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Review Article

Silica Nanoparticles: Navigating the Toxicological Terrain – An In-Depth Exploration of Multifaceted Health Impacts

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ABSTRACT

Silica nanoparticles have emerged as versatile materials with widespread applications, particularly in industries ranging from medicine to electronics. However, their increasing ubiquity raises concerns about potential adverse health effects. This review delves into the intricate landscape of the toxicological effects associated with silica nanoparticles, aiming to provide a comprehensive understanding of their multifaceted impact on human health. Drawing from a vast body of research, we explore diverse aspects, including respiratory, cardiovascular, and dermal effects, as well as potential implications for reproductive and immune systems. The intricate interactions between silica nanoparticles and biological systems are scrutinized, shedding light on cellular mechanisms and pathways involved in toxicity. Additionally, the influence of physicochemical properties, such as size, surface charge, and shape, on the toxicity profile is thoroughly examined. Insightful discussions on exposure routes, dosimetry, and risk assessment contribute to a holistic perspective on the potential hazards associated with silica nanoparticles. As we navigate through this toxicological terrain, it becomes evident that a nuanced understanding of the complex interactions between silica nanoparticles and the human body is imperative for informed decision-making in both scientific and regulatory realms. This review not only synthesizes existing knowledge but also identifies critical research gaps, paving the way for future investigations aimed at elucidating the intricacies of silica nanoparticle toxicity.

Keywords: Nanoparticles, Human body; Environment; Drug delivery; Adverse effect; Toxicology

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1.Introductiion

In recent years, silica nanoparticles have become ubiquitous in various industrial and technological applications, showcasing their versatility and adaptability. As these nanoparticles find their way into an increasing array of products, concerns about their potential impact on human health have escalated. This review endeavors to comprehensively explore the intricate landscape of the toxicological effects associated with silica nanoparticles, offering a nuanced understanding of their multifaceted influence on human health [1].

Silica nanoparticles, characterized by their unique physicochemical properties, have found applications in fields as diverse as medicine, electronics, and materials science. However, their pervasive presence raises critical questions about the potential risks they pose to human well-being. This review synthesizes existing research, providing a thorough examination of the various dimensions of health impacted by silica nanoparticles. From respiratory and cardiovascular effects to dermal, reproductive, and immune considerations, the exploration of these multifaceted health impacts is crucial for informed decision-making in both scientific research and regulatory frameworks.

Throughout this journey, we will delve into the intricate interactions between silica nanoparticles and biological systems, unraveling the cellular mechanisms and pathways that underlie their toxicity. Moreover, the influence of key physicochemical attributes, including size, surface charge, and shape, will be scrutinized, as these factors play a pivotal role in determining the toxicological profile of silica nanoparticles [2].

As we navigate this toxicological terrain, this review aims not only to consolidate current knowledge but also to identify critical gaps in research, paving the way for future investigations. By doing so, we contribute to a more comprehensive understanding of the potential hazards associated with silica nanoparticles, ensuring that scientific discourse and regulatory decisions are grounded in a holistic appreciation of their multifaceted health impacts.

2. Toxic Effects by Organ System

Numerous models have been used to test silica nanoparticles both in vitro and in vivo. Most of these studies on effects at the cellular, tissue, and organ levels made use of amorphous colloidal SiO2-NPs, which are primarily produced using the Stober process. Crystalline, pyrogenic, vitreous, or surface modified SiO2-NPs were employed in certain instances.

3. Respiratory System

SiO2-NPs dose-dependently decreased viability and induced apoptosis in human lung cells. Indicators of oxidative stress included DCF, GSH, MAD, and LDH. COX-2 expression and IL-8 release were indicators of inflammation. The following extracellular parameters were increased in a dose- and time-dependent manner: lactate, glucose, histidine, phenylalanine, and tyrosine. ER stress and DNA damage were also noted. JNK-mediated acetylation of p53 and SIRT11 was linked to apoptosis. In certain cases, cells were able to avert apoptosis by initiating autophagy. It was discovered that the fibrotic mechanisms were autophagic flux blockage and interactions between macrophage fibroblasts. Shape factors affected aggregation but did not significantly alter the release of IL-8 or LDH from mesothelial cells [3].

Overall, exposure to SiO2-NPs disrupted several pathways involved in global metabolism. The inflammatory response in mice was influenced by both sex and particle size. Allergy-related respiratory symptoms were dose-dependently

exacerbated when PEG-coated SiO2-NPs were co-exposed to a sensitising allergen. After being infused with silica, scavenger receptor class A type I/II null mice (CD204) did not exhibit fibrosis; instead, they displayed increased neutrophil accumulation and elevated TNF-α. This suggests that alveolar macrophages play a crucial role in mitigating inflammation caused by silica exposure. Follistatin (FST) expression in human lung cells and mouse lung tissues, mediated by Nrf2, provided protection [4].

