Chapter 14

Nanomaterials and Safety Concerns to End Users

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Abstract

Nanomaterials (NM) are part of the daily life since decades, and the advantages that nanotechnology has brought to humanity in relation to the novel nanoproducts with unique properties are undeniable. However, concern about engineered NM has raised because of the lack of both regulation to the increasing production and safety assessments in users (with emphasis on workers). As robust evidence suggests toxic effects of NM on human health in case of exposure, this chapter aimed to describe not only the main applications and benefits of NM but also their fate, exposure pathway, and ultimate toxicological effects.

Keywords

Applications, Engineered nanomaterials, Environmental fate, Exposure pathway, Nanoparticles, Nanotoxicology

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1. Introduction

Humans have been using nanomaterials (NM) since prehistoric times and first civilizations without knowing their existence [1]. For example, prehistoric humans used combustion products of fire, like carbon NM, for cave paintings. Ancient Egyptians synthesized palladium disulfide nanoparticles (NP) of 5 nm for the formulation of hair colorants. However, many years passed until in 1914, Richard Adolf Zsigmondy first introduced the term of nanometer. Since then, the “nano-universe” has been growing unlimited. In 1959, Richard Feynman installed the new concept of nanotechnology [2], and in 1974, Norio Taniguchi was the first Japanese researcher to use the term “nanotechnology” [3]. Over the years, the use of nanotechnology has expanded dramatically. Nowadays, it could be found in almost every field of science, such as cosmetics, wastewater treatment, environmental remediation, sensors, electronics, medicine, catalyst and energy-storage devices [4].

The fundamental constituents of nanotechnology are the NM. These materials of $10^{-9}$ m in size have at least one dimension between 1-100 nm. They can be of different shapes; like NP, nanofibers, nanoplatelets, nanorods and nanosheets, and different composition such as inorganic, organic, carbon and hybrid composites NM [5]. At the nanoscale, these materials exhibit different physicochemical properties when compared to their bulk, and can contribute to increase or improve the resistance, lightness, cleanliness and intelligence of the surfaces and systems were they are included [6].

Having been widely proved the advantageous properties of NM in comparison with the micrometric counterparts, the increased amount of production of these novel materials has raised concern regarding both their fate when released and potential exposure to humans. However, the knowledge about their safety remains under development despite the fact that there is updated evidence suggesting toxic effects in case of exposure (with emphasis in case of occupational one). In this sense, this chapter aimed to describe the main NM applications, the values towards the global market and production levels, and also to provide information about their potential fate and toxicological effects on humans.
2. Applications

Nanomaterials are now being applied in the manufacture of a wide variety of daily use products, ranging from cosmetics, paints and coating, food, automotive, toys, textile, electronic, plastic and sport industry to biomedical and pharmaceutical sector (Figure 1). In fact, according to a BCC report, there are more than three thousand commercial applications based on NM [7].

For example, in the cosmetic industry, nanosized materials can be found in moisturizers, hair care products, make up and sunscreens [8]. The incorporation of NM in personal care products seeks to prolong their useful life by increasing the stability of the cosmetic components and improving the delivery of the ingredients through the skin. Cosmetic industry also aims to develop new products whose nanometric elements can target the right amount of the active ingredients to the required part of the body and promote a controlled release of them. At the same time, NM are used to give new color, transparency, and UV protection. This is the case of titanium dioxide (TiO$_2$NP) and zinc oxide nanoparticles (ZnONP) that are incorporated in modern sunscreens as an UV filter and to make creams and lotions transparent [9]. Nanometric lipid vesicles, liposomes, have been another protagonist of cosmetic products since the 1980s to improve the topical delivery of cosmeceuticals [10]. The interest of cosmetics brands in incorporating liposomes into their products arose from the many advantages they offer: biodegradability, improved moisturization, recovery action, biocompatibility and controlled dermal release. Moreover, due to their similarity to cell membranes, they can penetrate epidermal barrier in contrast to other delivery systems, increasing cosmeceuticals accumulation in the skin [11]. Taking advantage of all these properties of liposomes, the L’Oréal group for Lancôme and Dior LVMH were the two pioneer brands to launch “Niosomes®” and “Capture®” onto the market in 1986, respectively.

