], [15], [17], [18].

## **1.2. Growing apprehensions regarding the possible health hazards associated with exposure to nanoparticles.**

Growing concerns have emerged about the health risks of nanoparticle exposure. While nanotechnology has made advancements in biomedical sciences, it is increasingly recognized that both naturally-occurring and synthetic nanoparticles can lead to human diseases. The lungs are especially vulnerable to nanoparticle entry, resulting in toxic effects. However, the precise effects of nanoparticles on health are not fully understood, highlighting the need to examine their properties and pathological effects on the respiratory system.

Research has shown that nanoparticles can enter the body through inhalation, ingestion, and skin contact, causing damage to cells, tissues, and organs. Factors such as size, shape, surface area, and chemical composition influence nanoparticle toxicity. The respiratory system is particularly susceptible to nanoparticle-induced toxicity due to its role in particle entry and its connection with other organs.

Inhalation of nanoparticles has been linked to adverse health effects including inflammation, oxidative stress, DNA damage, and immune responses. Efforts are being made to understand the mechanisms of nanoparticle toxicity and develop strategies to mitigate risks, such as safe synthesis methods, biomarkers of toxicity, and protective measures for workers. Continued research is necessary to ensure the safe application of nanoparticles in various fields and assess their long-term effects on human health and the environment. It is crucial to gain a comprehensive understanding of nanoparticle toxicological effects and develop effective strategies to address growing concerns about their potential health risks. See references: [1], [2], [3], [4], [5], [6], [7], [8].



**Figure 1:** Toxic effects of nanoparticles on health. (source: reference [3])

**Table 1:** (source: reference [3])

Type of NPs	Size (nm)	Study design	Action object	Findings	References
SiO <sub>2</sub> -NPs	220 nm	Animal experiment	Respiratory system	SiO <sub>2</sub> -NPs specifically adsorb apolipoprotein AI (Apo AI) in blood to improve its cytotoxicity, while rapid clearance of SiNPs from blood depletes plasma Apo AI and promotes SiNPs-induced atherosclerosis.	<a href="#">124</a>
CuO-NPs	50 nm	Animal experiment	Respiratory system	Intratracheal instillation of copper oxide nanoparticles induces oxidative stress, inflammation, and tumor lesions in rats.	<a href="#">126</a>
PS-NPs	100 nm	Animal experiment	Nervous system	Polystyrene nanoparticles induce intestinal inflammation, growth inhibition, and developmental restriction in zebrafish, which are closely related to dysregulation within the brain-gut-microbiota axis.	<a href="#">157</a>
SiO <sub>2</sub> -NPs	20 nm	Animal experiment	Nervous system	SiO <sub>2</sub> -NPs entered the brain by intranasal instillation and accumulated in the striatum. Exposure to SiO <sub>2</sub> -NPs also resulted in increased oxidative	<a href="#">158</a>

Type of NPs	Size (nm)	Study design	Action object	Findings	References
				damage and striatal inflammatory response.	
SiO <sub>2</sub> -NPs	20 nm	Cell experiment	N/A	SiO <sub>2</sub> -NPs decreased cell viability, increased lactate dehydrogenase levels, induced oxidative stress, disrupted the cell cycle, induced apoptosis, and activated p53-mediated signaling pathways.	<a href="#">159</a>
Fe <sub>2</sub> O <sub>3</sub> -NPs	150 nm	Animal experiment	Nervous system	Iron oxide nanoparticles exposure can cause oxidative damage and neurotoxicity in the mouse brain.	<a href="#">160</a>
SiO <sub>2</sub> -NPs	20 nm	Animal experiment	Endocrine system	SiO <sub>2</sub> -NPs increase thyroid hormone disruption in juvenile zebrafish coexposed to PCBPA by promoting PCBPA bioaccumulation and bioavailability.	<a href="#">175</a>
TiO <sub>2</sub> -NPs	150 nm	Animal experiment and cell experiment	Endocrine system and nervous system	TiO <sub>2</sub> -NPs increased the bioconcentration of lead, which led to the disruption of thyroid endocrine and neuronal systems in larval zebrafish.	<a href="#">176</a>
Cd-NPs	N/A	Animal experiment and cell experiment	Immune system	Cd-NPs exposure resulted in decreased hemocyte phagocytosis in <i>Crassostrea gigas</i> and resulted in immunosuppression.	<a href="#">191</a>
Cd-NPs	N/A	Cell experiment	Immune system	Cd-NPs lead to a severe decrease in the viability of monocytes in mice, accompanied by lymphocyte transformation, resulting in immunodeficiency.	<a href="#">192</a>

