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Nanotechnology From Engineers to Toxicologists:
Risks and Remedial Measures

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ABSTRACT

There is growing public perception that nanotechnology products are flourishing without sufficient care for the risks they pose to life, global, and local environments. The transparency of safety issues and impact on environment should be the prime focus while engaging a particular field with nanotechnology. Testing of nano products needs to be enforced before they are released to the market. Whether nanotechnology is good or bad for the environment is totally based on the nature of its use and considerations made during its application. The use of nanotechnology in any field requires great care, and any sort of negligence is likely to bring negative effects for the environment and its habitats. Recent studies show that the lack of knowledge as regard risks is found even at the expert level. The present work highlights the risks associated with the use of nanoparticles and the necessary preventive measures for using the technology in a safe and sound way.

KEYWORDS

Analytical Techniques, Engineering Control, Environment, Public Awareness, Recycling, Rules and Legislation, Social Risks, Waste Monitoring, Worker Protection

INTRODUCTION

Nanotechnologies is invariably perceived as the great white hope of the 21st century economy (Castillo, 2013). It has brought revolution in many fields like science, engineering, and medical. In engineering, various nanomaterials, devices and systems have been developed: They include carbon nanomaterials, nano-structured materials, polymers, nanocomposites and organic electronics (Varadan, Pillai, Mukherji, Dwivedi, & Chen, 2010). Nanotechnology is reported to enhance the life of materials exposed to aggressive environments, provide anti-reflection coatings on photovoltaic cells, and reduce friction & wear in automobiles (Korada & Hamid, 2017). In food sciences, nanotechnology is being used for food processing, packaging, development, safety, detection of food-borne pathogens and shelf-life extension (Singh et al., 2017). In addition, it has also found its application in increasing food nutrition and physical and organoleptic properties (He & Hwang, 2016). Nanotechnology has helped the medical scientists in synthesizing regenerative medicines and new drugs with enhanced targeted delivery (Shrivastava & Dash, 2009). It has also been used as developing sensors for early-state detection of cancer in human body (Perfézou, Turner, & Merkoçi, 2012; Y. Zhang, Li, Gao,

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Chen, & Liu, 2019). Nanobiotechnology leads to the development of pharmaceuticals and mechanical devices at nano-scale for the evaluation of biological systems and treatment of pathology (Saadeh & Vyas, 2014): It is estimated that by 2030, nanobots will be streaming through human veins and arteries for medical treatment (Trevor English, 2017).

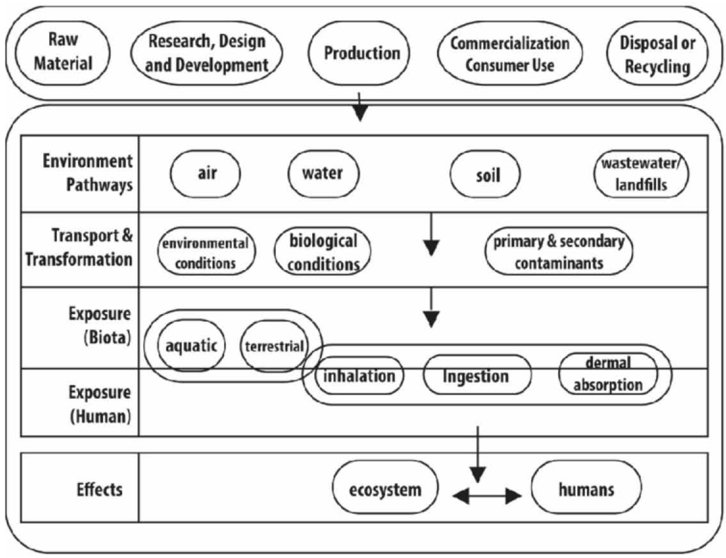
In civil engineering, smart cementitious composites with enhanced performance and strength have been developed (Anwar Khitab, M. Alam, Riaz, & Rauf, 2014). Surface paints with enhanced life and resistant to aggressive environment have been developed and applied in actual field conditions (A. Khitab & Arshad, 2014). Pavements with anti-pollutant characteristics are developed and constructed in Japan, considerably reducing the city pollution caused by the car-exhausts (A. Khitab, 2012). Nanotechnology has helped creating concrete that has self-cleaning properties, known as photo-catalytic concrete and it has been used in the construction of many important buildings like new jubilee church in Rome and police headquarters Bordeaux France (Han, Zhang, & Ou, 2017). Concrete with high damage tolerance and damage sensing has been developed using nano Carbon Black (M. Li, Lin, Lynch, & Li, 2012). Concrete pavements that melt snow and avoid use of heavy machinery for snow-removal have also been developed, using nanomaterials (Chen, Wu, Xia, Jing, & Zhang, 2018). The use of nanotechnology in public health is equally well-recognized: The nanoparticles have the potential for the treatment of water and waste water to a great degree. CNTs, nano sized magnetite, CeO_2 and TiO_2 have been considered as prime nanoparticles to remove pollutants from water (Deliyanni, Bakoyannakis, Zouboulis, & Matis, 2003; Mayo et al., 2007; Nawrocki & Kasprzyk-Hordern, 2010).

As a matter of fact, nanomaterials have given too much to humankind and its blessings are countless. But they become threat for the environment and its habitats when discharged in undesirable quantities and in wrong destinations (Anwar & Khitab, 2017). For example, while treating water, negligence may leave undesirable quantity of nanoparticles in water; thus instead of doing benefit, it may cause harmful impact on the environment and health of consumers. Therefore, the exact quantification of nanoparticles to be released in a medium is the first responsibility, the world should care of.

Nanomaterials may be released from point or non-point sources. Point sources include industries, storage units etc. and non-point sources include storm water runoff or wet deposition from the atmosphere. Exposure to nanomaterials may occur unintentionally in the environment or through the use of nanotechnology based products in our daily lives. Human exposure to these nanoparticles is more likely to happen during the manufacturing process. However, inhalation of nanomaterials released to the atmosphere and use of drinking water or food having accumulated nanoparticles is also possible. Moreover, absorption by soil and then transportation in saturated and unsaturated regions in the subsurface is also possible. This is very likely to affect the ground water table, which then needs proper treatment before it is used for drinking and irrigation purposes (Wiesner, Lowry, Alvarez, Dionysiou, & Biswas, 2006). Furthermore, from soil, nanoparticles may easily become the element of the vegetation; thus becoming a serious health threat to all consumers as well as the habitat, whose existence is equally important for the conservation of ecosystem. This concern seems to be justified as both natural and man-made filters might be too big to catch the nanoparticles.