![Figure 1. Nanomaterials are applied in a wide range of consumer nanoproducts from different sectors.](image-url)
Paints and coatings are other sectors that mainly include, for example, TiO$_2$NP, nanosized antimony tin oxide (ATONP), silver NP (AgNP) and nano silicon dioxide NP (SiO$_2$NP) to enhance durability and incorporate new functions to the products [12,13]. While TiO$_2$NP [14] and AgNP [15] provide antimicrobial properties against Gram positive and Gram negative bacteria, silica NP (SiNP) are included in paints to improve their physic-mechanical properties, and increase durability and resistance to abrasions, scratches and weather [16,17]. ATONP provides coatings thermal insulation and transparent protection against UV radiation, which was not seen with the bulk material [18].

Nanotechnology is widely used in various fields of food industry as well [19,20]. Production, processing, safety, and packaging of food have included NM to guarantee contamination-free products and provide end consumers with food of higher quality and enhanced properties. In this sense, nanostructured components aim to change textures and colors of food, give new tastes, and deliver and control the release of food ingredients, flavors, and additives. Nanofillers can also improve mechanical properties, increase durability, control gas permeability and provide antimicrobial action to food packaging, ensuring a well preserved product [21]. It is also possible to develop food nanosensors or nanobiosensors by using thin films, nanorods, NP, and nanofibers to detect pathogens in processing stages or in the food material, advising consumers and distributors about the condition of the product [22].

The electronic industry takes advantage of the magnetic, electrical, optical and chemical properties of NM to increase the capabilities of electronics devices, such as recording media, data storage devices, and computer components [23]. For example, nanoelectronics have allowed to reduce power consumption, weigh and thickness of the computer and television screens, but also helped to increase the computers response speed and the capacity of hard disk drive storage. Carbon nanotubes (CNT) [24] are incorporated in transistors to magnify the processing power of silicon chips, reducing the use of energy, the heat generated, and the size and weight of the components [25]. Additionally, nanotechnology is applied to conserve power and prolong battery life of small portable electronic gadgets. Magnetic ferrite-based NP with high saturation magnetization and electrical resistivity can be applied in magnetic recording media [26,27].

Sports technology also includes different nanoscale materials, specially CNT, to produce lighter but stiffer equipment and enhance strength and durability of conventional sporting equipment [28]. In this sense, CNT are used to improve the performance of tennis, badminton, golf, kayaking and archery equipment. TiO$_2$NP, SiNP and fullerenes [29] are included in tennis rackets; nanonickel [30] is used in golf clubs to increase their moment of inertia and stability; carbon nanofibers help to reduce the weight and increase stiffness of bicycles; and nanoclay enhances speed of water-boats [31]. In the case of textile industry, nanotechnology is used to improve specific functions in clothing, like water repellence, antimicrobial action, conductivity, and antistatic and antiwrinkle characteristics [32]. AgNP provide bactericidal protection to baby clothing, TiO$_2$NP acts as UV protector in swimwears, synthetic amorphous SiNP increases hydrophobicity of waterproof mountain jackets and tablecloths, and nano aluminium oxide and CNT enhance resistance
to scratches. It is noteworthy that these advantages can be achieved without altering
breathability or texture of textiles, and this is only possible with the application of the
nanoengineered materials [33]
Nanocomposites made of polymers entrapping several varieties of NM, are widely used to
improve physical properties and the efficiency of plastics manufacturing [34]. As well as
this, toys containing antimicrobial nanostructures, like AgNP, are already available in the
market [35]. Automotive sector appeals to nanotechnology to increase strength and
improve adhesion of tires to the road [36]. In fact, carbon black and silica fillers, nanoclay,
CNT, and graphene are incorporated in rubber of automobile tires to enhance security, fuel
efficiency, control, and handling performance. But also, NM are present in the surface
coating, fluids, interior and exterior parts, electronics, and batteries of the cars.
Pharmaceutics, biology and medicine are other fields where the use of nanotechnology has
grown remarkably [37–39]. In fact, NM are applied in different areas like drug delivery,
imaging, gene therapy, tissue engineering, diagnosis, nanoscale biochips, and alternative
therapeutics. Nanoparticles can be used to miniaturize biosensors and develop more
sophisticated biochemical and diagnostic analysis approaches. Currently, the use of NP for
diagnosis has extended to treatment of different diseases like cancer and diabetes. For
example, iron oxide NP are widely employed in Magnetic Resonance Imaging [40], gold
NP are used in cancer treatment, drug delivery and as antibacterial material [41], and AgNP
are used as antibacterial agents for dressing wounds [42–44]. Inorganic, polymeric and
lipid NP can help with targeted drug delivery, increasing bioavailability of the drug [45,46],
and biomaterials and nanofiber based scaffolds are favorable to stimulate growth,
proliferation, and cell attachment for tissue engineering [47,48].
Although these are just some examples, there are many other NM and applications that are
currently used to improve the quality and properties of countless products. In fact, it is
considered that NM have been introduced in consumerization category, as they migrated
from the laboratory research to enterprise and then into the market. As a result, there is a
constant exposure to different nanostructures. However, it has been reported that 70% of
the products do not include information about the NM employed [49]. This is particularly
the case for the automotive, cosmetics and electronics sectors, where 92%, 60% and 88%
of the products, respectively, do not declare and identify a specific NM. Although this
information should be available for final users, the determination and quantification of NM
content in commercial products lead to many technical problems for companies, as they
require special techniques and regulations to characterize them [50]. All this is especially
problematic since the adverse physicochemical effects that NM can have on living beings
remain ambiguous [51]. Not only the final users but also exposed workers and the general
public could experience side effects against NM.