Type of NPs	Size (nm)	Study design	Action object	Findings	References
carbon black nanoparticles	170-410 nm	Cell experiment	Immune system	After exposure to carbon black nanoparticles, increased levels of proinflammatory cytokines (TNF- $\alpha$ ) and chemokines and decreased phagocytic capacity were observed in macrophages.	<u>193</u>
NPs	N/A	N/A	Immune system	NPs can cross biological barriers that protect reproductive tissues and accumulate in the testes, causing oxidative stress, sex hormone disturbances, inflammation, and germ cell damage.	<u>204</u>
Au-NPs	5 nm	Animal experiment	Immune system	Au-NPs were able to internalize into endosomes/lysosomes of TM3 Leydig cells, induce autophagosome formation, increase reactive oxygen species (ROS) production, and disrupt the cell cycle in the S phase, resulting in condensation-dependent cellular Toxicity and DNA damage. Moreover, AuNPs significantly decreased testosterone production in TM3 cells by inhibiting the expression of 17 $\alpha$ -hydroxylase, an important enzyme in androgen synthesis.	<u>205</u>

## 2. The respiratory system as a primary route for Nanoparticles (NPs) entry

### 2.1. Unique position and function of the lungs in gas exchange

The respiratory system plays a crucial role in gas exchange, with the lungs being the vital organs responsible for this process. However, due to their unique position, the lungs also serve as the

primary route for the entry of nanoparticles (NPs) into the human body. This has raised concerns about the potential toxic effects of NPs on respiratory health.

Recent advances in nanotechnology have led to significant progress in various fields, including biomedical sciences. However, there is still limited understanding of how exposure to naturally-occurring and synthetic NPs affects human health. To address this gap in knowledge, researchers have examined the biophysical properties of NPs as well as their pathological effects on the respiratory system.

Studies have shown that NPs can enter the human body through inhalation, ingestion, and skin contact, leading to damage at cellular, tissue, and organ levels. The size, shape, surface area, and chemical composition of NPs are key determinants of their toxicity. Additionally, interactions between NPs and biological systems such as proteins, enzymes, and DNA can further impact their toxic effects.

The lungs are particularly vulnerable to the potential toxicity of NPs due to their direct exposure to inhaled particles and their role as a gateway for these particles into circulation. Moreover, since the lungs receive the entire cardiac output, any NPs that enter through inhalation can easily access other organs and tissues within the body.

In terms of specific organs targeted by NPs, research has shown that liver, kidneys, and lung are among the primary organs affected by NP exposure. Although most NPs demonstrate slight toxicity in animals upon exposure, certain adverse effects such as oxidative stress generation, inflammation, and DNA damage have been commonly observed.

To mitigate these risks associated with NP exposure, strategies need to be developed for safe NP synthesis and effective protective measures for workers in industries that utilize NPs. Long-term effects on human health and the environment also require further investigation.

In conclusion, while NPs have the potential to revolutionize various fields, including biomedicine, they also pose significant health risks. The respiratory system, being a primary route for NP entry into the human body, is particularly susceptible to the adverse effects of NPs. Therefore, it is imperative to continue studying the toxic effects of NPs on human health and developing strategies to mitigate these risks. See references: [1], [2], [3], [4], [5], [6], [7], [8].

## **2.2. Importance of understanding the effects of NPs on respiratory health**

The respiratory system serves as a primary route for the entry of nanoparticles (NPs) into the human body, making it crucial to understand the effects of NPs on respiratory health. Numerous studies have been conducted to assess the potential adverse effects of NPs exposure on various organs, including the lungs, liver, kidneys, and brain. It has been established that NPs can enter the body through inhalation, ingestion, and skin contact, leading to damage at cellular, tissue, and organ levels.

Recent research has focused on unraveling the mechanisms behind NPs toxicity and identifying factors that contribute to their harmful effects. It has been found that the size, shape, surface area, and chemical composition of NPs play a key role in determining their toxicity. Moreover, interactions between NPs and biological systems such as proteins, enzymes, and DNA can also affect their toxicity.

