

IMPACT ANALYSIS OF NANOPARTICLE FEATURES ON RESPIRATORY HEALTH AND IMMUNE SYSTEM DISRUPTION

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ABSTRACT

Nanoparticles, due to their small size and unique properties, are increasingly used in various industries, from electronics to medicine. Their potential to cause respiratory health issues and disrupt the immune system has become a growing concern. Research aims to analyze the effect of different nanoparticle features (such as size, shape, and chemical composition) on respiratory health and the immune system. With the growing use of nanoparticles (NP) in everyday products, understanding their potential health risks is essential. Research assessed the effects of nanoparticles (CuO, CNTs, SiO₂, ZnO) on respiratory health and immune disruption. In vivo, 60 rats were exposed to varying nanoparticle doses for 8 weeks, using BALF-measured indicators for inflammatory and oxidative damage. In vitro tests on pulmonary epithelial cells examined nanoparticle-induced cell viability, cytotoxicity, and inflammation. Nanoparticle exposure significantly increased oxidative stress markers (8-OHdG, HO-1, TNF- α , and MCP-1) and reduced the anti-inflammatory marker IL-10. CNTs had the strongest negative health impacts. Nanoparticles, especially CNTs, cause oxidative stress and inflammation, posing risks to respiratory health and immune function.



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1. INTRODUCTION

Nanoparticles (NP) are particles of material that range in size from 1 to 100 nanometers, and one nanometer is equal to 0.0000039 inches. Because of their size and properties, NPs often find their application in medicine, electronics, and cosmetics industries (Sajid & Płotka-Wasyłka 2020). However, as people make their use, the frequency that they appear in the environment, especially in the air, rises significantly assessed by

(Forest et al., 2021). Particles from vehicles, industries, and products, for instance, aerosols, can easily release particles into the atmosphere. Because NP are already present in the environment and are used so frequently, it is important to understand how these particles influence the bodies, especially the respiratory and immunity systems by (Tulinska et al., 2022). These small particles can be inhaled and penetrate deep into the respiratory tract, where they can have adverse effects on the body. They can cause inflammation, make

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the lungs function worse, and contribute to diseases like chronic obstructive pulmonary disease (COPD) and breathing problems (Jin et al., 2023). However, NP are also known to have some relations with immune cells, which are primarily responsible for protecting the body from diseases by (Jin et al., 2021). That interaction can alter the immune functions and make the individual more vulnerable to infections or chronic diseases. The role of the size, shape as well as chemistry of the NP has to be deciphered. These characteristics can affect the behaviour of NP in the body as well as their ability to engage the cells by (Baranov et al., 2021). Through these components, it is easier to determine the dangers being posed by NP and therefore establish measures to safeguard the population by (More et al., 2021). Whether NP are dangerous to human health and to help design safer environments and health policies that reduce human contact with NP and help to enhance lung health. This adaptive feature is an attribute common to all biological systems. Thus, exploring supply chain resilience through the immune system lens promises productive results. NP have found application in every industry from electronics to medicine, and are dependent on extremely small scales. The size enables interaction with biological systems unreachable by larger particles, thus imparting versatility in applications to many consumer and industrial products. However, the properties useful to nanoparticles themselves raise issues of concern regarding the impact on human health, especially in respiratory function and disruption of immune processes (Ivanov, 2024). Figure 1 illustrates the effects of NP on immune system disruption and respiratory health.

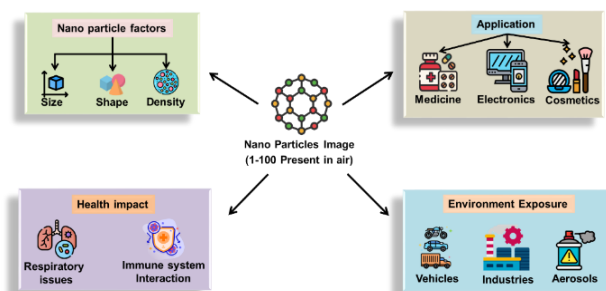


Figure 1. Impact of NP on respiratory health and immune system disruption

Globally, respiratory syncytial virus (RSV) was the primary factor contributing to children's lower respiratory tract infections. Viral infections, bronchitis, and asthma have all been related to environmental particulate matter exposure. Smallcombe et al. (2020) determined that co-exposure to NP intensifies the RSV-induced breakdown of the airway epithelial barrier. RSV and titanium dioxide NP (TiO₂-NP) were employed for incubating bronchial epithelium cells. By producing reactive oxygen species, the research found that prolonged exposure to TiO₂-NP increases inflammation and exacerbates RSV-induced AIC impairment. To find out how it affects lung conditions like asthma, more