3. Global market and production levels
Nowadays, the scientific community has successfully achieved the ability to integrate the
novel properties of nanoscale materials into new products and systems. In addition,
nanotechnology has generated considerable support and funding from Governments and industrial companies which drive the growth of the nanotechnology market. For example, in the United States, the National Nanotechnology Initiative enhances interagency coordination of nanotechnology research and development from early-stage fundamental science through applications-driven activities. In this way, new developments are transferred and manufactured into products to benefit society [52]. The United States President’s Budget provided $1.2 billion for the National Nanotechnology Initiative to support innovation competitiveness, economic growth, as well as national security [53]. In the year 2014, the incorporation of nanotechnology into the different industries of the United States increased the U.S. gross domestic product and at the same time created nearly 1.8 million new jobs in the process [54]. Indeed, the global nanotechnology market is supposed to overcome a net value of $124 billion by the year 2024 [55].

In parallel, the United State Food and Drug Administration (FDA) received an augmented demand for regulatory review of products containing NM. Furthermore, a Nanotechnology Task Force was created in 2006 to help FDA’s regulatory authorities. For example, since 1970, the Center for Drug Evaluation and Research of the FDA has received more than 600 applications for products containing NM. However, half of them were received during the last 10 years [56]. The nanomedicine’s market had an estimated value of $53 billion in 2009, while by 2025 the business of nanomedicines is expected to reach a total market value of approximately $334 billion [57]. Undoubtedly, nanoscience and nanotechnology are important players of economic growth and industrial revolution.

Products that result from nanotechnology take advantages of the better and new properties to the nanoscale, in relation to larger size materials. However, the same interesting properties that make NP useful from a technological point of view would be involved in toxic effects for human health and the environment. In this context, specific regulations that ensure the safety use of NM are of paramount importance in order to present technical and accurate information about NM. Until now, the number of publications that address the nanotechnology applications together with regulatory issues and environmental management of NP is scare, but it is a rapidly growing field [51,58,59].

Due to the different applications of nanotechnology, the impacts on society are many and diverse. The top three nanotechnological applications are electronics, energy and biomedical, altogether they reach ca. 70% of the global nanotechnology market [60]. It is worth to mention that NP represent more than 85% of the global nanotechnological product market [60]. The United State National Institute for Occupational Safety and Health (NIOSH) reported that more than 2 million persons were exposed to large amounts of NP, and this number would rise fast and reach 4 million soon, thus is vital to evaluate the exposure and develop efficient monitoring methods and control techniques [61].

