Section A-Research paper

Engineered nanoparticle risks and dangers to the environment and human health

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Abstract: This article's goals are to: (1) investigate the current state of knowledge regarding the risks of engineered nanoparticles for the environment and human health; (2) determine whether this knowledge is sufficient to enable a thorough and efficient risk assessment of these materials; and (3) offer recommendations for future research in this area. To achieve the goals, the applicability of each of the four steps of the risk assessment methodology—hazard identification, dose-response assessment, exposure assessment, and risk characterization—was assessed in the context of the current state of knowledge regarding the risks of nanomaterials. Limitations were then noted, and suggestions were made for how to get around them.

Keywords: risk characterization, dose-response analysis, exposure analysis, engineered nanoparticles, hazard identification, environmental sustainability, and human health.

1. Introduction

The scale of their applicability is enormous compared to the nanoparticles' modest size. Almost every industry and government area is impacted by nanotechnology, including those in healthcare, agriculture, transportation, energy, materials, and information and communication technologies.

In recent years, there has been much discussion about the possible advantages and hazards of using engineered nanoparticles (ENPs). Contrary to the widely held hopeful predictions that nanotechnology will significantly advance technology and improve society, it is thought that exposure to some ENPs may have negative effects on the environment and/or human health. The chemical risk assessment (CRA) has been promoted as the most pertinent method to comprehend, analyze, and quantify the dangers associated with ENPs since the early debates regarding those risks. A number of approaches are currently being vigorously debated and

reviewed on a global scale with the hope that, in the not too distant future, it will be able to conduct comprehensive and accurate risk assessments of ENPs.

The objectives of this article are to:
1. Examine the present state of knowledge regarding the hazards that ENPs pose to the environment and public health.

2. Determine whether this knowledge is adequate to enable thorough and efficient risk assessment of ENPs.

3. Make suggestions for upcoming studies in the area of ENP risk assessment.

2. Nanotechnology and Its Applications

The study of how matter is organized and controlled at the nanoscale—that is, between 1 and 100 nm—as well as the production of goods and devices with dimensions that fall within this range—is known as nanotechnology. It is an area of applied science and technology. One billionth of a metre is known as a nanometer (nm), which comes from the Greek word "nanos" for "dwarf."

All materials that are nanoscale in at least one dimension are referred to as nanomaterials [1], whereas materials that are nanoscale in at least two dimensions are referred to as nanoparticles [2]. The term "nanoparticles" refers to both fibres and tubes as well as particles, however it does not include multilayers, coatings, or films as materials.

There are two different kinds of nanoparticles (NPs): (1) naturally occurring NPs, which are created naturally by volcanoes, forest fires, or combustion byproducts, and (2) engineered nanoparticles (ENPs), which are created specifically to be used in applications. Examples of ENPs include carbon black, fumed silica, titanium dioxide (TiO2), iron oxide (FOx), quantum dots (QDs), fullerenes, and carbon nanotubes (CNT)

NPs that naturally exist are NOT covered by this article. Only ENPs are covered in the paper. Due to the dominance of quantum effects and the huge surface-area-to-volume ratio (sa/vol) in this size range, materials made of ENPs differ from their bulk counterparts in terms of their optical, electrical, magnetic, chemical, and mechanical properties [1]. Most materials' sa/vol steadily rises as their particle sizes decrease, changing the characteristics and behaviour of the surrounding atoms due to increasing adsorption. When particles are tiny enough, they begin to abide by the principles of quantum mechanics. Materials that have been scaled down to the nanoscale can suddenly display radically different properties from those that they do at the macroscale, opening up new uses.

2.1. Areas of Application

Today, a wide range of applications for nanotechnology are accessible on the market. For instance, stain-resistant clothing, more durable tennis balls, lighter tennis rackets, cosmetics and sunscreen, water filters, glare filters, ink, and dressings for burns and wounds [4].

Table 1 lists the fields of application for nanotechnology.