As size of nanoparticles is very small, they can easily stay in atmosphere and can cause air borne diseases and several harmful environmental effects (Maynard, Warheit, & Philbert, 2011; G. Oberdörster, E. Oberdörster, & J. Oberdörster, 2005). Size of nanoparticles can be as small as biological molecules such as proteins. They can easily be absorbed and may reach the inner bio molecules in the body (European Commission Joint Research Center (ECJRC), 2003). Availability of limited knowledge about this technology and its impacts on the habitats is a major reason to consider risks seriously. It is an emerging field at the moment and not all nanomaterials have been studied in detail regarding their harmful effects. So, there is need to adopt wide precautions and consider all available research findings very critically during the whole life cycle of the nano-based products (Dhingra, Naidu, Upreti, & Sawhney, 2010; Semenzin et al., 2019; Wardak, Gorman, Swami, & Deshpande, 2008). Basically, for any material its exposure and effects throughout the life cycle are important to be considered: This has been schematically shown in Figure 1, which shows and integrates the life cycle stages of nanoparticles with their pathways, transportation, exposure and effects in a simplified way.

Figure 1. Nanotechnology life-cycle stages integrated with pathways, transformation and exposure



Based on the previous and most recent studies, this work is a mere attempt to describe the possible risks from the use of nanotechnology and nanomaterials and suggest remedies and preventive measures, so that this technology can be used with least impact on the environment, we live in.

LITERATURE REVIEW

Risk

Risk is defined as a probability or threat of damage, injury, liability, loss or any other negative occurrence that is caused by external or internal vulnerabilities and that may be avoided through preemptive action (Bussinessdirectory, n.d.). Risks can be broadly distributed into two main categories: Known risks and potential risks. When the relation between the cause and its impact is established, the risks are 'known risks'. In case of known risks, the significance of danger is well known and prevention is easy to make. When a relation between the cause and the impact is not established, the risks are categorized as 'potential risks'. In potential risks, the significance and the certainty of dangers is not known.

Risks from nanotechnology fall in both categories. Though the potential risks are suspicious however, as a matter of public health and environmental safety, precautionary measurements are mandatory to be taken for both types of risks.

Risk Assessment

Cumulative Risk Assessment (CRA) is a process in which, scientific and regulatory principles are applied in a systematic way to identify and quantify the risks. It is considered as the most relevant system and is based on four major steps 1) Hazard identification 2) Dose response assessment 3) Exposure assessment and lastly 4) Risk characterization (Hansen, 2009; International Programme on

Chemical Safety & Organisation for Economic Co-operation and Development, 2015). Its main result is a statement of the probability, which depicts whether humans or other environmental receptors will be harmed or not when exposed to a pollutant and what would be the intensity of this harm? The CRA methodology is internationally recognized and employed by many well reputed organizations, such as World Health Organization (WHO), Organization for Economic Co-operation and Development (OECD), as well as by several European and U.S. agencies (Nielsen, Østergaard, & Larsen, 2008). It is considered as a very valuable tool for the regulation of chemicals including nanoparticles. CRA is also a fundamental ingredient of the new European Union (EU) chemical regulation policy, known as Registration, Evaluation and Authorization of Chemicals (REACH) ('Understanding REACH', n.d.).

Hazard Identification

Hazard identification (HI) is defined as the recognition of the undesirable effects, which a matter has an intrinsic capacity to cause (Hoshino, Hanaki, Suzuki, & Yamamoto, 2004; Lovrić et al., 2005). In 2007, 428 studies reporting on toxicity of Engineered Nanoparticles (ENPs) were identified (Green & Howman, 2005). In these studies, adverse health effects of 965 tested ENPs of different chemical compositions were observed. It is very important to note that the vast majority of the reviewed studies demonstrate some degree of hazardous effects on the tested organisms. Toxicity has been reported for many ENPs, but for most of them, further investigation and confirmation are needed before hazard can be identified. For proper hazard identification, data characterization and standardized tests are mandatory.

Dose-Response Assessment

Dose-response assessment (DRA) is defined as an approximation of the relationship between dose, or level of exposure to a substance and the occurrence as well as severity of an effect, which occurs (Hoshino et al., 2004; Lovrić et al., 2005). The dose is generally measured in mass units (i.e., µg, mg, g), however it has been concluded that toxicity of some ENPs is not mass dependent and is influenced by several physico-chemical properties including surface area, morphology and chemical composition (Valavanidis, Vlachogianni, Fiotakis, Loridas, & Perdicaris, 2013). Some studies conducted in past used the concept of mass units, while others considered the surface area or other characteristics for the assessment purposes (Rushton et al., 2010).

Exposure Assessment

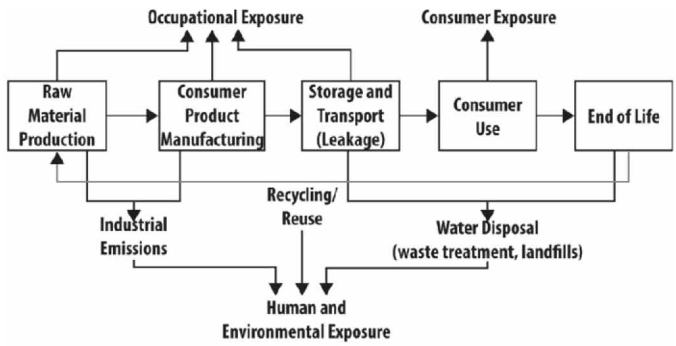
Exposure assessment (EA) is defined as the estimation of the concentrations/doses to which the specific human populations (i.e., workers, consumers and people exposed indirectly via the environment) or environmental compartments (aquatic environment, terrestrial environment and air) may be exposed (Hoshino et al., 2004; Lovrić et al., 2005). Figure 2 links each stage of a nanoparticle life with the specific exposure it may cause to the human beings and the environment.