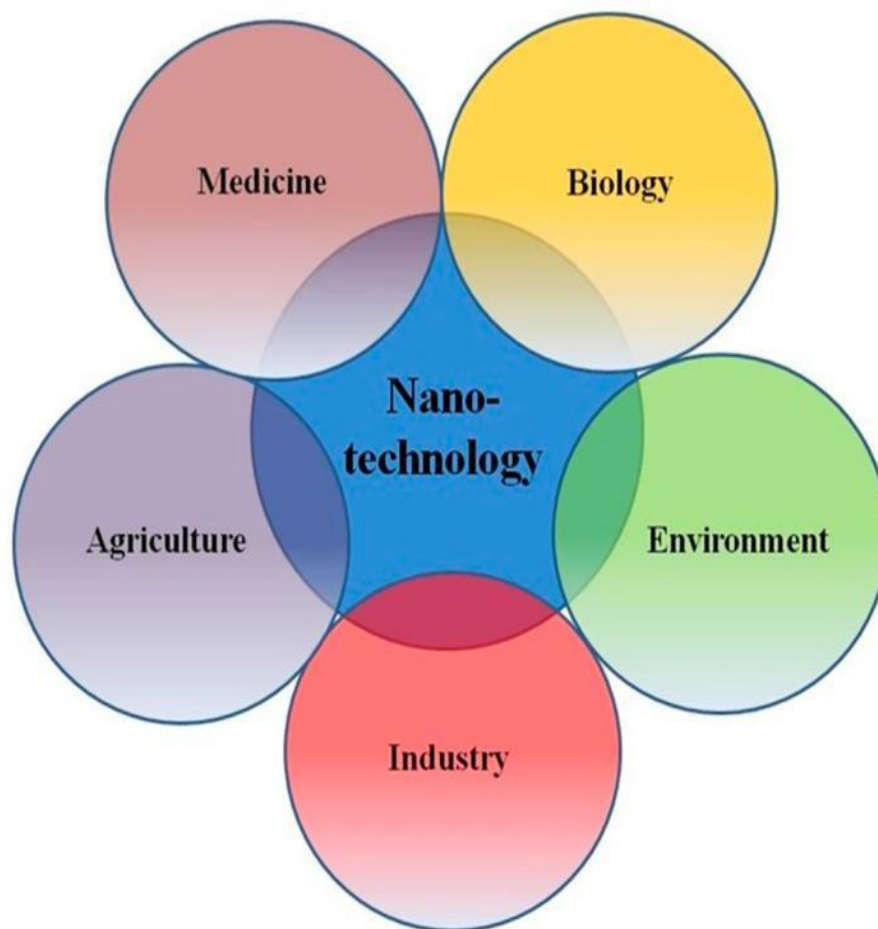
To mitigate the risks associated with NPs exposure, it is essential to develop strategies for safe and efficient synthesis of NPs. Additionally, biomarkers of NPs toxicity need to be identified for early detection and intervention. Protective measures should be implemented for workers in industries that utilize NPs. Furthermore, further research is needed to understand the long-term effects of NPs exposure on human health and the environment.

The importance of studying the toxic effects of NPs on human health cannot be overstated. While NPs have the potential to revolutionize various fields, they also pose significant risks to our well-being.

Therefore, continuous research is crucial in order to develop effective strategies for mitigating these risks.

In relation to respiratory health specifically, it is essential to consider how NPs exposure affects other organ systems such as the nervous system, endocrine system, immune system, reproductive system as well as their potential role in tumor development. Understanding these multifaceted effects will provide a comprehensive understanding of how NPs impact overall human health.

In conclusion, with increasing global use of NPs in various industries and applications, it is imperative to study their potential toxic effects. The respiratory system serves as a major entry point for NPs, making it vital to understand their impact on respiratory health. By identifying the mechanisms and factors contributing to NPs toxicity, strategies can be developed to mitigate risks and ensure the safe use of NPs. Continued research is needed to fully comprehend the long-term effects of NPs exposure on human health and the environment. See references: [1], [3], [4], [5], [6], [7], [8].



**Figure 2: Nanotechnology transformative innovations in medicine, agriculture, industry, environment, and basic biological sciences. (source: reference [6])**

**Table 2: Table 1. Summary of effects of nanoparticles on various organs and organ systems of the human body. (source: reference [7])**