The production of NM is expected to keep increasing through the years. In 2014 (with predictions that would last up to 2025), it was estimated that the global market for NM was from 300,000 tons up to 1.6 million tons. The Asian region accounts for largest market share (34%), followed by North America (31%) and Europe (30%). Among the most
produced NM, the SiO$_2$NP were between 185,000 and 1,400,000; TiO$_2$NP between 60,000 and 150,000; and CNT between 1,550 and 1,950 annuals tons [62].

Even though, recent surveys revealed that the majority of the population is aware about the nanotechnology and most of them recognizes its beneficial effects in medical and technological applications. Indeed, only a small fraction of the population declared aversion towards nanotechnology. The public perception about nanotechnology has a direct implication on both the implementation and regulation of NM or products that contains them [63].

4. Environmental fate

Massive production of nano-enabled products inevitably leads to the release of engineered NM into the environment. Along with the product life cycle, there could be potential emissions and wastes during production processes, usage, and final disposal of consumer nanoproducts [64–66]. For example, Kaegi et al. [67] confirmed TiO$_2$NP emission from exterior paints into runoff waters. Similarly, several studies have investigated the release of Ag$^+$ from silver nanoproducts such as textiles (shirts, towels, socks), medical devices (mask, commercial dressing, medical cloth), personal and health care products (detergent, shampoo, toothpaste, toothbrushes) and paints [44,68–73]. The presence of AgNP was confirmed in most products and Ag release was quantified in the wash water samples [73–75].

In the environment, emitted NM can be deposited on land and remain in the soil or can be transported by wind or rainwater runoff to aquatic systems [76]. In turn, homo- and heteroaggregation lead to an accelerated air or sediment bed deposition [77]. Resuspension of NM is possible via wind, water currents, or biological processes (e.g., disturbance of sedimentary deposits by living organisms). In addition, particles could slowly migrate into groundwaters [78].

Wastewater treatment plants (WWTP), landfills and waste incineration plants (atmospheric emissions) are the main sources of NP emissions. Thus, NP are expected to be found in various environmental compartments (air, soil, water). Several authors have made attempts to calculate final concentrations of NM in environmental matrices (surface waters, wastewater treatment plant effluents, biosolids, sediments, soils, and air), even taking into consideration dynamic material flow analysis models (i.e., the flow of NM from their synthesis to final disposal) [64,79–81]. Despite the predicted environmental concentrations (PEC) that have been modelled for several NM, their field validation has not been confirmed yet [65,82]. The order of magnitude of the modeled PEC in surface waters was estimated in the range of mg L$^{-1}$ (for TiO$_2$NP) or ng L$^{-1}$ (for ZnONP, AgNP, fullerenes, CNT, and CeO$_2$NP) [64], while the concentrations in waste incineration residues are at the mg kg$^{-1}$ level [82]. Analytical methods are currently under development, and the quantification of NM in environmental samples in the field is still not possible. Likely, this is due to the low concentrations and the technical difficulties in distinguishing the naturally occurring NM from engineered NM.
5. Exposure pathway

Exposure to NM could take place through various routes. Due to their small size, nanosized materials can easily enter into the human body by inhalation, ingestion, through the skin, and by injection, crossing numerous biological barriers and distributing throughout the organism. Thus, the immune system reacts and initiates a clearing process of the body. If these biological responses are not controlled, NM are considered toxic [83]. Ultimately, those NP will be accumulated in tissues meanwhile there is some evidence suggesting their biomagnification through the trophic web [84,85]. In addition, other research includes NP routes through both reproductive and circulatory systems [86]. The cycle of life of different NM in the human body, their residence times, and fate to each organ could be dissimilar and highly dependent on the exposure pathway apart from the chemical and physical properties of the particles [78]. Overall, the main documented routes of exposure are those described below and represented in Figure 2.