In another study, ENP-containing products were divided into several categories (including appliances, food and beverages, health and fitness, home and garden and goods for children). The researchers found out that the expected consumer exposure is more for products, which fall in the categories of appliances, home & garden and health & fitness (Jaiswal, Mattoussi, Mauro, & Simon, 2003).

Risk Characterization

The last step of Risk assessment procedure is the Risk Characterization, which is defined as the estimation of the occurrence and severity of the harmful effects expected to occur in human population or the environment based on the 'actual exposure' to the substance. The phase may also include risk estimation. In this last phase, all the information which is collected during the first three steps of risk assessment is combined, weighted and the then the risk is quantified. The quantitative risk characterization compares the predicted environmental concentration (PEC) of a chemical agent

Figure 2. Life-cycle stages of a nanoparticle integrated with specific vulnerable exposure



with its predicted no-effect concentration (PNEC). The PNEC is the concentration, below which the exposure to the substance is not probable to cause any adverse effects, while the PEC is the prognosticated concentration of a chemical in the environment. The ratio of PEC to PNEC is called risk quotient (RQ). If the RQ is lower than 1, no further testing or risk reduction measures are needed (European Commission Joint Research Center (ECJRC), 2003). If it is greater than 1, further testing or remedial measures are mandatory to reduce the RQ (European Commission Joint Research Center (ECJRC), 2003; Nielsen et al., 2008).

Risk assessment of nanoparticles is so important that scientists have developed a separate field by the name of 'Nano (eco)-toxicology'. It is a new field of research, which deals with the engineering of nano-devices and nanostructures to completely understand their impacts on living organisms (G. Oberdörster et al., 2005). The reason behind the development of this separate scientific discipline is the request of a number of scientists with the purpose of generating data and knowledge about nanotechnology effects on the environment and its habitats (G. Oberdörster et al., 2005; The Engineer, 2015).This field is still in the development phase, however it can have sufficient contribution towards the identification and assessment of risks (Kahru & Dubourguier, 2010; Pachapur, Brar, Verma, & Surampalli, 2015; Polonini & Brayner, 2015).

NANOTECHNOLOGY RISKS TO THE HUMAN HEALTH

Nanotechnology if used properly can have positive effects on the health of humans. Tiny nanotechnology based sensors are helpful to detect cancer in its early stages (Perfézou et al., 2012; Rachel's Environment and Health News, 2003; Y. Zhang et al., 2019). European commission has also talked about nano-sized robots (nanobots), which may have the potential to cure several diseases (RAY, YU, & FU, 2009). Gold nanoparticles have been found to help in early diagnosis of heart attacks (R. Wang et al., 2015). Nano-technological transport capsules make it possible to release medications specifically to the target organs only (Patra et al., 2018; Siegrist, Keller, Kastenholz, Frey, & Wiek, 2007). Just like any other product, ENP based products if taken in toxic quantities or applied to those, who do not need it would definitely lead to the occurrence of disastrous effects. Throughout the recent past, considerable number of people are exposed to the nanoparticles (Kaluza et al., 2009). In 2004, a British report (Aitken, Creely, & Tran, 2004) following estimates for the United Kingdom were established:

1. Five hundred workers are directly exposed during nanoparticle production, and 102,000 are possibly exposed during their handling in the industries that use them;
2. Within 15 years, approximately 660, 000 workers will be exposed to nanoparticles either by industrial production and/or use.

Not all nanoparticles are equally dangerous to the human health if taken in undesirable quantities either by direct or indirect contact. Some can have acute effect on human health while others can be fatal to the human beings and other living organisms. Moreover, upper intake limits also vary from one nanoparticle to the other. Nanoparticles can affect different parts of the human body from skin to the brain. Moreover, their presence on many consumables is very difficult to find and using any product having excessive quantities of nanoparticles can affect several organs within the human body. A potential route of inhaled nanoparticles within the body is the olfactory nerve; nanoparticles may cross the mucous membrane inside the nose and then reach the brain through the olfactory nerve (Selvaraj, Gowthamarajan, & Karri, 2017).

Studies have shown that inhaling nanoparticles can even affect the central nervous system (Maynard et al., 2011; G. Oberdörster et al., 2005). Moreover, their extremely small size is very tangible to affect the skin and eyes of people exposed to them (G. Li, 2004). It has also been found that increased breathing rate due to exercise further promotes the deposition of these particles in lungs (Peter A. Jaques, 2000). Deposition of nanoparticles may occur in the cardiovascular system, liver, brain, testis, spleen, stomach, and kidneys. This in turn may lead to apoptosis of cells, inflammation and changes in the immune responses (Fubini, Ghiazza, & Fenoglio, 2010; Maynard et al., 2011; G. Oberdörster et al., 2005).

However, the potential hazard is always dependent on the type and concentration of the particles, an individual is exposed. Some important nanoparticles along with their potential hazards are briefly discussed below.

Titania (TiO_2)

TiO_2 nanoparticles are widely used for a variety of applications: It is one of the top five commonly synthesized nanomaterial (Shakeel et al., 2016). Many procedures have been reported for producing TiO_2 nanoparticles; most commonly used procedures involve the synthesis by hydrolysis and calcinations (A. Khitab et al., 2018; Pottier, Chanéac, Tronc, Mazerolles, & Jolivet, 2001). However, these procedures might induce toxic amounts of TiO_2 in the workers dealing with them. It has been found that, nano-sized particles of TiO_2 can easily get through the human body via inhalation, ingestion (food and drinks), medical injections, outermost layer of the epidermis and some hair follicles (Lademann et al., 1999; Shah, Shah, Hussain, & Khan, 2017). It has been reported that TiO_2 nanoparticles cause oxidative stress, histopathological changes, carcinogenesis, genotoxicity and immune disruption (Shakeel et al., 2016). Moreover, The International Agency for Research on Cancer (IARC) has classified Titanium dioxide dust as an IARC Group 2B carcinogen, meaning it is possibly carcinogenic to humans. In addition to cancer, titanium dioxide toxicity is also associated with the DNA damage (Fubini et al., 2010). The risks associated with exposure to TiO_2 nanoparticles necessitate that these particles need to be stringently managed to moderate risks for human and animal health in many circumstances.