Areas	**Applications**
Automotive	Lightweight construction; Catalysts; Painting; Tires; Sensors; Windshield and body coatings
Construction	Materials; Insulation; Flame retardants; Surface coatings; Mortar
Electronics	Displays; Data memory; Laser diodes; Fiber optics; Optical switches; Filters; Conductive coatings; Antistatic coatings; Transistors
Engineering	Protective coatings for tools, machines; Lubricant-free bearings
Food and Drink	Packaging; Storage life sensors; Additives; Juice clarifiers
Medicine	Drug delivery systems; Contrast medium; Rapid testing systems; Prostheses and implants; Antimicrobial agents; In-body diagnostic systems
Textiles	Surface coatings; –Smart clothes (anti-wrinkle, stain resistant, temperature controlled)
Chemical	Fillers for paints; Composite materials; Impregnation of papers; Adhesives; Magnetic fluids
Cosmetics	Sunscreen; Lipsticks; Skin creams; Toothpaste
Energy	Lighting; Fuel cells; Solar cells; Batteries; Capacitors
Environmental	Environmental monitoring; Soil and groundwater remediation; Toxic exposure sensors; Fuel changing catalysts; Green chemistry
Household	Ceramic coatings for irons; Odor removers; Cleaners for glass, ceramics, metals
Sports	Ski wax; Tennis rackets; Golf clubs; Tennis balls; Antifouling coatings for boats; Antifogging coatings for glasses, goggles
Military	Neutralization materials for chemical weapons, bullet-proof protection

3. Defining “Hazard” and “Risk”

The word "hazard" has numerous meanings. The United States Environmental Protection Agency (EPA) defines "hazard" as the "inherent toxicity of a compound" [5]. This definition is used in this essay. This definition states that a chemical compound is dangerous if it has the property of being toxic. Any exposure to a potentially harmful material might

result in negative health impacts in people or even death.

Regarding the definition of "hazard" provided above, the EPA defines "risk" as "a measure of the probability that damage to life, health, property, and/or the environment will result from a given hazard" [5]. This definition states that a risk is high if there is a high likelihood of exposure to a hazardous material and a high likelihood that there will be severe negative health or environmental effects. To calculate risk, it's critical to take into account both the frequency of the incident and the severity of the hazard [2].

In literature, "known risks" and "potential risks" are typically distinguished as two different forms of risk. We speak of "known" hazards once the causal relationship between a cause and an effect has been established. Generally, someone is accountable for these risks. Preventive action is available after the causal connection has been established. We speak of "potential" dangers when it is unclear how a cause will affect damage. When there are possible dangers, it is unclear whether there is a threat, how serious the harm could be, or what the likelihood of it happening is [2, after 6]. It is acknowledged that a precautionary strategy can be used in this situation because it is marked by a state of suspicion (rather than awareness) [2, 3].

The potential threats posed by ENPs to the environment and human health are insufficient. The evaluation of hazardous agent risks is crucial. How cautious one should be and what preventative or precautionary actions should be taken will depend on how likely it is that a dangerous material would cause harm (the risk).

4. Risk Assessment of ENPs

Since the beginning of the discussion regarding the potential risks posed by ENPs, the risk assessment of chemicals (CRA) method has been advocated as the most pertinent method to comprehend and quantify the associated concerns [7]. CRA is a procedure that applies scientific and regulatory principles in a methodical way to describe the risks associated with exposure to chemical compounds by humans and/or the environment. It is described as "a process, intended to calculate or estimate the risk to a given target organism, system, or (sub)population, including the identification of attendant uncertainties, following exposure to a specific agent," taking into account both the inherent properties of the agent of concern and the properties of the particular target system [8]. The CRA is a four-step process with the following steps: hazard identification, dose-response assessment, exposure assessment, and risk characterization. Its primary output is a statement of the likelihood that people or other environmental receptors (such as plants or animals) exposed to a chemical agent will be harmed and to what extent.

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In order to accomplish the goals of this study, the most significant scientific findings were highlighted, and limitations were identified and discussed. The current state of knowledge regarding the risks of ENPs for the environment and human health was summarized and evaluated in relation to each of the four elements of the CRA framework.

4.1. Hazard Identification

Hazard identification (HI) is the process of identifying the negative consequences that a chemical has the potential to produce [10, after 11]. Up until recently, a lot of the debate over the potential dangers of ENPs to the environment and human health was seen as more speculative than practical. But during the past few years, a number of experimental studies have discovered that exposure to specific ENPs can have harmful impacts on living things' health. 428 studies reporting on the toxicity of ENPs were found in 2007, according to Hansen et al. [12]. 965 investigated ENPs with different chemical compositions were found to have negative health consequences in these investigations [12].

The most significant scientific discoveries that are pertinent to the HI of ENPs are briefly described in the sections that follow. They serve as a summary of the current body of knowledge regarding the risks posed by ENPs, which is based on experimental investigations.