5.1 Inhalation

Toxicity through airborne exposure to NP has been a major concern as it was considered one of the main routes of exposures for humans. Intrinsic properties of the particles such as their size and spreading pattern will ultimately determine the area of the respiratory tract in which the NP will settle. However, once settled, the NP are able to enter the blood circulation and reach different parts of the body including the brain [87]. Particularly, a complete review carried out by Garcés et al. [86] explained that AgNP caused lung toxicity by altering O₂ metabolisms and generating oxidative damage in mice, which was related to alveolar epithelial injury after an acute exposure. In addition, the presence of NM in the air has been associated with low quality indexes and related to a cause of a variety of cancers depending on the particle density. Urban air can contain up to 10,000-50,000 NP cm⁻³. For example, in the case of AgNP having a density > 6 g cm³, the proposed exposure threshold is 20,000 NP cm⁻³ [78]. Urban air could have up to 50,000 NP despite the real concern regarding work safety is increased in the case of the proximity of industries which process NM (like leather tanneries) as the level increases in multi-fold ways [88].

5.2 Penetration through skin

Despite that inhalation has been considered the primary route of exposure to NP for humans, there is an ongoing debate about the potentiality of NM passage through the skin and its significant health hazard in humans [89]. The increasing number of products containing NM or nanoproducts has reached an amount of 3,000 and they belong to various fields of applications with emphasis on personal care category (including baby products). Therefore, the current concern lies in the fact that those nanoproducts are being applied directly to the skin, being the most used the TiO₂NP, ZnONP, and AgNP [90,91]. In addition, the aforementioned particles are also applied in textile industries (for deodorizing and antibacterial purposes), antibacterial products, and even some NP has a direct use like nanosilver as biocide [92]. For example, a toxicological study about a nanocrystalline silver-impregnated coated dressing showed high amounts of silver ions release when
dispersed in saline solution (simulating the human body’s fluids) up to 150 µg ml⁻¹ [44]. NP are able to cross over the skin and reach the basal layers, and the smaller they are, the easier they cross given the size of skin pores (< 4 nm) [93]. Therefore, people who suffer from dermatitis or chronic eczema can have severe toxic effects as it has been proved regarding SiO₂NP [94]. A review carried out by De Matteis [90] explained that the particle shape also will determine the ultimate skin penetration as rods have more ability to penetrate in comparison with sphere and triangles. Lastly, the NP ultimate distribution will depend on the application as it was proved in mice that exposure to gold NP (AuNP) induced a flux in the blood vessel only after an intravenous administration, and it did not in the case of the topical one [95].

5.3 Ingestion

Food and beverages widely contain NM, therefore, gastrointestinal tract is a vital route of exposure [78]. As examples, TiO₂NP can act as a food coloring agent in sweets, which concentrations generally are between 1-5 µg mg⁻¹, and they are also present in chewing gums, confectionery, sauces and dressings, creamers, and dietary supplements. Average consumption was estimated as 0.2-0.7 mg kg⁻¹ weight per day in the United States and 1 mg kg body weight per day in the United Kingdom and Germany [96]. Particularly, concern about TiO₂NP ingestion raised in relation to the highest exposure scenario in the case of the children (1-2 mg kg⁻¹ body weight per day, < 10 years old) [97]. Unluckily, there is still a lack of studies addressing the safety of TiO₂NP consumption [78]. On another hand, AgNP use is also a matter of concern. Wijnhoven et al. [98] highlighted the addition of AgNP into the food production chain as their application occurs at all stages: during the processing of food (the particles are applied in food preparation equipment), for conservation purposes (the refrigerators storage containers are applied with AgNP), and at the ultimate food consumption (nanosilver is applied as a supplement). In all cases, the authors stated that the AgNP application has antibacterial purposes and avoids pathogens growth although the expected consumer exposure remains low and hard to estimate. Lastly, another study showed that commercially available plastic food containers were proved to release up to 3.1 ng of AgNP cm⁻² after 10 days, and that the particles were capable of migrating to food [72]. Regarding SiNP, Dekkers et al. [99] explained in those particles widely present in food products could led to a daily oral intake of the particles at 1.8 mg kg⁻¹ bw per day for an adult of 70 kg. Notably, the authors listed a diverse variety of food-based products where they detected SiNP such as mix for lasagna sauce, pancake mix, coffee creamer, instant soups, and steak and vegetable rubs.
6. Toxicological effects

The benefits that NM have brought to humanity are countless, so their widespread use is expected to keep growing through the years. However, consumer knowledge regarding their functionality, benefits, and potential dangers of nanotechnology to final users is still modest [63]. According to Rodríguez-Ibarra et al. [100], the PubMed database showed 25,000 papers published related to engineered NM applications while less than 3% included occupational safety. In this sense, an updated search in Scopus database showed that 4,700 articles included the keyword “engineered nanomaterials” (ENM), but only the 43% contemplated their applications, and just a 20-30% included their toxicity or risks. Unluckily, less than 8% took into account occupational-exposure implications (Figure 3).