Carbon Nanotubes (CNTs)

CNTs are widely used in civil engineering applications specifically for ground improvement, water cleaning and air purification: Its use to produce high performance cementitious composites and paints is also growing (A. Khitab & Arshad, 2014). Nevertheless, its exposure to construction workers carries some risks. To assess the risks of CNTs, several studies on animals in laboratories have been carried out. Moreover, advanced intensive research is also in process. Based on the data available, some of the conclusions regarding adverse effects of CNTs toxicity have been made; a few of them are discussed here. One study showed that carbon nanotubes may lead to mesothelioma, a lung cancer previously associated with asbestos fibers (A. Khitab et al., 2013; ScienceDaily, 2011). With nanotubes being used in new technologies like solar panels, construction materials, batteries, medical devices and plastics, the probability that they will enter into our environment is becoming more certain. According to Lam (Lam, 2003), it has been found that, single walled carbon nanotubes can cause interstitial inflammation and lesions in rats and topical application of raw single walled carbon nanotubes to nude mice has been shown to cause dermal irritation (Murray et al., 2009). Multi walled CNTs have also shown some toxicity in rats and have led to significant inflammation as well as damage to the tissues (Carrero-Sánchez et al., 2006; Poland et al., 2008). Most studies on the toxicological effects of C60 fullerenes suggest that these materials tend to induce oxidative stress in living organisms (Lai, Chen, & Chiang, 2000; E. Oberdörster, 2004; Zhu, Oberdörster, & Haasch, 2006), which is a condition associated with the oxidative damage in a cell, tissue, or any organ, caused by the reactive oxygen species. According to a report published in ScienceDaily, the CNTs, having a diameter of 10-100 nm and a length of 1-10 mm, can make way far into the lungs and alveoli, posing a serious health risk (ScienceDaily, 2011). Though use of CNTs is revolutionary in various disciples, the risks found in lab studies have made it clear to adopt necessary precautions during their application.

Engineered Zinc Nanoparticles (Zn ENPs)

ZnO ENPs are widely used in pigments, photo catalysts, semiconductors, plastics, ceramics, lubricants, paints and coatings (Chaúque, Zvimba, Ngila, & Musee, 2014). The harmful effects of zinc ENPs specifically on humans have also been studied. After experiencing a specific dose for a certain time period, the individuals started feeling sore throat, chest tightness, headache, chills and fever (Gordon et al., 1992). Moreover, one study on mice indicated that environmental exposure to Zn ENPs causes lung inflammatory response (Sayes, Marchione, Reed, & Warheit, 2007). Wang et al. (B. Wang et al., 2008) also found that Zn ENPs can cause severe symptoms of lethargy, vomiting, anorexia, and diarrhea, reduction in weight and even death in mice. All these tests on animals have unveiled the potential risks associated with Zinc engineered nanoparticles and as these are used in lubricants, paints and coatings, which due to wreathing and passage of time may peel off from the applied surfaces; chances are that their toxic amount may enter into the environment and affect the human beings.

Alumina (Al_2O_3)

Alumina nanoparticles (AlNP) are more inflammatory and they also penetrate into brain very easily adopting a number of routes, which may include the blood and olfactory nerve. Olfactory neural tracts connect directly to the area of the brain that is most effected by Alzheimer's disease (Blaylock, 2013). In a recent study carried out by Zhang et al., female mice were exposed to AlNP during pregnancy: It was concluded that the exposure induced neurodevelopmental toxicity in offspring (Q. Zhang et al., 2018). Zaitseva et al. studied the effect of AlNP, having dimensions 30-40 nm, and specific surface area of 113 m^2/g on human body (Zaitseva, Zemlyanova, Stepankov, & Ignatova, 2018): They have concluded that AlNPs have a high degree of potential hazard to human body. The particles were found responsible to generate ROS (Reactive Oxygen Species), damage DNA, depolarize cell membrane, result in morphological changes and cell death and affect metabolism.

NANOTECHNOLOGY RISKS TO THE ENVIRONMENT

Nanotechnology has the potential to improve the inventory storage as well as enhance the ability to grow at higher yields and more variety of crops (Zahedi, Karimi, & Teixeira da Silva, 2020). This can be a good positive contribution to the environment. Moreover, nanotechnology based improvements in the energy technology can reduce the dependence on fossil fuels by making the photovoltaic energy production competitive with other energy sources. This may improve the renewable energy systems including biomass (Roco & Bainbridge, 2005).

But as explained earlier, nanotechnology if misused can have serious impacts on the environment and these harmful impacts on the environment are definitely linked with the habitats. It is more like a cycle; nanotechnology may directly affect the human beings or it may first disturb the environment thus ultimately affecting the habitats. Sometimes, nanotechnology is used for the betterment of environment and carelessness and lack of knowledge leads to more harm than good. Johansson et al.

have categorized two types of scientists working with nanotechnology, upstream or engineers and downstream or toxicologists: According to their study, while the former always downplay risks, the later always focus at risks (Johansson & Boholm, 2017). This makes the lack of knowledge even at expert level.

Water is the most important matter on earth not merely for human beings but for all creatures. One of the fundamental Humanitarian aims is the provision of clean and affordable water to the community: However, it is still a major challenge for the 21st century (Mayo et al., 2007). In recent decades, water treatment using nano-technological based expertise has gained significant attention of researchers all around the world. It has been reported that there are abundant challenges faced by water/wastewater treatment nanotechnologies including misuse of nanoparticles, technical hurdles, high cost, and potential environmental and human risk (Qu, Alvarez, & Li, 2013). The use of engineered nanoparticles and nanomaterials for water treatment and groundwater remediation has raised concerns for human exposure. These concerns are based on the fact that nanoparticles will be highly mobile in porous media because of their small size; thus implying a greater potential for exposure as they are dispersed over greater distances and their effective persistence in the environment increases (Dunphy Guzmán, Taylor, & Banfield, 2006). It is concluded that nanoparticles can enter into the environment from a number of sources but the most likely doorways are sewage water and wastes: According to Schlich et al., silver nanoparticles absorbed onto the sewage sludge caused toxic effects on soil micro-organisms (Schlich, Klawonn, Terytze, & Hund-Rinke, 2013). The production of the raw materials, the manufacture of products with nanomaterials, as well as at the end of the products' lifecycle generates all these wastes. Some specific nanoparticles and their harmful effects on the environment are discussed below.