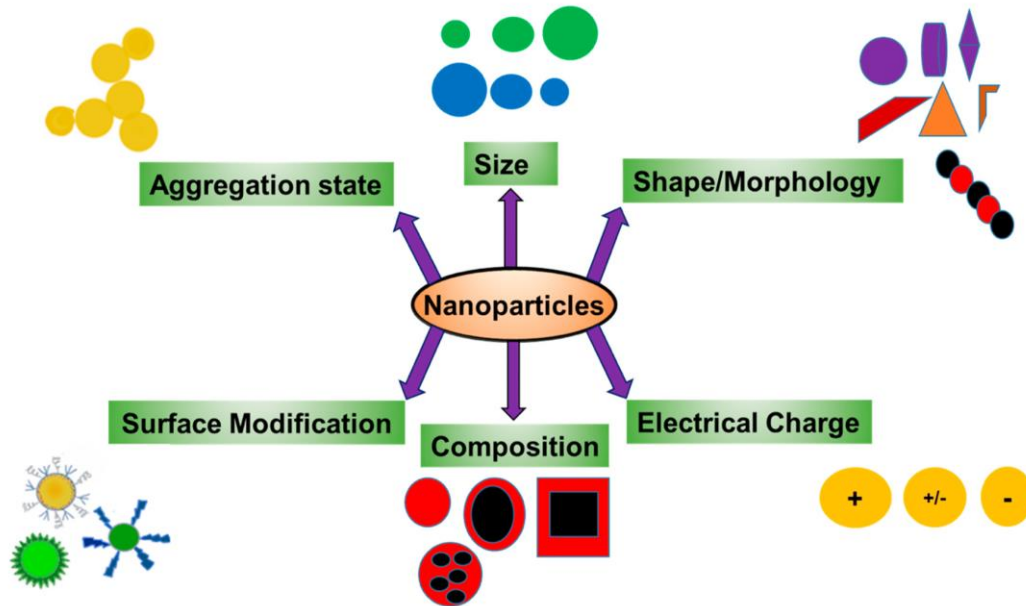
S. No.	Biological system	Target organ	Effect of nanoparticles	References
1.	Respiratory system	Lungs	Inflammation Oxidative-stress Genotoxicity Tumorigenicity	Clift et al., 2011 Sharma et al., 2012 Zhu et al., 2013 Stueckle et al., 2017
		Alveoli	Activation of macrophages causing pro-inflammatory cytokine release	Nho, 2020
2.	Digestive system	Stomach	Increased mucus production and Inflammation	Georgantzopoulou et al., 2015
		Intestine	Accumulation in lamina propria and degenerating goblet cells	Zhang et al., 2014
3.	Cardiovascular system	Heart	Increased blood pressure and decreased heart rate	Yu et al., 2016
		Endothelial lining	Increased ROS production leading to oxidative stress Heart muscle fibre degeneration and cellular necrosis	Miller et al., 2012 Yu et al., 2016
4.	Excretory system	Kidneys	Inhibition of NO pathways and vasoconstriction Accumulation in Proximal convoluted tubules	Mills and Miller, 2011 Pujalté et al., 2011
		Epithelial lining	Nephrotoxicity and DNA-Damage Shrinkage of kidney cells and nuclear condensation leading to oxidative stress	Sramkova et al., 2019 Wang et al., 2009; Pujalté et al., 2011
5.	Neural system	Brain	Cytotoxic effects on glomerular and renal cells Cytotoxicity in HK-2 cell lines of the lining Accumulation and effecting expressions of genes Apoptosis, cell cycle alterations and oxidative DNA damage	Pujalté et al., 2011 Pujalté et al., 2011 Yang et al., 2010 Valdiglesias et al., 2013
		Ovary	Inflammation and hormone imbalance Decrease in tissue weight and abnormal cell structures	Haase et al., 2012; Feng et al., 2015 Asadi et al., 2019
6.	Reproductive system	Testes	Inflammation and cytotoxicity	Santonastaso et al., 2019
		Gametes	Loss of integrity of sperm DNA Problems in the process of oogenesis leading to hormone disbalance	Santonastaso et al., 2019 Iavicoli et al., 2013
7.	Endocrine system	Thyroid	ROS-Overproduction, Oxidative stress and Apoptosis Overproduction of T-3 Thyroid hormone and decrease in thyroid-stimulating hormone	Iavicoli et al., 2013 Jiang et al., 2019
		Hormone receptors	Blockage of signal cascades, Overstimulation of hormones	Leso et al., 2018
		EDCs (Endocrine-disrupting chemicals)	Cytotoxicity and imbalance in production	Iavicoli et al., 2013; Lu et al., 2013
		Kidney	Degrading effects on testes and kidney hormones	Li et al., 2009
		Liver	Elevated serum levels of • Alanine aminotransferase • Alkaline phosphatase Lipid peroxidation and pathological lesion	Miller et al., 2012; Sharma et al., 2012