research was required. Aerosolized antimicrobial treatment is being utilized more often to treat recalcitrant respiratory tract infections, which are a worldwide health concern. Infected lung tissue presents a difficult set of biological obstacles to overcome. To get beyond these obstacles and accomplish site-specific administration, respiratory medication delivery via nanoparticle-mediated means is becoming increasingly popular. Huang et al., (2021) addressed developments in drug delivery systems based on nanoparticles, obstacles encountered when transferring laboratory-based research to clinical settings, and possible remedies. NPs were being utilized more frequently in common products such as food, cosmetics, medications, and home items. Nanotechnology was the manipulation of matter at the nanoscale. With NPs connected to toxicity via raising reactive oxygen species (ROS) and anti-inflammatory medication stages, conventional NP categorization based on size has been called into question. Inflammation and oxidative stress were highlighted as the primary pathways for NP toxicity in biological systems by (Garcés et al., 2021). The extremely contagious SARS-CoV-2 virus was the source of COVID-19, which has spread to millions of individuals in 213 countries. Inhibiting the virus's harmful effects remains not possible through clinically validated treatment approaches, and COVID-19 vaccines are indeed being developed by (Medhi et al., 2020). The possible applications of NPs include COVID-19 as well as coronavirus immunization, therapy, and diagnosis. In particular, viruses belonging to the Coronaviridae genus were discovered to be effectively combated by NPs. To provide NP-based pandemic preparedness measures, research integrated contemporary SARS-CoV-2 investigation with earlier antiviral findings. Despite investigations using NPs have become more common, much is known about its health effects, underlying processes, and assessment methodologies. Xuan et al., (2023) included an in-depth analysis of the uses of NPs in medicine, covering medical evaluation, treatment, and toxicity on different systems. Along with the fundamental functions of ROS build-up, harm to mitochondria, responses to inflammation, apoptotic DNA damage, cell division, and epigenetic control, it also analyses the cancer-causing potential of NPs. Further, the paper presents established and developing approaches for assessing NP toxicity. The purpose of the article was to close information gaps and advance the comprehension of NPs toxicity. Globally, chronic respiratory diseases (CRDs) constitute the primary contributor to disabilities-adjusted life years (DALYs), death, sickness, along with economic and social difficulties. The pulmonary vasculature, parenchyma, and airways are all impacted by these illnesses. Instead of administering medications for the best treatment and mitigation, the present emphasis on therapy was on pain relief. Exploration has been done on parenchymal recovery, oxidative damage, chronic inflammation, and airways. Growth hormones, antioxidants, chemokines, inflammatory substances, and other proteins were

instances of biological mediators and enzymes that impact the pathophysiology of CRDs. The aim of the Hussain et al., (2021) prescribed treatments was to ease airway constriction and lessen inflammation of the airways. Searching for ways that pharmaceutical chemical research and personalized medical care could interact together to develop customized Nanotherapeutics. Sanna & Sechi (2020) highlighted the challenges in clinical translation and investigated the targeting concept in drug delivery by nanoparticles. The findings highlight the primary barriers to a productive clinical trial and the potential of nanotechnologies to ease prescription restrictions. Silver NP(AgNPs) may be widely dispersed and incorporated through blood circulation, according to (Rosário et al., 2022) conducted on rats exposed to AgNPs and Silver Nitrate (AgNO₃). AgNP5 produced toxicity that persisted longer and raised lung glutathione (GSH) levels, whereas AgNP50 raised liver GSH levels. The small intestine, liver, kidneys, and plasma had the highest levels of silver, which remained there for a minimum of 28 days. Considered a significant content in faces, the urethra was the primary excretory pathway. The actual findings for both the liver and cardiac matched the modelled silver material. The important environmental factor that could impact health and the transmission of illness is relative humidity (RH) examined Guarnieri et al., (2023). It alters the rheological characteristics of mucus, which impacts mucociliary elimination and pathogen defense. To stop the spread of germs and viruses, RH must be controlled. The impact of a single risk factor is unclear, though, because RH imbalances can be connected to various irritants, allergies, and infections. Although normalized RH could contribute to a healthier atmosphere, it is not always a direct risk factor.

