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Silicon Micro- and Nanoparticles: Size-Dependent Physicochemical Properties and Toxicological Implications

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Abstract

Silicon-based micro- and nanoparticles are now widely used in fields like medicine, industry, agriculture, and the environment because of their special properties. Research shows that the size of these particles has a big impact on how they react, interact with living things, move through the body, and cause toxic effects. This review brings together what is currently known about how the size of silicon and silica particles affects their properties, how they are made and studied, and how they cause biological and toxic effects. It focuses on issues like oxidative stress, inflammation, lung toxicity, how the particles spread in the body, and how long they last. The review also looks at regulatory challenges and ways to design safer materials. Understanding how size affects both the usefulness and risks of these materials is key to making sure they are developed safely and responsibly.

Keywords: Silicon nanoparticles; Silica microparticles; Size-dependent toxicity; Oxidative stress; Nanotoxicology

1. Introduction

Silicon-based materials, such as elemental silicon and silicon dioxide, are widely used because they can be engineered for many applications, including electronics, medicine, catalysis, agriculture, and environmental cleanup (1,2). As nanoscale technologies develop rapidly, there are growing safety concerns, as the size of these particles strongly affects how they react, interact with living systems, and their potential toxicity (3,4).

Studies show that nanoscale silica causes stronger inflammation and oxidative stress than larger particles when compared by equal mass. This highlights the need for hazard assessments that consider particle size (5).

2. Classification of Silicon Micro- and Nanoparticles

Elemental silicon nanoparticles and silicon dioxide particles differ in their crystal structure, surface chemistry, solubility, and biological behavior. These differences affect their toxicity (6). It is important to distinguish micro- and nanoscale materials because nanoscale particles have much greater surface area and behave differently in the body than larger particles (4).

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2.1. Size-Dependent Physicochemical Properties

2.1.1. Surface Area and Reactivity

As particle size decreases, the surface area relative to volume increases significantly, exposing more atoms or groups on the surface. This makes silicon-based micro- and nanoparticles much more reactive, better at adsorbing substances, and more active as catalysts. At the nanoscale, higher surface energy helps these particles interact more strongly with proteins, lipids, and nucleic acids, thereby affecting how they spread, clump, and behave in the body (7,8).

Silica and silicon-based nanoparticles have many silanol (Si–OH) groups on their surfaces, which makes them more reactive. These groups can form hydrogen bonds, interact electrostatically, and participate in redox reactions, leading to the production of reactive oxygen species and increased oxidative stress in cells. Because of this, smaller particles are often much more biologically active than larger ones when compared by equal mass (3,4).

The higher reactivity from increased surface area is closely linked to inflammation in the lung and immune cells, such as activating macrophages, releasing cytokines, and damaging cell membranes. Studies show that surface area is a better predictor of the toxic effects of silicon-based particles than particle mass alone, especially after breathing them in (7,8). This means risk assessments should consider surface area, not just mass, especially for workplace and environmental safety.

2.1.2. Porosity and internal architecture

Mesoporous silica nanoparticles have well-organized pores and a large internal surface area, sometimes several hundred square meters per gram. This structure affects their properties and how they interact with living systems. The even pore sizes allow these nanoparticles to bind proteins, lipids, and small molecules, forming complex layers on their surfaces. These layers can change how cells recognize, take up, and process the nanoparticles.

Porosity influences the degradation rate of particles and the release of ions. Porosity affects how quickly particles break down and release ions, which in turn changes how long they stay inside cells and where they go. Mesoporous structures can retain nanoparticles in specific regions of the cell for longer, potentially disrupting those areas, causing cell stress, and triggering inflammation. Solid silica particles of the same size usually have less internal surface area and break down differently, leading to other effects in cells. This shows that the inside structure of the particles, not just their size, is important for their behavior and safety, and a key determinant of their toxicity. Crystalline forms, such as quartz and cristobalite, are strongly associated with pulmonary fibrosis and carcinogenesis, particularly following chronic inhalation. Their rigid lattice structures and reactive surfaces sustain immune cell activation, enhance the release of pro-inflammatory mediators, and contribute to persistent alterations in lung tissue.

Amorphous silica, which does not have a regular crystal structure, is usually thought to be less dangerous. However, new studies show that very small amorphous silica particles can still be harmful in some situations. Research with human immune and skin cells found that these nanoparticles can cause cell stress, energy problems, and inflammation, especially when there is a lot of surface area or high particle concentrations. This means that having less crystal structure does not always make nanoparticles safer.

Overall, these findings show that the porosity and order of the particles, along with their size and surface features, all play a role in how harmful they can be. To fully understand the risks of silicon micro- and nanoparticles, it is important to examine their internal structure and form, not just their weight and size.

In living systems and the environment, silicon micro- and nanoparticles rarely stay as single particles. They often clump together due to various forces and interactions with ions and biomolecules. This aggregation alters their size, surface charge, and settling behavior, thereby affecting where they end up in the body, how they are absorbed, and how often they contact cells. As a result, the dose cells actually experience can differ significantly from the amount administered, making it harder to compare results across studies (9,10).