### 3. Biophysical properties of naturally-occurring and synthetic NPs

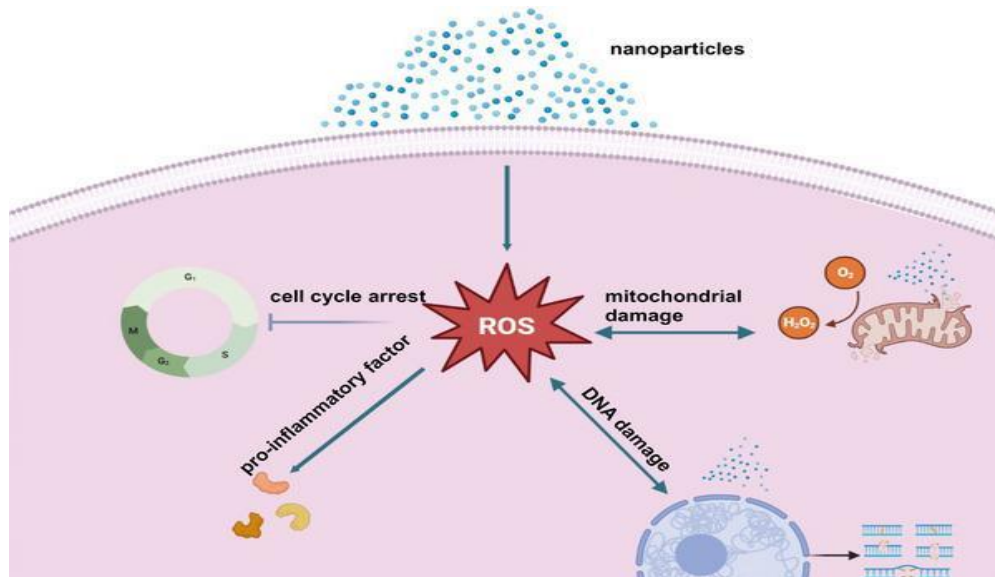
#### 3.1. Examination of the physical characteristics of NPs

Nanoparticles (NPs) are being widely used in various applications, but their effects on human health and the environment are not fully understood. The physical characteristics of NPs, such as size, surface modification, shape, and composition, greatly influence their toxicity profiles. Smaller-sized NPs tend to have higher tissue distribution and more serious toxic effects in certain organs, like the liver. Long fibrous particles are difficult to clear from the body, leading to organ accumulation. Surface chemistry, including charge and coating materials, also affects NP toxicity. While NPs show promise for treating lung diseases, factors like physical characteristics, routes of administration, and lung physiology need to be considered. Nanoparticle toxicity is linked to mechanisms like reactive oxygen species generation and modulation of cell signaling pathways. Current toxicity assessment models have limitations, and interdisciplinary collaboration is needed to develop robust models. Understanding the physical characteristics and toxicological mechanisms of NPs is crucial for safe and effective application. Ongoing research aims to enhance our understanding of NP toxicity at various levels and develop mitigation strategies. Standardized regulatory frameworks can be established based on advances in nanotoxicity research. See references: [1], [3], [10], [11], [13], [14], [17].





**Figure 3:** Physicochemical properties of nanoparticles that dictate their toxicities. Size, surface modification, surface charge, composition, shape and aggregation state of NPs are key factors in dictating NPs distribution in different organ systems following their exposure. (source: reference [11])



**Figure 4:** Nanoparticles are mainly related to the mechanism of toxicity induced by the accumulation of ROS. (source: reference [3])

### 3.2. Differentiating between naturally-occurring and synthetic NPs

Nanoparticles (NPs) can have different effects on the respiratory system and organs, whether they are naturally occurring or synthetic. Human exposure to NPs has increased due to global climate change and their use in therapeutic and diagnostic applications. Research shows that both types of NPs can be more toxic than larger particles of the same substance.

The lungs are vulnerable to the adverse effects of inhaled NPs. Short-term and long-term exposure can harm our health. Efforts are being made to reduce cellular toxicity caused by NPs.

Naturally occurring nanosized particles have existed throughout human evolution, but we have only recently gained the ability to manipulate matter at the nanoscale. Nanotechnology has promising applications in many industries, but its potential adverse effects on human health and the environment are not well understood.

Nanoparticles are defined as particles with a dimension of 100 nm or less. Due to their small size and unique properties, they may have different toxicity profiles compared to larger particles of the same material. Different types of nanoparticles also have specific mechanisms of toxicity.

The respiratory system is especially vulnerable to nanoparticle toxicity as it is the entry point for inhaled particles and connected to the circulatory system. There has been increased research on the effects of nanoparticles on the respiratory system.