CNTs

As far as environmental negative effects of CNTs are concerned, certain studies have been done for their evaluation. However, the results are controversial; some studies were even unable to determine any negative effect, however others did. One of the important parameter to find the environmental hazards of nanotechnology is to study aqueous creatures in detail. The data available have shown considerable negative effects on the aqueous creatures including the fishes and amphibian larvae when, exposed to the nanoparticles. According to Das et al., risks linked with CNTs are growing via waste water treatment routes and there are knowledge gaps in the risk assessment (Das, Leo, & Murphy, 2018).

Actually, carbon nanotubes usually do not settle under the action of gravity in water thus they are regarded as surface functionalized and their extremely fine distribution in water remains stable. Such behavior promotes the accumulation of several heavy metals, which then influences their transport in the water bodies and in biological systems (Schierz & Zänker, 2009). According to Cornelis et al., CNTs dissolved in water and deposited in soil through sewage sludge, aerial nanoparticles or soil remediation can prompt toxic effects in various micro-organisms (Cornelis, Kirby, Beak, Chittleborough, & McLaughlin, 2010).

Nano-TiO_2

Titanium dioxide is one of the most commonly investigated nanoparticles and its impacts on environment are well concluded (Caramazana-González et al., 2017; Shah et al., 2017; Simonin et al., 2016; Wilson, 2018). Research has come up with the establishment of a number of standardized nano TiO_2 tests for fishes, crustaceans and even algae. According to Battin et al., microorganisms are very sensitive to nano TiO_2 (Battin, Kammer, Weilhartner, Ottofuelling, & Hofmann, 2009). Nano-TiO_2 shows photo catalytic behavior under ultra violet radiations, which causes the development of Reactive Oxygen Species (ROS) (F. Li et al., 2015; Xue et al., 2010). These species have the potential to damage the cell membrane of several microorganisms. Many studies have also been conducted for the simulation of actual condition in natural running waters on the laboratory scale, which have shown that TiO_2 nanoparticles and small concentrations of larger naturally developed agglomerates can both damage the cell membranes of living organisms (Asztemborska, Jakubiak, Stęborowski, Chajduk, & Bystrzejewska-Piotrowska, 2018; Shah et al., 2017). Damage to these living organisms is definitely a big threat to the environment.

TiO_2 nanoparticles can also attach themselves to the chitinous (a protective substance) exoskeleton of the animals leading to obstruct molting, which is necessary for the growth in juveniles. This phenomenon may kill such animals thus having serious negative effects on the environmental balance in long term. Regarding this particular molting obstruction effect in juveniles, dose of the nano-TiO_2 was kept at 0.24mg/liter in one study and a comparison was also established between dosages of nano and larger form of the TiO_2 particles: Nanoparticles proved to be twice as harmful at this dose as compared to the larger forms (Dabrunz et al., 2011).

Nanosilver

The use of nanosilver technology has more recently been expanded from medical field, textiles to personal electronic devices and appliances such as humidifiers, air cleaners, room sanitizers and water purification units (Thamilselvi & Radha, 2017). Silver nanoparticles have antimicrobial properties and may also have some role to play in preventing or managing infections (Salomoni, Léo, Montemor, Rinaldi, & Rodrigues, 2017). However, their uncontrolled discharge in the environment is harmful. The primary pathway for nanosilver in the environment is the waste-water washed out of textiles, cosmetic units and several other industries (Reed et al., 2016). Furthermore, nanosilver in waste water has been identified by an international group of researchers from different scientific disciplines as one of fifteen areas of concern that can threaten biological diversity (Sutherland et al., 2011) and it is well known that biodiversity is very important for maintaining balance of the ecosystem, provision of biological sources and for social benefits (recreation, cultural value, research). Once bio diversity is disturbed, the whole environment starts to suffer.

Microorganisms including bacteria, fungi and algae are all vital part of the environment. They have their own roles and importance in our world. For example, bacteria are the most diverse group of microorganisms; although some are parasitic for the habitats, most of them are either neutral or have beneficial relationship with the humans, animals and plants (Venkova, Yeo, & Espinosa, 2018). Similarly, algae are a source of oxygen for aquaculture and natural food for the cultured animals (Weiss, 1952). It is therefore very important not to disturb their presence up to a certain degree. As the world is developing day by day, these microorganisms are getting very close to lose their balance in the environment. As far as nanotechnology is concerned, it has also shown some negative effects on these microorganisms.

Silver ions from silver compounds or those, which develop from nanosilver particles through contact with water are very toxic to several microorganisms including bacteria, fungi and algae (Hegde, Brar, Verma, & Surampalli, 2016). In addition to these, there are many useful organisms in soil, therefore, when sewage sludge having nanosilver pollutants is spread on fields, it negatively affects these microorganisms. For fishes and crustaceans, even low concentrations of nanosilver are enough to cause considerable damages however for mammals, the material is toxic only at high concentrations. According to Yin et al., very limited research work is available on harmful impacts on nanosilver on plants (Yin et al., 2011). However, the available data at the moment conclude that the growth impairment of grass seedlings due to cell damage, when exposed to nanosilver in abundant quantities (Budhani, Egboluche, Arslan, Yu, & Deng, 2019).

Fe ENPS

Fe ENPs have found wide applications with organic and inorganic coatings for stabilizing their suspension. Fe ENPs have also gained attention due to its super-magnetism characteristics (Ali et al., 2016): They are suggested for hyperthermic treatment of patients using an external magnetic field. They are also found suitable for cancer diagnosis and treatment (X. Zhang et al., 2018). It is reported that long exposure period (~2 days) Fe ENPs might lead to cytotoxicity owing to production of free radical (Abakumov et al., 2018). The growing application of high concentration of zero-valent Fe NPs has raised concerns as regard their environmental behavior and potential ecological impact (Lei, Sun, Tsang, & Lin, 2018). Zero-valent iron ENPs undergo chemical transformation, when used in environmental remediation techniques (W. Zhang, 2003). After transformation, they are oxidized to FeO in the reaction path. The oxidized form is reported to be more harmful than the corresponding free metals. Same behavior is observed, when some other metal ENPs are converted to oxides in air or water e.g. Cu, Si. (Morris & Willis, 2007).