1.1. Research gap

Medical research was limited for several reasons. The long-term effects of NPs on human health, especially under realistic exposure scenarios, require clinical researches. Many animal studies could not adequately represent human responses to NP exposure. In addition, variation in the NPs with respect to their characteristics (size, shape, dose) and the absence of standardized protocols for testing makes it impossible to generalize most findings across diverse NP types and bio-systems. More research is needed to understand accumulated health effects, particular mechanisms of toxicity, and the entire difficulty of getting from lab results to effective clinical treatments. The present research aims to examine the effects of various kinds of NP on respiratory health and immune system disruption. It focuses on the oxidative stress and inflammatory responses caused by these particles. The research will help to understand health risks and safe design of nanoparticles as well as future therapeutic approaches for respiratory diseases by stressing various nanoparticle characteristics and their effects on oxidative stress, inflammation, and immune markers.

2. METHODOLOGY

Different approaches were applied in the effects of nanoparticles on respiratory health and immune function, namely in vivo and in vitro approaches. The in vivo part involved 60 rats that were exposed to CuO, CNTs, SiO₂, and ZnO nanoparticles in different doses for 8 weeks. Bronchoalveolar lavage fluid (BALF) was collected for the determination of inflammatory and oxidative stress markers. In vitro, pulmonary epithelial cells were exposed to the nanoparticles, followed by assessment of cell viability, cytotoxicity, and inflammation. Oxidative stress markers, such as 8-OHdG and HO-1, and pro-inflammatory cytokines (TNF- α , MCP-1) and anti-inflammatory cytokines (IL-10), were quantified to assess the effect of nanoparticles on immune function and respiratory health.

2.1 Nanoparticles Selection

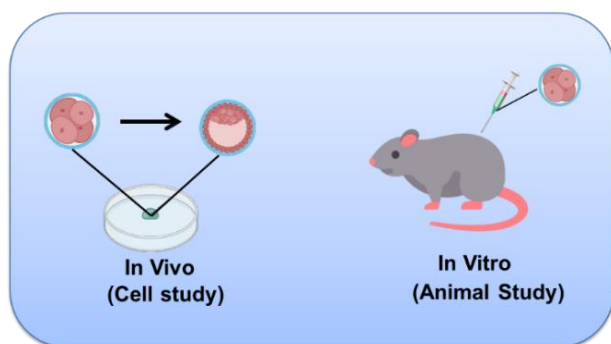
To investigate potential inhalation exposure health risks, some nanoparticles such as copper oxide, carbon nanotubes, silica, and zinc oxide were considered for respiratory health and immune system adverse effects. By evaluating inflammatory response, oxidative stress markers, and immune cell distribution, a broader understanding will be achieved concerning the influences on respiratory health and immune disruption by such nanoparticles, shown in Table 1.

- **Copper Oxide (CuO):** The antibacterial characteristics of CuO can lead to oxidative stress and inflammatory inhalation, which may affect immune function and exacerbate respiratory disorders.
- **Carbon Nanotubes (CNTs):** CNTs, which are constructed materials with different structural characteristics, are essential to examine the long-term health impacts of nanomaterial inhalation because of their association with lung inflammation and potential immune system variations.
- **Silica Nanoparticles (SiO₂):** SiO₂ NP are often discovered in consumer items and have been scientifically associated with respiratory damage and inflammation. Therefore, it is needed to determine how these NP affect the immune system and the functioning of the lungs.
- **Zinc Oxide (ZnO):** ZnO, which is frequently used in sunscreens because of its antibacterial qualities, can produce reactive oxygen species (ROS) and possibly cause oxidative stress, which can impair immunological and respiratory health.

Extensive studies have been done on the deleterious effects of NP in both vivo and in vitro. Despite their settle in peripheral lung tissue, NP that enters human tissue through the airways can travel through the interstitium and pulmonary epithelium. Figure 2 shows the variation of vivo and vitro studies.