Biophysical properties like size, shape, surface modification, surface charge, composition, and aggregation state differentiate naturally occurring and synthetic nanoparticles. Size affects distribution, cellular uptake, and overall toxicity. Smaller nanoparticles can have higher tissue distribution and cause more serious toxic effects.

Shape also impacts distribution, deposition, and clearance in the body. Long fibrous particles are difficult to clear and tend to accumulate in organs.

The surface chemistry of nanoparticles affects their pharmacokinetics and accumulation in target organs. Charged nanoparticles accumulate more in target organs. Coating materials can modify surface properties and reduce toxicity.

Understanding the toxicological mechanisms of nanoparticles is crucial for safe and effective use. Nanoparticle-induced toxicity is often associated with the accumulation of reactive oxygen species. Reliable toxicity assessment models considering human exposure scenarios and nanoparticle-organism interactions are needed.

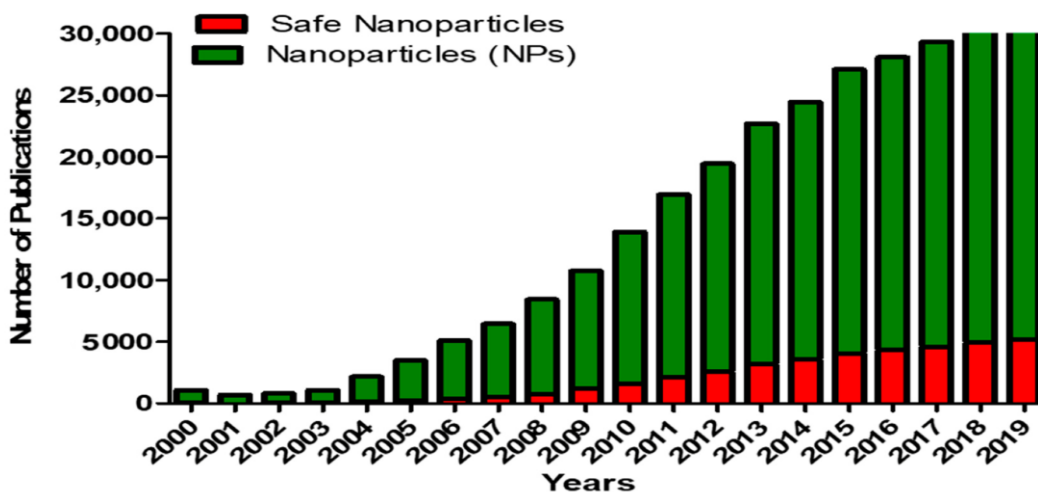
In conclusion, both naturally occurring and synthetic nanoparticles can affect human health. Understanding the biophysical properties that differentiate these particles is vital for assessing their toxicity. Further research is necessary to develop reliable toxicity assessment models and ensure safe nanoparticle use. See references: [1], [3], [10], [11], [13], [17].

#### 4. Pathological effects of NPs on the respiratory system

##### 4.1. Impact on lung function and structure

Nanoparticles (NPs) have gained attention for their wide range of applications, but it is important to understand their potential adverse effects on human health, specifically on the respiratory system. Inhaled NPs can harm our health both in the short-term and long-term. The toxicity of NPs depends on their size and composition, with naturally-occurring and synthetic NPs being more toxic than larger particles of the same substance. When NPs enter the body through inhalation, they can cause damage to tissues and cells, even reaching the brain by breaching the blood-brain barrier. The interaction between NPs and cells is influenced by factors such as particle shape, size, surface charge, dispersity, and protein corona effects. Studies have shown that NPs activate oxidative stress and inflammation, leading to adverse respiratory effects like fibrosis and lung cancer. NP exposure has a greater impact on individuals with preexisting respiratory diseases. The deposition of NPs in the respiratory system is determined by their size, shape, and surface chemistry, with smaller NPs being more likely to interact with lung cells in the lower airways. NPs generate reactive oxygen species (ROS) and induce oxidative stress, damaging cellular components and activating the immune system, causing inflammation. NPs can also have detrimental effects on other body systems, such as the

cardiovascular and gastrointestinal systems, leading to cardiac arrest and ulcers. Comorbid individuals are at higher risk due to NP accumulation. Understanding the toxicological mechanisms of NPs and developing strategies to mitigate their adverse effects is crucial for their safe use. Further research is needed to fully comprehend these mechanisms and establish guidelines for the design of safe and biocompatible NPs. Overall, inhaled NPs can cause significant harm to the respiratory system and organs, including inflammation, oxidative stress, fibrosis, and the development of lung cancer. It is important to develop safe NPs to minimize potential health risks while utilizing their benefits in various industries and medicine. See references: [1], [3], [6], [7], [9], [11].