Al_2O_3 ENPs

It has been found that the root growth of five plant varieties (corn, beans, cucumber, carrots and cabbage) is affected by a brief exposure to alumina nanoparticles (Yang & Watts, 2005). Sadiq et al. (2011) studied the effect of exposure of Al_2O_3 ENPs on two species of microalgae, Scenedesmus sp. and Chlorella sp.: They have concluded that the nanoparticles interact with the cell surface, decrease chlorophyll content and have growth inhibitory effect (Sadiq, Pakrashi, Chandrasekaran, & Mukherjee, 2011). Doskocz et al. (2017) compared the effect of macro Al_2O_3 and Al_2O_3 ENPs on the growth of Pseudomonas putida (bacteria found in soil and water habitats) (Doskocz, Affek, & Załęska-Radziwiłł, 2017): They found that nano form is highly toxic than the macro form.

SOCIAL RISKS OF NANOTECHNOLOGY

Terrorism

There are some social concerns about nanotechnology that it may also allow us to create more powerful weapons, both lethal and non-lethal. Some organizations are concerned that the implications of nanotechnology in weaponry should remain in ethical limits. They urge scientists and politicians to examine carefully all the possibilities of nanotechnology before planning to use it in a large number of weapons. It is also important to note how uncomplicated is the application of nanotechnology in weaponry. Any easily doable or portable use of nanotechnology in weapons can raise some concerns for illegal use of this technology. According to Altmann, new options for nuclear artillery might also include nanotechnology materials extraction and processing, weapons production, and perhaps new types of nuclear weapons (Altmann, 2004). Use of nanotechnology for terrorism is not out of question as several terrorist groups have shown interest in using potential of chemical and biological weaponry. According to I. Puscas, following threats posed by the use of nano-weapons by terrorist groups, the international community needs to adapt solid approach for regulating nanotechnology (Puscas, 2015).

Privacy

Privacy concerns necessitate ethical use of nano devices. As nanotechnology based products reduce in size, spy devices too can become invisible to the naked eye and even more mobile. This would make it easier to invade one's privacy. These devices can even be planted into human bodies and as technology is thriving in the recent era, it would not be outlandish to state that mind controlling may be developed to affect one's thoughts by manipulating the brain processes. According to Hoven, nano technology has given rise to the production of devices, which are cheap, easily available and even not clearly visible (van den Hoven, 2014): He refers to Radio Frequency Identification Tag (RFID) as a disruptive device, affecting privacy.

However, social risks are never too difficult to cope with; all it needs is to keep the right information among the right people to avoid any misuse of the technology. As far as other risks are concerned, there is need to adopt a number of specific remedial measures which are discussed in the 'Remedial Measures' section.

Fire and Explosion Risk

Combustible nanomaterial possesses higher risk of fire explosion as compared to the same material at macro-level. Rate of combustion also increases leading to the possibility of relatively inert materials becoming more reactive in the nanometer size range. Furthermore, combustion leads to the dispersion of materials in air and here again nanoparticles offer more safety risk, when dispersed in air as compared to the macros having same composition. For instance, nanoscale Al/MoO_3 thermites ignite more than 300 times faster than corresponding micrometer-scale material (Granier & Pantoya, 2004). According to Krietsch et al. (2014), the enhanced specific area of ENPs leads to an increase in its ignition capacity and pyrophoric (capable to ignite spontaneously) behavior (Krietsch, Scheid, & Schmidt, 2014).

REMEDIAL MEASURES

Advancement in Analysis Techniques

Conventionally, it is good approach to measure the toxicity of nanoparticles in terms of their mass and surface area. However, it may also be reasonable to determine particles size, shape, and morphology. Conclusions about the toxicity potential of nanoparticles on human beings are concluded from the tests carried out on animals. However, it is possible that certain nanoparticles affect only specific form of living organisms and these animal test based results may lead to erroneous conclusions. Moreover, sometimes tests are carried out on healthy animals. Studies have shown that some toxins may not be harmful for healthy organisms but may have ruinous effects on unhealthy or already diseased organisms (European Commission Joint Research Center (ECJRC), 2003). There is need to bring new advancements particularly related to the nanoparticles toxicity tests for detecting their possible harmful effects on human beings. Long term studies are also necessary to determine delayed impacts of engineered nanoparticles and to help determine prospective adaptive mechanisms. Additionally, more studies on bioaccumulation of ENPs in the food chain and their interaction with other pollutants are also mandatory.

As far as instruments for the exposure assessment are concerned, there is need to bring new advancements because nanotechnologies are diverse and the exposure to nanoparticles also vary widely, so multiple sensors operating under different conditions are required. Three zones stand out as productive ground for this particular novel research: monitors for airborne exposure, detectors for waterborne nanomaterials, and smart sensors that can measure both exposure and potential hazards. Different characterization techniques are available, which can help assessing the risks associated with particular ENPs (Mourdikoudis, Pallares, & Thanh, 2018).

Continuous Research and Education

Nanomaterials are frequently being used across the globe in many ways without any awareness to the end-user. Owing to many risks associated with nanoparticles, the school science curricula need to be integrated with nanotechnology concepts, which are closely connected and evocative to students (Ghattas & Carver, 2012). Ban et al. are of the view that some topics related to nanotechnology should be included within the middle and high school curricula (Ban & Kocijancic, 2011). According to Marikar et al., majority of even undergraduate medical students lack understanding of nano-medicines and its underlying biological principles (Marikar et al., 2014). Past surveys indicate that careful examination of the existing data and planning of new research in this field is required. Research should also examine how social and economic forces affect allocation of benefits and risks, both across social classes and across societies of the world. There is need to introduce several worker transition programs and postdoctoral trainings in the physical and toxicological sciences, but more important is to inaugurate trainings that combine specialties in the social sciences and humanities with knowledge of nanoscience and nano-engineering. For the completion of these projects, there is need to develop infrastructure of nanoscience laboratories, shared social science information systems and simulated virtual laboratories. Moreover, several new statistical software should be developed for creating linkage between nanoparticles and their harmful effects to human health and the environment.