How well nanoparticles are dispersed matters a lot in lab studies. How evenly nanoparticles are distributed is very important in lab studies. If they are not well dispersed, they can settle quickly on cell layers and create high local concentrations. Stable dispersions, however, allow for more interactions and cell uptake. Factors such as the medium, salt content, pH, and proteins all affect how particles clump. This highlights the need for standard ways to disperse particles and measure doses in nanotoxicology research (10). Particles can be made using different physical, chemical, or biological methods. Each method produces particles with different sizes, shapes, and surface features. Common methods for making them include sol–gel synthesis, flame pyrolysis, laser ablation, and newer green methods that use

plant extracts or biopolymers. The Stöber method is especially popular for producing uniform, round silica nanoparticles with controlled sizes, typically ranging from a few dozen to several hundred nanometers (1).

By adjusting factors like the amount of starting materials, solvent, pH, and temperature, researchers can control the size, porosity, and surface features of the particles. These traits are important for how particles function and interact with living systems. So, the way the particles are made plays a big role in their safety and potential risks.

When silicon-based nanoparticles come into contact with biological fluids, they quickly pick up a layer of proteins, lipids, and other molecules called the protein corona. This new layer changes how cells recognize and take up the particles, and how the immune system responds. The corona often has a greater effect on the particles' surfaces than the original surface (11-13).

In comparison to microparticles, nanoparticles demonstrate greater cellular internalization. Nanoparticles are taken up by cells more easily than larger particles, mainly through different endocytosis pathways. This means more nanoparticles enter cells and interact with structures such as mitochondria and lysosomes, which can increase the risk of toxic effects (14). How well particles are taken up and the effects they have depend on their size, surface charge, and the makeup of the protein corona, well-documented mechanism underlying the toxicity of silicon-based nanoparticles. Smaller particles, with higher surface area and reactivity, exhibit greater redox activity, leading to excessive ROS production, depletion of antioxidant defenses, and mitochondrial dysfunction. These oxidative imbalances can trigger lipid peroxidation, protein oxidation, and disruption of cellular signaling pathways (15).

3. Inflammation and immune activation

Silica nanoparticles strongly activate the body's first line of immune defense. When macrophages take up these particles, they can disrupt lysosomes and trigger inflammatory pathways, such as the NLRP3 inflammasome. This causes the release of cytokines such as IL-1β and TNF-α, leading to tissue inflammation and, with long-term exposure, changes in tissue structure (16,17). linked to silica nanoparticles are primarily indirect and mediated by oxidative stress rather than direct DNA in silica nanoparticles mainly causes genetic damage indirectly, through oxidative stress rather than by directly affecting DNA. Higher levels of reactive oxygen species (ROS) can induce DNA strand breaks, alter DNA bases, and destabilize chromosomes. Although ROS do not typically cause direct mutations, prolonged oxidative and inflammatory stress can elevate the risk of long-term genetic alterations and disease (18). Nanoscale particles, compared with microscale forms on an equivalent mass basis, elicit stronger biological responses due to their higher surface area and reactivity. Short-term exposure to these particles can trigger increased neutrophil recruitment, elevated pro-inflammatory cytokine release, and epithelial cell injury, highlighting their potential for acute tissue damage. Together, these observations underscore the interplay between particle size, oxidative stress, and inflammatory mechanisms in determining the genotoxic and cytotoxic potential of silicon-based nanoparticles Long-term pulmonary outcomes are influenced by factors such as particle bio persistence, surface reactivity, and clearance efficiency, with chronic inflammation increasing the risk of fibrotic changes (5,8,19).

3.1. Biodistribution, clearance, and bio persistence

After inhalation or ingestion, silicon nanoparticles can cross body barriers and accumulate in organs such as the liver, spleen, and kidneys. Where the particles go depends mostly on their size, surface chemistry, and how fast they dissolve. Smaller, more soluble particles are usually cleared faster, whereas those that do not dissolve well or clump together can remain in tissues longer, increasing the risk of systemic effects (20).

3.2. Environmental fate and ecotoxicology

In the environment, silicon nanoparticles can clump together, settle, dissolve, and react with natural organic matter. These changes affect how particles move, how readily they are available to living things, and how easily plants and animals can take them up. Agricultural studies show that while these nanoparticles can help plants cope with stress, they could also pose risks to ecosystems if they accumulate or move through food chains without proper management (21).

3.3. Regulatory considerations and safety-by-design

Current regulations struggle to address the risks of silicon micro- and nanoparticles, which depend on their size and properties. Standard exposure limits based on mass may not fully capture the dangers posed by high surface area, reactivity, or the duration of particle residence in the body. Because of this, more experts support safety-by-design methods that include careful control of material properties, standard testing, and early hazard checks. These

approaches match new regulatory trends that focus on understanding how nanomaterials work and their full life cycle (3).

4. Conclusion

This review demonstrates that the biological behavior and toxicity of silicon micro- and nanoparticles are determined primarily by particle size, surface area, porosity, crystallinity, and aggregation state, rather than by chemical composition alone. Nanoscale forms exhibit greater cellular uptake, oxidative stress, and inflammatory responses than their microscale counterparts. These findings underscore the importance of property-based risk assessment and safety-by-design strategies to promote safer industrial and biomedical applications of silicon-based materials. Furthermore, they highlight the need for standardized testing protocols and responsible nanomaterial development to maximize societal benefit.

Compliance with ethical standards

Disclosure of conflict of interest

The author declares no conflict of interest.

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