![Figure 3. Articles available in Scopus database. Last update: May 2022. Modified from Rodríguez-Ibarra et al. [100]. Published by Elsevier. License number: 5315960975965.](image-url)
Technically, a product including nanosized materials or implicating the use of nanotechnology cannot be considered as strictly dangerous. The harmfulness and toxicity of a certain new NM should be determined by its applications, the production, and the final disposal. By considering the wide variety of possible application sectors, the list of NM that are spread in the environment and represent a risk for human health is very extensive. However, they have different impact on the market. Inorganic non-metallic NM, metal NP, and carbon-based NM are the groups of nanostructures with the largest market volume that require an immediate regulatory attention.

Some effort was made experimentally in order to assess and, in the best-case scenario, prevent deleterious effect to users and consumers of nanoproducts. In this sense, the research field of “nano-ecotoxicology” emerged and gained importance in the last decades [65]. Nevertheless, despite several discussions and reviews about such field of study, official descriptions of health implications and environmental risk to users exposed to NM are severely lacking [101].

For example, a global report called “EMERGNANO” attempted to identify and assess worldwide progress in relation to nanotechnology risks and highlighted the need for a better characterization of nanotechnology constructs and for the production of “reagentgrade” NM. This matter of “nanosafety” has become under the spotlight since some unfortunate events such as a fatal one regarding women who worked for a paint factory in China and NP found in their lungs were associated with disease [102]. Therefore, it results of vital importance the availability of detailed information about the NM (chemical composition, morphology, aspect ratio, particle size, zeta potential, solubility, known hazards) as well as the complete description of how the NM should be used and how they were produced [101].

The most common toxic effects produced by nanostructured materials include oxidative stress caused by reactive oxygen species (ROS) release, protein denaturation, and alteration of mitochondrial and phagocytic functions. Other mechanisms are also related to physiological parameters that can go from physiological implications to reproductive failure by modifying hormones or hatching enzymes [65]. Additionally, when NM are deposited and accumulated in specific organs during an extended period of time, they can generate organelle damage and organ dysfunction, and lead to chronic health diseases, like asthma and cancer. However, these toxicity effects depends on many factors, like the chemical composition, morphology, core material, size and aging of each nanostructure [91]. For example, it has been demonstrated that nanotoxicity increases as size decreases [103]. Smaller materials can penetrate cells more easily and, due to their high specific surface area, they are more reactive and can have more interactions with cellular components. This increases the risk of suffering a prolonged inflammation, which can lead to the disruption of cellular machinery and finally to cellular death.

Despite short-term exposures to human were already considered to have a low risk, long periods of time at low dose of NM are a current matter of concern regarding safe implications. In this sense, a review carried out by Cronin et al. [104] explained that the
immune system is particularly affected (with emphasis on the innate immune system). The authors highlighted that the exposure to nanosized particles could be related to deleterious effects in immune functions like penetrating into neutrophils, disrupting epithelial barriers, influencing the form of active uptake used by phagocytic cells, and even deleterious effects were analyzed on fetus in case of exposure.

Interestingly, Akçan et al. [87] detailed the main chemical composition of NP and the main reported toxic effects. For example, carbon-based NM were related to cytotoxicity on alveolar macrophages, meanwhile quantum dots core metalloid complexes were proved to cross the blood-brain barriers and placenta and also distribute to all body tissues (being the liver and kidney the target organs of toxicity). Other metallic NP (made of silver, molybdenum, iron, aluminum, etc.) reduced cell proliferation and even cause death. Lastly, other kinds of NP like the ones doped with cerium, showed low toxicity in relation to cell proliferation. The charge of the NP, apart from their main component, will also have influence on the ultimate effects to users. In this sense, positively charged poly amidoamine dendrimers showed higher deposition in comparison with the neutral ones.