Table 1. Key features of Nanoparticles affecting Respiratory Health and Immune System Disruption.

Nanoparticle	Size	Shape	Density (g/cm ³)	Specific Surface Area (m ² /g)
Copper Oxide (CuO)	<100 nm	Typically, spherical	~6.0	~20-40
Carbon Nanotubes (CNTs)	<100nm (varies)	Fibrous (cylindrical)	~1.3-2.0	~200-1000
Silica Nanoparticles (SiO ₂)	<100 nm	Spherical or irregular	~2.0	~100-400
Zinc Oxide (ZnO)	<100 nm	Spherical or rod-like	~5.6	~20-60

**Figure 2.** Impact of NP on respiratory health and immune system disruption

2.2 Vivo research

The in-vivo involved the proper selection of animal models, with rat models chosen as appropriate for significance in researching respiratory health. Animals were grouped in accordance with doses of nanoparticles. This provided different levels of representation regarding health impacts. Different exposure types included inhalation or direct administration of NP under controlled

environmental conditions to resemble real exposure scenarios, for instance, constant temperature, humidity, and lighting, ensuring accurate results.

Nanoparticle Treatments and Dosing

60 Sprague-Dawley Rats were separated randomly into seven groups: control and treatment groups with varying NP CuO, CNTs, SiO₂, and ZnO. The rats were kept under standard conditions and the exposure to the NP was done through intratracheal instillation twice a week for eight weeks.

Detection of oxidative damage and inflammation in BALF

Following the euthanasia of the rats, biomarkers like 8-OHdG, HO-1, TNF- α , IL-10, and MCP-1 were determined in the Broncho alveolar lavage fluid (BALF). To assess immune system distribution, C-reactive protein levels were quantified in BALF so as to determine the degree of immune system interference. Table 2 also highlights a detailed description of the research component.

Table 2. Research components of vivo study.

Research Component	Particulars
Animal Model	60 Sprague-Dawley rats (250 to 300 g)
Groups	7 groups: 1 control and 6 treatment groups (3.5 mg/kg and 17.5 mg/kg doses of CuO, CNTs, SiO ₂ , ZnO)
Housing Conditions	Controlled environment (24°C, 50% humidity)
Exposure Method	Intratracheal instillation every 2 days for 8 weeks
Assessment of Respiratory Health and Immune System Distribution	Measured biomarkers: 8-OHdG (oxidative DNA damage), HO-1 (oxidative stress and inflammation), TNF- α (pro-inflammatory response), IL-10 (anti-inflammatory response), MCP-1 (immune cell recruitment)
Sample Collection	Broncho alveolar lavage fluid (BALF) was collected post-euthanasia and centrifuged at 3000 rpm for 10 minutes to obtain supernatants for biomarker analysis, assessing respiratory health and immune response disruption.

Note: RPM stands for revolutions per minute

2.3 Vitro research

In vitro tests conducted through the different types of pulmonary epithelial cells were designed to study the effects of selected nanoparticles (CuO, CNTs, SiO₂, and ZnO) on cell viability, cytotoxicity, and immune response. Several doses were used for NP exposure to

evaluate alterations in various other cellular functioning assessments, including inflammation and oxidative stress. Thus, the present research focused on improved understanding the interaction between these nanoparticles and lung cells that lead to respiratory health complications and disturbing the immune system.

Nanoparticle exposure paired with cell culture

Pulmonary epithelial cells are the cells derived from the Sprague-Dawley rats (250 to 300g), which help with breathing and prevent germs and dust from entering the body. The cells were then grown in suitable culture media and kept under a physiological environment for 60 hrs.

Cells were exposed to different doses of each nanoparticle for 30 hours. The following assays were conducted to assess different nanoparticles' effect on cell viability, cytotoxicity, and inflammatory properties to foster cell understanding of respiratory health and immune system interference. Table 3 demonstrates various features of vitro investigation.

Table 3. Research components of vivo study.