4. Circulatory system

SiO2-NPs demonstrated cytotoxicity, LDH leakage, inflammatory cytokine production, necrosis, apoptosis, ER stress, and autophagy in human umbilical vein endothelial cells. Potassium ion channel activation was linked to cytotoxicity and LDH leakage. Independent of ROS and AMPK, autophagy was linked to the PI3K/AKT/e NOS/NO signalling pathway; blocking autophagy reduced necrosis but not apoptosis. SiO2NPs demonstrated apoptosis, oxidative stress, LDH leakage, and an increase in Ca2+ in erythrocytes and platelets. Platelet aggregation and haemolytic activity resulted from this. Particle size had an inverse relationship with haemolytic activity, which was higher for aged mesoporous or nonporous particles (assuming the ageing effect was not due to degradation products). Haemolytic activity was reduced by PEG surface modification. Intratracheally administered SiO2-NPs in rats to serum and the heart moved to the heart and serum, where it caused dose-dependent harmful alterations in the production of cardiac enzymes, body weight, blood factors, apoptosis (as confirmed by protein expression), and histopathology. In cardiac cells, silica nanoparticles resulted in cytotoxicity and metabolic disruption. SiO2-NPs also prevented D3 murine embryonic stem cells from differentiating into cardiomyocytes, even at low concentrations where cytotoxicity was not noted [5].

5. Digestive system

Silica nanoparticles increased ROS production, mitochondrial damage, and apoptosis in human liver cells. Even at low doses, where there was no morphological alteration or rise in reactive oxygen species, proteomic analysis showed changes in protein expression. SiO2-NPs grafted with polymer were less cytotoxic in human colon cells, and there was a positive correlation between biocompatibility and higher grafting density. SiO2-NPs smaller than 300 nm that were injected intravenously in mice resulted in liver damage linked to sinusoidal endothelial cells and Kupffer cells. Four weeks of subacute exposure led to hepatic fibrosis. Over the course of six weeks, an intraperitoneal injection increased early fibrosis, lymphocytic infiltration, Kupffer cell activation, and inflammatory cytokines [6].

6. Immune System

Silica nanoparticles stimulated caspase1 in macrophages in a way that was dependent on Nalp3. Changes in the regulation of potassium and an increase in ROS production followed this. Both crystalline and vitreous SiO2-NPs exhibited NOS activation, TNF-α production, and cytotoxicity. The SiO2-NPs in both crystalline and vitreous forms exhibited strong hydrophilic surface sites, sustained hydroxyl radical release, and sharp edges. Oxidative stress was typically linked to cytotoxicity. Macrophages stimulated by exposure to lipopolysaccharides released Inflammasomes of the interleukin-1 family following a subsequent exposure to silica nanoparticles. Via NADPH oxidase in the cell membrane, ATP released from the P2X7 receptor caused the production of ROS [7].

7. Nervous System

Silica nanoparticles reduced extracellular acidification and cellular respiration in human neuronal cells. During differentiation, there was a decrease in mitochondrial function and a destabilisation of the mitochondrial membrane potential. Cell stiffness was also observed as a result of cytoskeletal aberrations. Many aspects of hippocampal function, such as reactive oxygen species (ROS), lipid peroxidation, protein oxidation, nitrite production, antioxidant activity, GSH, AChE, and inflammatory markers, were impacted by intraperitoneal exposure to rats. Vacuolation was found in the histopathology, and oral abnormalities in spatial learning and memory were noted [8-10].

8. Renal System

SiO2-NPs resulted in lipid peroxidation, apoptosis, nuclear condensation, increased ROS, reduced GSH, and decreased viability of human embryonic kidney cells. When rats were given silica nanoparticles, the kidneys experienced secondary effects. After seven and thirty days, fibrotic indicators and inflammatory markers were noticed [11].

9. Integumentary System

SiO2-NPs with an average diameter of 30 to 535 nm were all absorbed by mouse keratinocytes. For particles larger than 100 nm, cytotoxicity and LDH leakage were not observed, but they were dosedependent. GSH reduction was observed to follow a similar pattern [12].

10. Reproductive system

SiO2-NP exposure caused oxidative stress in the testis, DNA damage, histopathological alterations, and a reduction in the quantity and quality of sperm in male mice. SiO2-NP exposure in female mice caused uterine inflammation, trophoblast apoptosis, atresia, oxidative stress in the ovaries, DNA damage, and an imbalance in sex hormones [13-15].

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Conflict of Interest

The authors declare no conflicts of interest.

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