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NANOMATERYALLER: ÇALIŞANLAR İÇİN MESLEKİ AÇIDAN SAĞLIKLI VE GÜVENLİ Mİ?

NANOMATERIALS: OCCUPATIONALLY HEALTHY AND SAFE FOR WORKERS?

PhD Stud. İbrahim EYİ

Istanbul Aydın University, Institute of Science and Technology, Occupational Health and Safety, Florya Campus, Istanbul / TURKEY, ORCID: 0000-0002-9604-6876

Assoc. Prof. Banu Yeşim BÜYÜKAKINCI

Istanbul Aydın University, Faculty of Engineering, Textile Engineering, Florya Campus, Istanbul /TURKEY, ORCID: 0000-0001-7597-4406

ABSTRACT

This review describes identified health risks, toxicity/scientific findings; general characteristics of nanomaterials, worker's exposure to nanomaterials, exposure routes, and aims to give a perspective about risk of occupational disease in terms of Occupational Health and Safety. Studies based on experimental tools indicate for a specific bio-reactivity of nanoparticles associated with the high chemical surface reactivity because of nano dimensions and nanoparticles present potential hazards to humans.

An appropriate risk management, risk assessment and toxicity assessment are needed to protect employees. Inhalation exposure, dermal and other potential routes of exposure to nanoparticles should be assessed. To mention an occupational illness, it should be clinically proven that is result of an exposure of any spesific nanomaterial in the working area within required times. In this context, more epidemiological, vivo/in vitro and toxicological studies are needed to shed light on. Even tough there is not enough evidence for any occupational illness, it can be said that directly/indirectly new legislations on possible occupational diseases in the regulations of countries will take place or be nedded to protect workers against nanomateral exposures.
Keywords: Nanomaterial, Nanoparticle, Ocuupational Health and Safety, Occupational Disease.

ÖZET

Bu çalışma nanomateryallerin genel karakteristikleri mevcut çalışmalarla belirlenebilen potansiyel sağlık riskleri, toksisite ve bilimsel bulguları ve çalışanların maruziyeti, maruziyet yolları, meslek hastalığı risklerini iş sağlığı ve güvenliği açısından bir perspektifle derlemeyi amaçlamıştır. Deneysel çalışmalar nanopartiküllerin nano-boyut'ları nedeniyle spesifik bio-reaktivitelerini ve insan sağlığı için potansiyel tehlikeler içerdiğini ortaya koymuştur. Çalışanları korumak için doğru bir risk yönetimi, risk değerlendirmesi ve toksisite değerlendirmesi gerekmektedir. Solunumla, dermal yolla maruziyet ve nanomateryallerin diğer potansiyel maruziyet yolları değerlendirilmelidir. Herhangi bir meslek hastalığından söz edebilmek için çalışma ortamındaki spesifik bir nanomateryale maruziyet sonucunda belirli bir süre sonunda oluştuğu klinik olarak kanıtlanmalıdır. Bu bağlamda daha fazla epidemiyolojik, vivo/vitro ve toksikolojik çalışmaların yapılması gereklidir. Meslek hastalığından söz edebilmek için henüz yeterli bir kanıt olmasa da direk ya da indirek olarak potansiyel meslek hastalıkları için yeni mevzuatların çalışanları maruziyetten korumak için yerini alacağı ve gerekli olacağı söylenebilir.
Anahtar Kelimeler: İş Sağlığı ve Güvenliği, Nanomateryal, Nanopartikül, Meslek Hastalığı

1. INTRODUCTION

Nanomaterial definition is used for materials with dimensions between 1 to 100 nm. Nanomaterials can have one or several components and with their different structures and production methods. They can be currently in forms of nanoparticles (Np), nanofibers and nanotubes, composite materials and Nano-structured surfaces (BORM, Paul JA, et al., 2006). All of these forms can be released to environment as a single small particle with a diameter < 100 nm as a result of production process or wastes or during usage.

Nanotechnology, Engineering Nanomaterials (ENm) and Nanoparticles (Np) are used today in engineering applications, fuel-economy, high memory supercomputers, cancer treatment, pharmaceutical production, water purification, wearable health products, cleaners, solar panels, food packaging and preservation, cell renewal, sensors and medical fields [Table 1 (GREEN, Carolyn J et al., 2012)] and continue to penetrate increasingly into all areas of our lives (NSTC/NSET, 2016).

Table 1. Applications of ENPs

MNp Class	Applications
Carbon Compounds	
Carbon Nanotubes and derivatives	Aircraft, sporting goods, batteries, car parts, ceramics, computers, concrete, conductive coatings, electronics, orthopedic implants, plastics, catalysts, solar cells, super capacitors, textiles, water purification systems,
Fullerenes	Anti-viral therapy, cancer treatment, cosmetics, magnetic resonance imaging, removal of organometallic compounds, X-ray contrasting agent,
Metal Oxides	
TiO_2	Bioremediation, cement, clothing, cosmetics, electronic coatings, food colorant, paints, skin care products, solar cells, sporting goods, sunscreen lotions, windows
ZnO	Bottle coatings, contaminant sensors, gas purification, skin care products
CeO_2	Medical imaging, photovoltaic cells, security links, solar cells, targeted therapeutics, telecommunications
Semi-Conductor Devices	
Quantum Dots	Medical imaging, photovoltaic cells, solar cells, telecommunication, targeted therapies
Zero-Valans Metals	
Zero- Valent Iron	Detoxification of organochlorine pesticides, remediation of water, sediments and soils to remove nitrates, polychlorinated biphenyl
Nano particulate Silver	Air filters, appliances (hair dryers, vacuum cleaners, washing machines, refrigerators), baby products (milk bottles, teethers), coatings/paints, cooking utensils, cosmetics, deodorants, disinfectant sprays, food additive/supplements, food storage containers, hardware (computer, mobile phones), laundry soaps, medical instruments, textiles (e.g., socks, shirts, pants), toothpaste, wound dressings,
Colloidal Elemental Gold	Anti-microbial coatings, cosmetics, catalyst, flexible conducting inks or films, tumor therapy, pregnancy tests
Polymers	
Dendrimens	Chemical sensors, colored glasses, drug delivery, manufacture of macro capsules, modified electrodes, Nano latex, tumor treatment