Characteristic	Particulars
Cell Type	Pulmonary epithelial cells isolated from Sprague-Dawley rats (250 to 300 g).
Culture Conditions	Refined in appropriate growth media at 37°C with 5% CO ₂ for 60 hours.
Nanoparticle Treatment	Each nanoparticle was treated for 30 hours at doses of 10, 20, 50, 100, and 200 µg/mL.
Assessments	Cell Viability: Assessed using the MTT assay for metabolic activity.
	Cytotoxicity: Evaluated using Annexin V/PI staining for cell death and apoptosis.
	Inflammatory Response: Levels of inflammatory markers quantified in culture supernatants.

3. STATISTICAL ANALYSIS

For statistical significance determination, the data was analyzed by using SPSS software. The data were presented as mean ± standard deviation (SD) so that the central tendency and variation would be highlighted. Differences among groups were tested by the T-test, while proof for correlation helped understand the interrelationship between different variables. Regression analysis provided insight regarding the predictive power of nanoparticles over respiratory health and immune disruption. A threshold of $p < 0.05$ was considered statistically significant, indicating that the available data had significant

variation in all measured outcomes across the experimental groups.

3.1 T-test

The T-test outcomes compares biomarkers between the control and treatment groups exposed to nanoparticles, presenting differences in markers of oxidative stress, inflammatory cytokines, and other biomarkers. The evidence is based on statistically significant p-values of the effects of nanoparticle exposure on respiratory health and immune function. Table 4 illustrates the comparison of control and treatment groups.

Table 4. Comparison of control and treatment groups.

Biomarkers	Mean ± SD (Control)	Mean ± SD (Treatment)	t-Value	p-Value	Direction of Significance
8-OHdG	3.5 ± 0.5	5.2 ± 0.8	-4.5	<0.001	Negative
TNF-α	1.2 ± 0.3	3.0 ± 0.5	-5.25	<0.001	Negative
HO-1	2.1 ± 0.4	4.0 ± 0.6	-4.85	<0.001	Negative
IL-10	1.0 ± 0.2	0.5 ± 0.1	3.2	0.002	Positive
MCP-1	2.5 ± 0.4	4.5 ± 0.7	-4.00	<0.001	Negative

Table 4 depicts that treatment raised the oxidative stress marker 8-OHdG from 3.5 ± 0.5 in the control group to 5.2 ± 0.8 in the treatment group with $t = -4.50$; $p < 0.001$. The control was 1.2 ± 0.3 and the treatment was 3.0 ± 0.5, with a significant t-test of -5.25, $p < 0.001$ for TNF-α suggesting inflammatory status. The marker HO-1 from control = 2.1 ± 0.4 to treatment = 4.0 ± 0.6 with $t = -4.85$, $p < 0.001$. On the contrary, the anti-inflammatory cytokine IL-10 reduced from 1.0 ± 0.2 in the control to 0.5 ± 0.1 in the treatment group with $t = 3.20$, $p = 0.002$, indicating that immune response could have been affected by the

nanoparticles. MCP-1 levels increased from 2.5 ± 0.4 in controls to 4.5 ± 0.7 in the treatment group with t-value: -4.00, p-value: <0.001. The indicated biomarkers, 8-OHdG, TNF-α, MCP-1, and HO-1, all point to higher oxidative stress and inflammation because of nanoparticles. Reduced IL-10 indicates that the patient may have compromised immune control, resulting in poor health. When the level of IL-10 decreases, it suggests that the treatment may be reducing the body's ability to fight inflammation. Figure 3 depicts the result of the T-test analysis.