**Figure 6: The number of scientific papers published in the last two decades. Papers were identified in Pubmed database from the year 2000 until 2019 using the key words nanoparticles (green) and safe nanoparticles, toxicity of NPs (nanoparticles), risks of NPs (red). (source: reference [11])**

#### 4.2. Toxic effects on lung cells and tissues

Nanoparticles (NPs) have become widely used in various industries and scientific fields due to their unique properties. However, the toxicity of NPs is a major concern that limits their use in the diagnosis and treatment of diseases. NPs can enter the body through inhalation, skin, and digestion, and they can access vital organs through the bloodstream. The respiratory system is particularly susceptible to the toxic effects of NPs.

When NPs are inhaled, their size, shape, and surface chemistry affect their deposition in the respiratory system. Smaller NPs are more likely to penetrate deep into the lungs and interact with lung cells. They can be recognized and engulfed by different types of lung cells, triggering cellular responses such as the generation of reactive oxygen species (ROS), cytokine release, and activation of inflammatory pathways.

Exposure to NPs has been linked to various adverse effects on the respiratory system, including inflammation, oxidative stress, fibrosis, and even lung cancer. For example, titanium dioxide (TiO<sub>2</sub>) NPs have been shown to induce lung inflammation and fibrosis in animal studies. Preexisting respiratory diseases can exacerbate these adverse effects.

The toxic mechanisms of NPs are complex and involve the generation of ROS and induction of oxidative stress. ROS can damage cellular components such as proteins, lipids, and DNA, leading to

cell death or dysfunction. Inflammation is also triggered by NP exposure through activation of the immune system.

Furthermore, NPs have been found to have carcinogenic properties. Their ability to generate ROS and induce oxidative stress plays a key role in this carcinogenicity. It is important to note that more research is needed to fully understand the toxicological mechanisms of NPs and develop strategies for mitigating their adverse effects on human health.

In conclusion, NPs pose significant risks to human health, particularly on the respiratory system. Their small size allows them to penetrate deep into the lungs and interact with lung cells, leading to inflammation, oxidative stress, and even cancer. It is crucial to develop safe and biocompatible NPs for their successful application in various fields while considering their potential toxic effects. Strict guidelines for toxicity testing and the design of safe NPs are needed to ensure their clinical applicability and minimize health risks. See references: [3], [6], [7], [9], [11].

5. Potential human health risks associated with NP exposure

### **5.1. Reviewing existing evidence on the health effects of NP exposure**

This review focuses on the toxic effects of nanoparticle (NP) exposure on human health, particularly on the respiratory system and other organs. The size, shape, and surface chemistry of NPs play a significant role in their deposition in the respiratory system, with smaller and elongated particles having a higher probability of deposition. NPs that are deposited in the respiratory system can interact with lung cells, triggering cellular responses such as the generation of reactive oxygen species (ROS) and inflammation. Adverse effects on the respiratory system include inflammation, oxidative stress, fibrosis, and lung cancer. Biomarkers have been used to study the interaction between NPs and health outcomes, revealing damage to the respiratory system. NPs can also have adverse effects on other body systems, including the cardiovascular and gastrointestinal systems. NPs pose a potential threat due to their small size and longer residence time in the atmosphere, allowing them to accumulate in the alveolar region and enter other internal organs. Epidemiological and toxicological studies have demonstrated their ability to penetrate deep inside the lungs. NP exposure can lead to oxidative stress, inflammation, and various lung diseases. DNA damage, mutations, neoplasms, carcinomas, cardiac arrest, and ulceration are among the health complications associated with NP exposure. Comorbid individuals are at a higher risk due to NP accumulation. Despite their potential clinical applications, some studies indicate that NPs can be toxic, highlighting the need for safer NPs and strict guidelines for toxicity testing. Further research is necessary to fully understand the mechanisms underlying the effects of NP exposure and develop safer nanoparticles. It is crucial to take precautions to minimize NP exposure. See references: [3], [7], [9], [11], [12].

### **5.2. Identifying gaps in current knowledge**

Identifying gaps in current knowledge for potential human health risks associated with nanoparticle (NP) exposure is crucial for understanding the implications of these tiny materials on respiratory systems and organs. While there is a growing body of research on the health effects of NP exposure, there are still significant gaps in our understanding.