CNTs, or carbon nanotubes

Single-walled carbon nanotubes (SWCNTs) have been shown in a study by Lam et al. [13] to have a dose-dependent effect on interstitial inflammation and lesions in mice and rats (0-0.5 mg•kg-1 for 7 to 90 days). Rats exposed to SWCNT soot (1 and 5 mg•kg-1 for 24 hours to 3 months) developed pulmonary grandulomas, according to Warheit et al. [14]. However, unlike Lam et al. [13], Warheit et al. [14] found that the effects were not dose-dependent. When Smith et al. [15] evaluated the ecotoxicity of SWCNTs on young rainbow trout (0.1, 0.25, and 0.5 mg•L-1 for 24 hours to 10 days), they found that the rate of ventilation increased in a dose-dependent manner. Additionally, they noticed a large dose-dependent decline in thiobarbituric acid reactive substances (TBARS), a hallmark of oxidative stress, particularly in the liver, brain, and gills.

It was established by Carrero-Sanchez et al. [16] that MWCNTs showed acute toxicity in rats with LD90 of 5 mg•kg-1. Poland et al. [17] shown that whereas shorter MWCNTs generated less inflammation, longer MWCNTs significantly increased inflammation and tissue damage in mice, suggesting that particle morphology affects CNT toxicity. They also came to the conclusion that mice do not exhibit significant inflammatory responses to water-soluble MWCNT components.

In the literature, a variety of cytotoxicity tests using SWCNTs were reported. After being exposed to unprocessed (iron-containing) SWCNTs at concentrations ranging from 0.6 to

0.24 mg•mL-1 for 2 to 18 hours, human epidermal keratinocytes showed signs of oxidative stress and cellular damage, according to Shvedova et al. [35]. After being exposed to SWCNTs at concentrations between 0.8 and 200 g•mL-1, Cui et al. [36] noticed a dose- and time-dependent suppression of cell proliferation and a decrease in cell adhesive ability in human embryo kidney cells. According to Sayes et al. [37], SWCNTs' surface functionalization significantly influences how hazardous they are to human dermal fibroblasts. While Monteriro-Riviere et al. [39] noted a decrease in the viability of human osteoblastic lines and human epidermal keratinocytes after exposures to 0.1, 0.2, and 0.4 mg•mL-1 of MWCNTs for 1 to 48 hours, Bottini et al. [38] noted that MWCNTs were more cytotoxic when oxized towards Jurkat T leukaemia cells. The highest toxicity was seen when the nanotubes were uncapped, debundled, short, and dispersed in solution, according to Kang et al.'s [40] comparison of the cytotoxicity of commercially generated MWCNTs in bacterial systems before and after physicochemical modification. When reporting the toxicity of CNTs, Kang et al. [40] came to the conclusion that comprehensive documenting of their physical and chemical properties is necessary.