Morphology and crystal structure also affect nanotoxicity levels. As an example, amorphous TiO$_2$ generates more ROS than the two crystalline polymorphs, anatase and rutile [105]. Furthermore, rutile TiO$_2$NP can cause DNA damage in the dark, while anatase TiO$_2$NP do not disturb genetic material in the same conditions. As well as this, rod-shaped iron oxide NM have shown much higher cytotoxic effect in a murine macrophage cell line compared to spherical NM [106]. In addition to this, concentration, aggregation, and time exposure are other factors that condition the degree of nanotoxicity [107–109]. It is considered that the amount of NM that penetrates into the cells keeps a directly proportional relationship with its concentration and period exposure. Nevertheless, at the same time, the higher the concentration, the greater the possibility that the nanomaterial aggregates and cannot cross the biological barriers.

Surface functionalization is also crucial to modulate the nanotoxicity since it determines uptake, the body’s immune response and biocompatibility of the nanosized material [110]. Biochemical modification of the outside part of nanostructures with specific targeting, such as small proteins, peptides, polymers, and oligosaccharides, also improve their stability and increase specificity and efficacy. For example, polyethyleneglycol (PEG), dextran, chitosan and lipids are commonly used to reduce cytotoxicity and enhance biocompatibility of NM, while hydrophilic polymers can reduce the response of the immune system [111].

The application of NM in consumer products and the use of nanotechnology are constantly growing, but the available information about their possible effects in living beings is not enough. Therefore, more studies of toxicity, health impact, biological interaction of NM, is urgently necessary, as well as regulations to control the potential risks of nanosized structures. Overall, given the variety of NM regarding their composition, and together with the different kinds of exposure (via airborne, skin penetration or digestion), it results a challenge to characterize the toxicity response in human/user in case exposure. The Table 1 summarizes some interesting findings based on previous evidence. Notably, there is
robust evidence suggesting the toxicity of carbon-based NM meanwhile there is a lack of research into other kinds such as AgNP despite their wide use and multiple applications.

Table 1. Cases of studies based on NM exposure to workers. Modified from Schulte et al. [112]. Published by Scandinavian Journal of Work, Environment & Health. License under Creative Commons Attribution 4.0.

<table>
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<th>Nanomaterial (NM)</th>
<th>Exposure</th>
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<td>Silica-based NM</td>
<td>Spray painting, manufacturing.</td>
<td>Shortness of breath, pleural and pericardial effusion, and pulmonary inflammation. Anomalies in cellular cytoplasmatic components. Decreased global DNA methylation. Lower blood and white blood cells.</td>
<td>[102,120,121]</td>
</tr>
</tbody>
</table>
Titanium dioxide-based NM

| Process and handle of NM and manufacturing. | Suspected effects on heart rate variability. Oxidative damage of nucleic acids and proteins. Augmented lipid peroxidation levels and altered antioxidant enzymatic activities. Altered biomarkers related to lung damage and cardiovascular disease. Decreased in blood and white blood cells number. | [120,122–124] |

Silver-based NM

| Manufacturing. | Detectable concentrations of silver in blood but not in urine. Altered activities of antioxidant enzymes (with great alterations after 6 months of exposure). Increased cardiovascular makers. | [125–127] |

Conclusions

Nanotechnology has become a vital tool for human being daily life and a key field of study for many subjects, from pharmaceutics to automotive industry. In this sense, the development of novel materials or NM inevitably has increased in an exponentially manner, leading to concern about the unregulated production and consumption of nano-based products, together with their release into environment as exposure to humans also may occur. From that concern, other fields of research such as “nanotoxicology” have emerged, despite the fact that the latter is still under development and available and robust information remains scarce. Since “nanosafety” is a matter of key importance, more studies aiming to guarantee both the correct manipulation by users and discharge of NM are mandatory. Only after an appropriate balance between the design and application of further NM and their side effects and risks (with emphasis on occupational exposure), nanotechnology will probably be one of the most promising fields of study worldwide in the long run.

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Emerging Nanomaterials and Their Impact on Society in the 21st Century


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