It is also important how early a risk is identified and strategy is established; it may save additional costs, which usually occur for risk remediation once the technology is already in use (Dunphy Guzmán et al., 2006). For this purpose, different well-funded pilot projects in different countries must be introduced.

Rules and Legislations

Most of the government regulatory frameworks, which are used today, were generated almost 40 years ago when, nanotechnology was not introduced (Paradise, 2019). Therefore, these frameworks lack the coverage of many unique properties, which are sole feature of nanoparticles.

In order to mitigate the risks associated with the use of nano building materials, specific guidelines for nanotechnology should be developed at national level to regulate the use as well as disposal of nanoparticles (J. Lee, Mahendra, & Alvarez, 2010). Another suitable approach would be to only allow professionals to work with nanotechnology (Reynolds, 2007). It has been found that there is no obligatory registration for any nanoparticle and most of the companies producing the nanomaterials are not willing to disclose their production volumes; this aspect should also be considered critically.

In addition to all this, a federal registry should be established for all companies and organizations manufacturing, importing and supplying products containing nanomaterials. It must register the organization's name and its products containing nanomaterials and all this information should be made publicly available.

The EU regulatory framework takes in nanomaterials: The legislation includes nanomaterials, addresses labelling on the products and its safety assessment. But nanomaterials are flourishing so enormously with new novel qualities and new behaviors that their exact safety and evaluation is a question mark. In USA, nanomaterials are regulated by Food and Drug Administration (FDA) (Smith, 2018). According to Paradise, FDA faces three core challenges with the progress of nanomedicines: (1) Adequacy of the regulatory framework as it is based on old definitions of chemical and mechanical action, which may not be applicable to nanomedicines, (2) Products may be associated with novel risks, which outclass traditional safety and efficacy requirements, (3) Labelling of the products may provide insufficient information regarding use of nanotechnology (Paradise, 2019).

Public Awareness and Feedback

Engineers, corporate management and societal policy-makers may not know very much about the best implementation of the possible technological developments, nor about what the indirect or second-order societal effects might occur; for example, at the intersection of nanomaterials and nano-systems with biological and ecological systems (Roco & Bainbridge, 2005). Feedback from well-informed public and international partners has become essential for progress in this field. More interactions between scientists, engineers, economists, health professionals and the public are needed to identify and reach the robust balance between benefits and limiting factors of nanotechnology.

There is need to inform general public about this technology. In recent years, several studies examined public opinion of nanotechnology in Europe and United States. A U.S. survey showed that more than 80% of the respondents indicated that they had heard "little" or "nothing" about nanotechnology (cobb & Macoubrie, 2004; Sabliov, Chen, & Yada, 2015). In addition to this, the results of a 2010 survey found that an average of 45% of Europeans from 32 countries said they had heard of nanotechnology (Joubert et al., 2020). According to a survey conducted by Senocak, it is reported that the majority of Turkish public is unfamiliar with nanotechnology (Senocak, 2014). The studies suggest that the public's awareness of nanotechnology is low, and that knowledge about nanotechnology is very limited. One way to cope with lack of knowledge is to employ social trust, when assessing the risks of a new technology (Lam, 2003; C.-J. Lee, Scheufele, & Lewenstein, 2005).

However, there are still some people who are aware of this technology and the products based on it. These people should be involved in feedbacks through various survey programs. The consumption of nanotechnology based products by a community must be recorded for study purposes. The record must include the type, duration and quantity of products, people use. Any harmful effects people experienced due to nanotechnology based products must also be recorded and analyzed. These measurements would further unclear the risks and uncertainties associated with this technology.

Workers Protection

The results of the surveys, even in developed countries, show that the industries have a very poor level of concern about the risks to which the workers are exposed (Castillo, 2013). The companies were found to refuse the answers, which depicted that the available data were not correct and the workers were not sufficiently safeguarded.

According to Schulte et al., for responsible development of nanotechnology, five criteria should be adapted: (1) anticipation, identification and tracking potentially risky nanomaterials at places of work, (2) assessment of exposure to workers, (3) communication of hazards/risks to workers, (4) control occupational health and safety risks, (5) Adaptation of safe development (Schulte et al., 2014).

Like many other emerging technologies, nanotechnology also poses several risks to the workers and their protection remains a key issue. People who work in the molecular nanotechnology field should develop and utilize professional guidelines that are grounded in reliable technology. Persons dealing with the nanotechnology should use Personal Protective Equipment (PPE) and go through regular checkups for avoiding any serious harmful impacts. Continuous workers training is also an important aspect, which could minimize the risks of the technology. Furthermore, there is need to develop specific procedures for the installment of various engineering controls including exhaust ventilations and good working practices at those locations, where exposure to nanomaterials may occur. Examples of good working practices include cleaning of work areas using HEPA (High Efficiency Particulate Air) vacuum pickup and wet wiping methods, preventing the consumption of food/ beverages in workplaces, providing hand-washing facilities, and facilities for showering and changing clothes (Bortolassi, Guerra, & Aguiar, 2019). Exclusion of pregnant or nursing women from the jobs and availability of enhanced medical surveillance at sites is also mandatory. These are very simple steps but can reduce risks to a considerable degree.

Suitable steps should be taken to lower the risks of worker exposure through the implementation of a risk management program (Hansen, 2009). Risk management programs for nanomaterials should be seen as a fundamental part of an overall occupational safety and health program in any organization producing or using nanomaterials or nano-enabled products.

Engineering Control

Engineering control techniques such as isolation of the generation source from the workers to minimize the interaction and application of efficient exhaust ventilation systems for capturing airborne nanomaterials can play an important role in worker's health and safety. Current knowledge indicates that a well-designed exhaust ventilation system with a HEPA filter should effectively remove nanoparticles (Bortolassi et al., 2019; Hinds, 1982). Furthermore, continuous monitoring of nanoparticles in air using appropriate devices is also very important to avoid any unnecessary effects on workers (Occupational Safety and Health Administration, 2013).

Development of Models and Robust Systems

There is requirement to develop models for predicting the potential impact of ENPs on human health and the environment. These models would help scientists for assessing the safety of many complex multi-component and multi-functional nanomaterials. According to Bora et al., predicting physical properties of nanomaterials require information over entire range of particles sizes (Bora et al., 2019). Thinking in terms of life cycles leads to a comprehensive approach for managing risks and benefits.