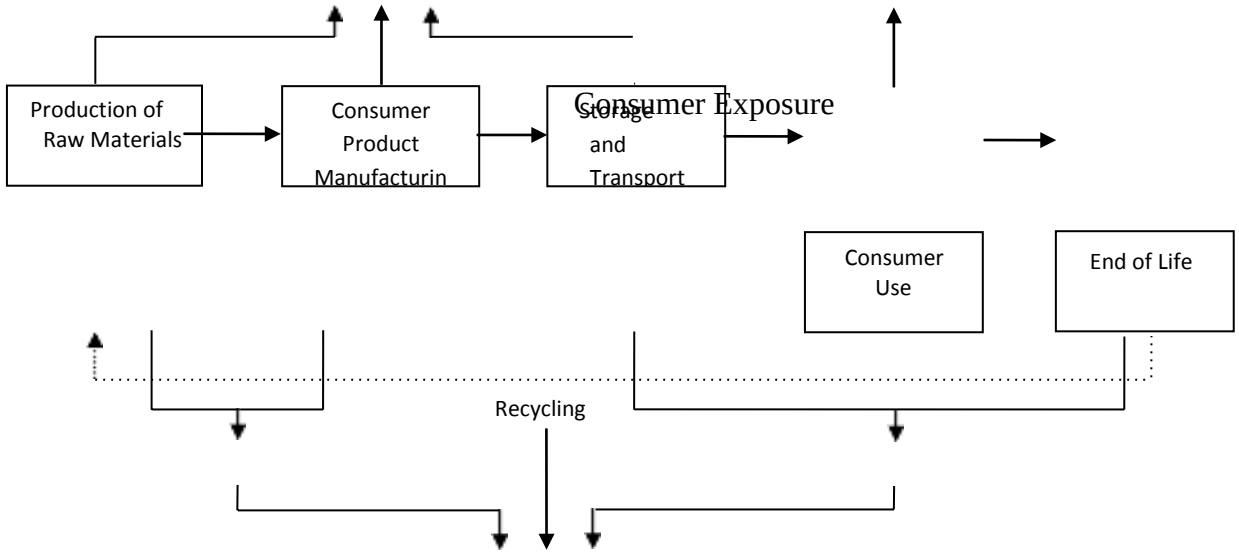
4.1.1. Characterization of ENPs

Table 2 lists studies on the metrology, characterization, and standardization of ENPs from 2004 through 2022 along with the total grant amount allocated to each study.

Specific Research Field		**State of Progress**			**Total**
		Unknown	In Progress	Completed	
Identification of metrics and associated methods for the measurement of ENPs and their properties	Number of studies	4	12	12	28
	Funding value (mill. €)	-	16.23	6.80	23.02
Development of standardized, well- characterized reference ENPs	Number of studies	1	1	6	8
	Funding value (mill. €)	-	0.28	0.20	0.47
Understanding the properties of ENPs in the context of their ignition and explosion potential	Number of studies	-	1	2	3
	Funding value (mill. €)	-	5.57	0.32	5.89

According to its definition, exposure assessment (EA) is "an estimation of the concentrations/doses to which human populations (i.e., workers, consumers, and man indirectly exposed via the environment) or environmental compartments (aquatic environment, terrestrial environment, and air) are or may be exposed."

Figure 1 shows potential routes for human, environmental, and occupational exposure to ENPs.



5. Conclusions and Recommendations

The major findings from this investigation are presented in this chapter. Additionally, recommendations and proposals for additional research are made, and research target points are highlighted.

Examine what is now known about the dangers of ENPs to the environment and human health.

ENPs may result in brand-new environmental issues, present concerns to human health, or both. However, it is impossible to reach a consensus at this juncture and level of information regarding the potential dangers of nanomaterial exposure. ENPs are projected to have different effects on living things than their bulk substitutes, and given their substantial

diversity, it is anticipated that ENPs will also vary greatly from one another in terms of toxicity.

The majority of the evaluated toxicity tests using ENPs show some risky effects on the examined species. CNTs may have a propensity to trigger interstitial inflammation and lesions in animals, according to several in vivo toxicological investigations [13,14]. Shorter MWCNTs were shown to induce less severe inflammation than longer MWCNTs, and dissolved MWCNTs nearly had no negative effects, suggesting that particle form rather than chemical content is what determines MWCNT toxicity [17].

According to Kang et al. [40], who examined the cytotoxicity of commercially available MWCNTs in bacterial cultures before and after physicochemical modification, the most dangerous MWCNTs are those that are uncapped, debundled, short, and distributed in solution. The majority of in vivo experiments with C60 fullerenes point to the fact that these substances frequently cause oxidative stress in living things [18–21]. It was discovered that the toxicity of QDs was affected by their composition, size, surface charge, coating, exposure to light, and temperature [46-49]. According to studies [51], smaller QDs are more hazardous than larger QDs, and exposure to UV radiation and higher temperatures also tend to make QDs more toxic. Zn ENP exposure results in pulmonary (lung) inflammatory disease. Human monocyte macrophages and human lymphoblastic cells are both less viable after exposure to FeO and TO2 ENPs, respectively [52,54]. Additionally, it has been demonstrated that nano-Ag works well as a bactericide [55,56]. The physical and/or chemical properties of ENPs that cause this toxicity are yet unknown, despite the fact that the majority of (eco)toxicity studies with ENPs found some level of toxicity. The main cause of the confusion in this regard is that the majority of ENPs utilised in toxicity testing are rarely adequately characterized.

The environmental fate of ENPs has only been the subject of a very small number of research, therefore their behaviour in the environment is still mostly unknown. The majority of the research on the environmental destiny of ENPs makes comparisons with data found for larger particles and uses vague general principles. Understanding the paths via which ENPs are exposed to the environment and to humans requires extensive investigation of their environmental destiny. The most common ways that workers are exposed to ENPs at work are by inhalation and/or skin contact [7, 88]. Exposures are typically more likely to happen when handling and bagging of the materials after manufacturing is finished, as well as when performing cleaning tasks [85,88].

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