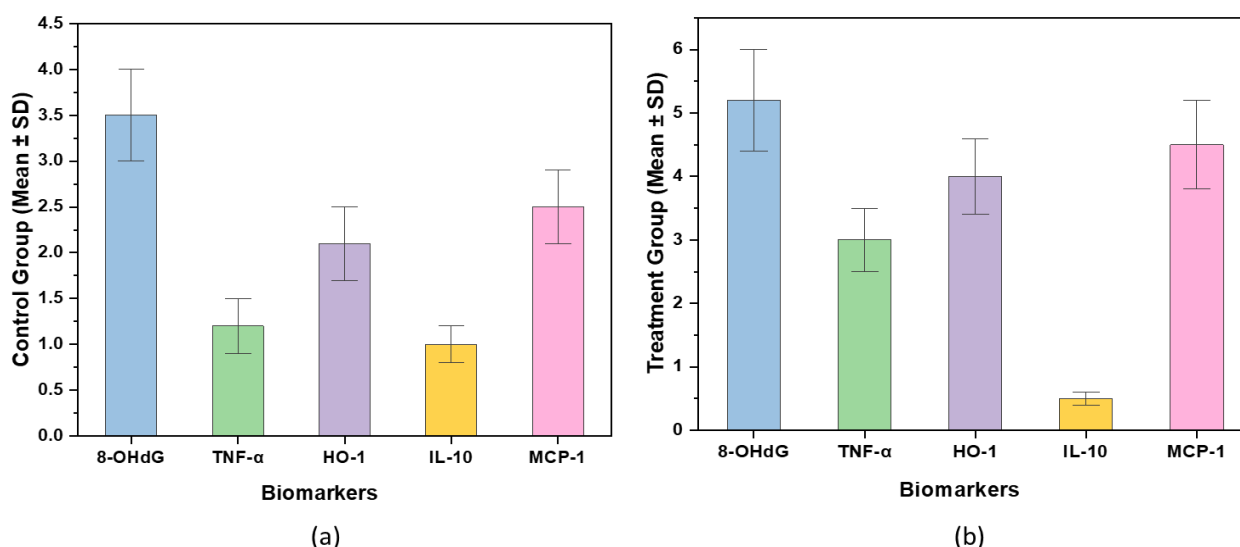


Figure 3. Biomarker control group and treatment outcomes (mean ± SD)

3.2 Correlation Analysis

The strength and direction of the relationship among the characteristics of nanoparticles (size, shape, and chemical composition) and the health effects presented by oxidative stress markers and immune responses were evaluated by means of correlation analysis. This analysis

assesses the degree of correlation between variation in nanoparticle properties and variation in various biomarkers to give us an insight into how specific properties of the nanoparticles may lead to respiratory health problems and disruptions in the immune system. Table 5 demonstrates the different biomarker concentrations in various nanoparticles.

Table 5. Level of Various Biomarkers in Different NP.

Biomarkers	Concentration of CuO (µg/mL)	Concentration of CNTs (µg/mL)	Concentration of SiO ₂ (µg/mL)	Concentration of ZnO (µg/mL)
8-OHdG	0.65	0.7	0.55	0.6
TNF-α	0.68	0.72	0.53	0.59
HO-1	0.75	0.74	0.57	0.62
IL-10	-0.56	-0.58	-0.5	-0.55
MCP-1	0.66	0.65	0.58	0.61

The correlation analysis test indicated that nanoparticle concentrations were indeed related to health issues. Larger mean CuO and CNTs concentrations tended to increase pro-inflammatory markers significantly; the relationship of TNF-α being significant at 0.68 for CuO and 0.72 for CNTs; HO-1 had significant correlations with 0.75 for CuO and 0.74 for CNTs. Conversely, the anti-inflammatory marker was inversely related to CuO (-0.56) and CNT (-0.58), suggesting that a higher concentration of NP could offer less anti-inflammatory protection. Based on the results obtained in this work, an increased concentration of NPs is associated with increased stress and inflammation, which can be dangerous for health.

Regression analysis

Regression analysis was performed to determine the level of effect of several characteristics of nanoparticles (size, shape, density, and dosage) on the respiratory bioindicators. The analysis quantified the degree of change in biomarkers related to oxidative stress, inflammation, and immune function in relation to the extent of altered parameters of the nanoparticles. Most importantly, by modelling the characteristics of nanoparticles to health outcomes, regression analysis provided answers to what the specific properties of nanoparticles that contribute to respiratory damage and/or the disruption of the immune system would be, thereby identifying potential dose-dependent effects and critical determinants of risk. Table 6 indicates the analysis of regression for the biometric properties of nanoparticles.

Table 6. Level of Various Biomarkers in Different NP.