Developing robust ways of evaluating the potential impacts both good and bad of a nano-product from its initial manufacture, through its use, to the final disposal will lead to new methodologies that would be widely applicable (Gilbertson, Wender, Zimmerman, & Eckelman, 2015).

Maintenance of Workplaces

Buildings, machines and equipment require regular maintenance for keeping the environment reliable and safe. Maintenance can be proactive for the prevention of machine & structure failures or reactive to repair equipment or building modules. Maintenance can be done in a variety of ways including servicing, inspecting, repairing, adjusting and replacing parts: It is accompanied by opening closed production units, replacing filters, removing paints affected by nanoparticles in air, grinding and sanding etc. According to a research based on the questionnaire jointly conducted by the Japan National Institute of Occupational Safety and Health (JNIOSH) and the National Institute of Advanced Industrial Science and Technology (AIST) from September 2007 through to February 2008, it was observed that more than 50% of the occupational health supervisors in workplaces gave a notion that nanoparticles may be leaked outside of the workplaces during the production process and workers may get exposed to the nanoparticles (Report of Review Panel Meetings on Preventive Measures for Worker Exposure to Chemical Substances Posing Unknown Risks to Human Health (Nanomaterials), 2008).

Waste Monitoring

As nanotechnology is rapidly emerging, therefore, the waste in recent era may have considerable amount of nanomaterials in it, which can easily become the part of the environment. For example, LEDs contain nano-scale coatings of the semiconductor materials arsenic, phosphorus, gallium and their compounds. Therefore, they belong to the waste category requiring special treatment or monitoring. In particular, the semiconductor material gallium arsenide is very problematic and could create environmental damage in a normal landfill (Steinfeldt et al., 2004). Therefore, it is very important to monitor the waste. Solid wastes should be packed in preserved containers for handling until incineration or other processing is carried out. Gas emissions and liquid effluents from nanoparticle industries must also be treated and final releases must be monitored (Ministry of Ecology and Sustainable Development (MOE & SD), 2006).

Recycling

An approach for reducing the undesirable quantities of nano-waste in the environment is to recycle them. The recycling of macro and micro waste materials is not a new topic and many industrial wastes have been successfully recycled to create high performing materials (Ahmed, Khitab, Mehmood, & Tayyab, 2020; Riaz, Khitab, Ahmad, Anwar, & Arshad, 2019). However sufficient precautions and considerations should be made during recycling. At present knowledge regarding the recycling of nanoparticles may not be sufficient however the scheme seems to have very high potential in it and ongoing research has also shown many positive results.

Manufacturers of nano-based materials should make plans for the efficient recovering and recycling of nanomaterials into the product life cycle. They should emphasis the production of those products, which allow easy separation and re-use of nanoparticles. This recovery can be done using a variety of ways, two important procedures are briefly explained below.

Nanoparticle Recovery Using a Micro-Emulsion

Myakonkaya et al. (2010) worked on the separation of cadmium and zinc nanoparticles using a special solvent. The solvent is a stable micro emulsion of oil in water but when heated it breaks down into two layers and all of the nanoparticles in the solution end up in one of the layers, which is simply separated (Myakonkaya, Guibert, Eastoe, & Grillo, 2010). The technology has been successfully used in many other studies (Lakshmanan, Okoli, Boutonnet, Järås, & Rajarao, 2014; Nazar, Myakonkaya, Shah, & Eastoe, 2011).

Nanoparticle Recovery by Cloud Point Extraction

Another process was reported by another group of researchers in 2011 (Nazar, Shah, Eastoe, Khan, & Shah, 2011). They employed a technique known as cloud point extraction (CPE) to separate gold and palladium nanoparticles from an aqueous solution. The cloud point of an emulsion is the point when the two phases are on the verge between mixing fully and forming two layers, causing clouding of the solution. In their method, the nanoparticle solution was heated to this cloud point and later on centrifuged for the efficient separation of the layers. This led to the recovery of nanoparticles from the solution. Hadri et al. (2017) investigated CPE for the analysis of AuNP in a soil matrix, reporting a recovery of more 90% (El Hadri & Hackley, 2017).

CONCLUSION

This work summarizes the hazards of nanotechnology (Figure 3) and the remedial measures (Figure 4). The information is intended for ensuring the responsible management and control of the potential risks raised by nanoparticles. Nanotechnology is reported a to be a major concern not only for human health but also for the whole ecosystem. Identification of metrics and development of methods for measuring, characterizing, assessing the behavior and characteristics of nanoparticles have prime significance. The study shows that there is a coordination gap between the engineers and the toxicologists: While the former consider nanomaterials as revolutionary, the later regard as potentially hazardous.

Figure 3. Risks of nanotechnology

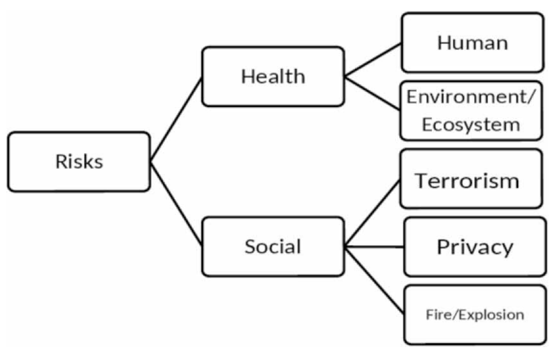
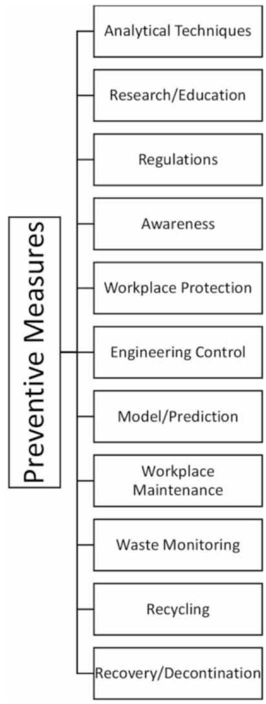


Figure 4. Remedial measures



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