Firstly, the composition and properties of NPs play a crucial role in determining their toxicity. However, there is a lack of comprehensive studies investigating the specific effects of different types of NPs. Further research is needed to evaluate the precise effects of various NPs and their potential long-term consequences.

Additionally, the route of entry for NPs into the body is an important consideration. Inhalation is a common route for NP exposure, but other routes such as dermal and gastrointestinal absorption also need to be explored. Understanding how different routes of exposure contribute to NP toxicity can provide valuable insights into prevention and control measures.

The extent of NP exposure, including factors such as duration, frequency, and concentration, also needs to be further investigated. The development of accurate sampling and analytical methods can help assess the level of exposure and its potential health risks. In cases where such methods are not available, alternative approaches like control banding models may be considered.

Furthermore, more studies are required to examine the effectiveness of control measures in reducing NP exposure. Evaluating the efficiency of engineering controls, personal protective equipment, and other preventive strategies can aid in developing effective guidelines for minimizing NP-related health risks.

Importantly, there is a need for comprehensive risk assessments that encompass all engineered nanomaterials commonly encountered in daily life. The current understanding of nanoparticle safety relies on existing data that may not adequately consider the unique properties and behaviors of nanomaterials. Developing standardized methods for assessing NP safety will help ensure appropriate protection measures are implemented.

Toxicological studies should also focus on systemic toxic effects rather than solely examining organ-specific impacts. Nanoparticles exhibit different properties and behaviors compared to larger particles, necessitating a reevaluation of traditional toxicology frameworks. Understanding the mechanisms behind NP toxicity on a systemic level can inform safety assessments and the establishment of appropriate standards.

In conclusion, while there have been significant advancements in understanding the potential health risks associated with NP exposure, several gaps in knowledge remain. Further research is needed to comprehensively evaluate the effects of different types of NPs, explore various exposure routes, assess the effectiveness of control measures, and develop standardized methods for assessing NP safety. Addressing these gaps will contribute to a more accurate understanding of the potential human health risks associated with NP exposure and guide efforts to mitigate these risks effectively. See references: [7], [11], [12], [13], [14], [15], [16].

## 6. Conclusion

### 6.1. Summary of key findings from the review

In conclusion, the review of data on the effects of nanoparticles (NPs) on the respiratory system and organs has provided key findings that highlight the potential risks and impacts of NPs on living organisms. The pathways of NPs into organisms can occur through both anthropogenic and natural routes, with anthropogenic nanoparticles being more likely to exhibit toxic effects. The structure, size, surface charge, and concentration of NPs determine how they enter organisms, either directly through external surface epithelia or gills, or indirectly through inhalation or ingestion via soil, water, and food. The toxicity of NPs often manifests as changes in reactive oxygen species levels, inflammation, cell damage, and DNA damage.

Furthermore, the introduction of organic and inorganic NPs into the food chain can lead to alterations in plant organs such as leaves, flowers, stems, and roots. In animals, NP impacts primarily affect metabolic systems, behaviors, and locomotive functions. Accumulation of NPs has been observed in various organs including the liver, kidney, lung, heart, gills, and even brain tissues.

Given the significant impact of engineered NPs on the environment and living organisms and the lack of preventive measures against their potential toxicity effects, there is a crucial need for risk assessment. Understanding the natural processes involving NPs is essential for developing safety protocols. To assess the impact of NPs on ecosystems and particularly on the food chain, it is important to consider their unique dimensional properties as well as surface characteristics that influence their interaction with biological systems.

It is necessary to identify which aspects of NP impact should be evaluated based on their specific features and biologically significant characteristics. This will enable the development of reasonable approaches for impact assessment that can reduce the risks associated with NP toxicity. Additionally, there is an urgent need for standardization in nanoparticle safety assessment methods to ensure accurate evaluation of their potential health hazards.

In conclusion studies focusing on systemic toxic effects and investigating the mechanisms underlying harmful effects of NP exposure are crucial. Nanotoxicological effects may differ from those of larger particles, necessitating the establishment of databases and safety assessment results specific to nanomaterials. Understanding the hazardous effects of nanoparticles, particularly in industrial waste gas, will enable their proper utilization while minimizing potential risks.

Overall, the review underscores the importance of considering the potential toxicity of nanoparticles when assessing their applications in various fields. The rapidly advancing field of nanotechnology offers immense possibilities for improving human health but also raises concerns regarding its impact on health and the environment. Therefore, it is essential to address these concerns through collaborative efforts among industry, academia, government agencies, environmentalists, and scientists to ensure the safe and responsible use of nanomaterials. See references: [3], [7], [8], [10], [12], [14], [15], [16].

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