Biomarkers	Variable	Coefficient (β)	SE	t-Value	P-Value
8-OHdG	Size of NP (nm)	0.25	0.05	5	<0.001
	Shape (Circular = 1)	0.80	0.1	8	<0.001
	Density (g/cm ³)	0.15	0.03	5	<0.001
	Dose (mg/kg)	0.20	0.04	5	<0.001
TNF- α	Size of NP (nm)	0.30	0.06	5	<0.001
	Shape (Circular = 1)	0.70	0.09	7.78	<0.001
	Density (g/cm ³)	0.25	0.04	6.25	<0.001
	Dose (mg/kg)	0.10	0.02	5	<0.001
HO-1	Size of NP (nm)	0.22	0.04	5.5	<0.001
	Shape (Circular = 1)	0.75	0.08	9.38	<0.001
	Density (g/cm ³)	0.18	0.03	6	<0.001
	Dose (mg/kg)	0.15	0.02	7.5	<0.001
IL-10	Size of NP (nm)	-0.15	0.05	-3	0.005
	Shape (non-circular = 0)	-0.50	0.09	-5.56	<0.001
	Density (g/cm ³)	-0.1	0.03	-3.33	0.003
	Dose (mg/kg)	-0.05	0.02	-2.5	0.015
MCP-1	Size of NP (nm)	0.28	0.05	5.6	<0.001
	Shape (Circular = 1)	0.65	0.07	9.29	<0.001
	Density (g/cm ³)	0.2	0.03	6.67	<0.001
	Dose (mg/kg)	0.12	0.02	6	<0.001

Note: Shape (Circular = 1, non-circular = 0)

Table 6 shows how nanoparticle characteristics (size, shape, density, and dose) affect health outcomes related to respiratory health and immune system disruption. The circular shape of 8-OHdG, TNF- α , HO-1, and MCP-1 has positive coefficients (0.80, 0.70, 0.75, and 0.65, respectively). However, the non-circular shape of IL-10 (tube-shaped) has a negative coefficient ($\beta = -0.50$, $P = 0.005$), indicating that certain features may suppress anti-inflammatory effects. Overall, these results emphasize the significant health risks associated with nanoparticle exposure. Figure 4 presents the result of the nanoparticle shape.

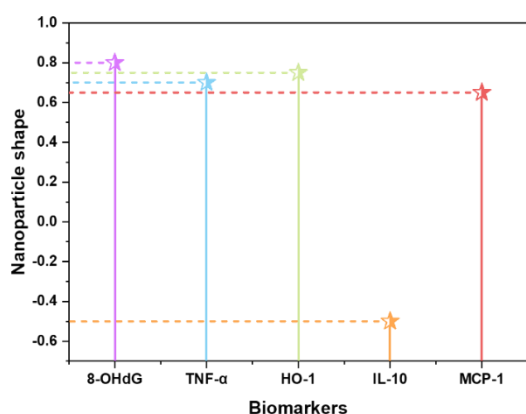


Figure 4. The outcome of nanoparticle shape

4. DISCUSSION

NP have direct and immunological impacts on pulmonary health, as the research emphasizes. The indicated biomarkers, 8-OHdG, TNF- α , MCP-1, and HO-1, all point to higher oxidative stress and inflammation. On the contrary, the body's anti-inflammatory evidence of IL-10 reduced abruptly, indicating that NP inhibits the body's capability of regulating inflammation. The correlation findings also reveal that inflammation and stress markers increase significantly with increased concentrations of NP, specifically CNT. Conversely, CNTs correlated strongly with the inverse of IL-10, demonstrating decreased anti-inflammatory properties. According to the regression analysis, various properties of NP, such as size, shape, density, and dose, determine the health effects experienced. Circularity was beneficial to stress and inflammation levels, while an absence of circularity in shape was associated with lesser anti-inflammatory benefits, specifically IL-10. Concisely, NP-related findings suggest that noncircular two-dimensional NP increases stress and inflammation as well as decreases the body's anti-inflammatory ability.

5. CONCLUSION

Therefore, the present research proves that NP such as CNTs cause increased levels of both inflammation and

oxidative stress in vitro and vivo methods. Increases in the biomarkers of oxidative stress, inflammation, and endothelial dysfunction, 8-OHdG, TNF- α , MCP-1, and HO-1, and reduce in the anti-inflammatory cytokine IL-10 support the pathogenic impact of these NP on respiratory diseases and immune stress. This is important for regulation development and reduction of harm that can be posed to human health due to the increased use of

NP in consumer products. Research findings are dependent on certain NP and experimental animals; thus, further research is needed to look at long-term implications and the processes of action in various biological systems. Further research should also examine the potential synergistic effects of several NP under practical exposure scenarios.

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