Given that nanomaterials is increasingly becoming a part of daily life, whether their exposures can be a threath to human health and particulary to the workers is an unanswered question yet. Occupational Illness results from immediate or continous exposure of physical, chemical, biological agents or working conditions and situations in the workplaces and as a result of that exposure workers health is damaged to some extents. To identify something as an occupational illness, it should be clinically evident and exposure ways should be proven that may result in disease by a specific exposure time with a spesific agent. It could become an new and challenging issue to be researched that whether Nanomaterial exposurement of workers in the working area may result as an occupational illness in the long term for workers.

2. NANOPARTICLE EXPOSURE AND EFFECT ON OCCUPATIONAL HEALTH

Ultrafine particles can have similar or close dimensions with Nanomaterials and particles but Nanoparticles is produced deliberately to achieve some properties. A good many of study findings reveals acute and chronic effects on urban and workplace pollution and their health status because of particulates in the atmosphere.

The literature refers to some researches showing a connection and resemblance in exposure to ultrafine particles in the atmosphere with laboratory and functional characteristics. Ultrafine particulates could have similar dimensions with Nanomaterials but they are released to environment unintentionally and not produced with engineering techniques as Nanomaterials. Therefore, comparatively it can be concluded that Nanoparticles can have negative effects in the occupational places and for urban pollution (Stone, Vicki, et al., 2017). Ultrafine particle effects on health (such as; asbestos) become apparent thanks to long years' studies. With regards to their similar dimensions with ultrafine particles, it can be said that nanomaterials can have same or similar effects on health of exposed people but their different production processes and Nano additives in the other harmless substances is still unknown areas which needs specifically more studies. Nanotechnology workers are exposed to nanometer-scale particles (DEBIA, M., et al., 2013). Nano-Exposure of workers has potential negative health effects (TSUJI, Joyce S., et al.,2005).

Nanomaterials can pass through the tissues and damage the cell as well as cause toxicity. Nanoparticles can migrate into the bloodstream, easily overcome cell barriers, in conclusion affects organs and tissues at the cellular and molecular level6. The easiest and major exposure to nanomaterials is via respiratory exposure [Fig.1 (Babaarslan E., 2014)] and nanoparticles can easly pass to bloods and other tisues from respiratory system.

For this reason, to protect employees a toxicological risk assessment from the very beginning has to be part of the design and manufacture of Nanomaterials (BAKAND, S; HAYES, A., 2016).

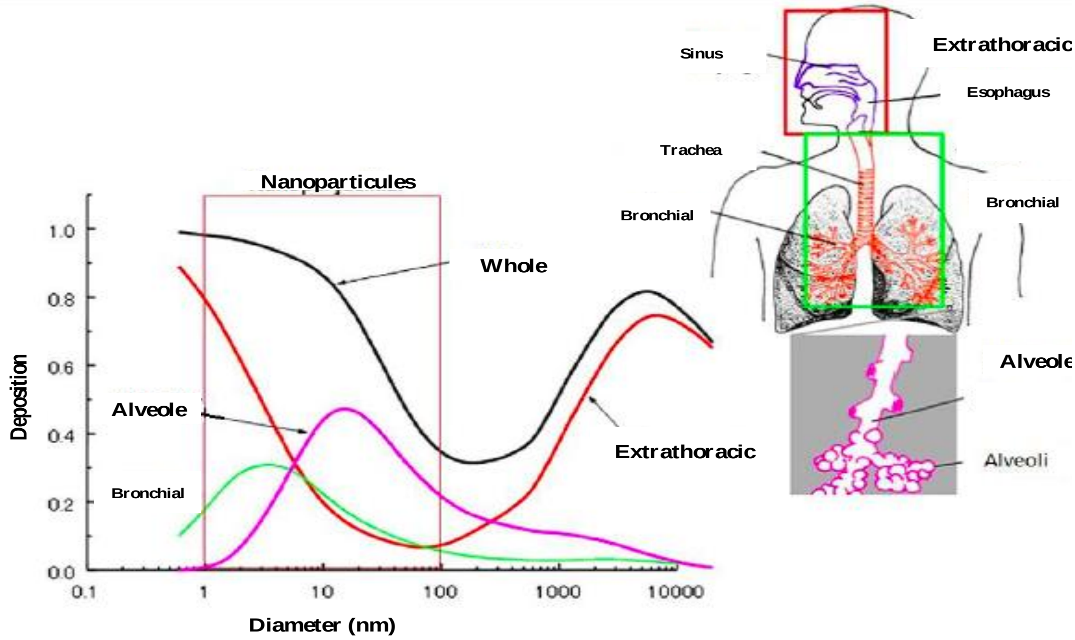

Figure 1. Accumulation Points According to Particle Size in Human Respiratory System

According to literatures, the main nanoparticle exposure routes are; injection into the human body (drug delivery, etc.), oral administration, inhalation (Figure 1), to penetrate through digestion and skin, gastrointestinal (GI) way, the blood-brain barrier (BBB) and NPs have the ability to overcome biological barriers (Figure 2) (TSUJI, Joyce S., et al., 2005).

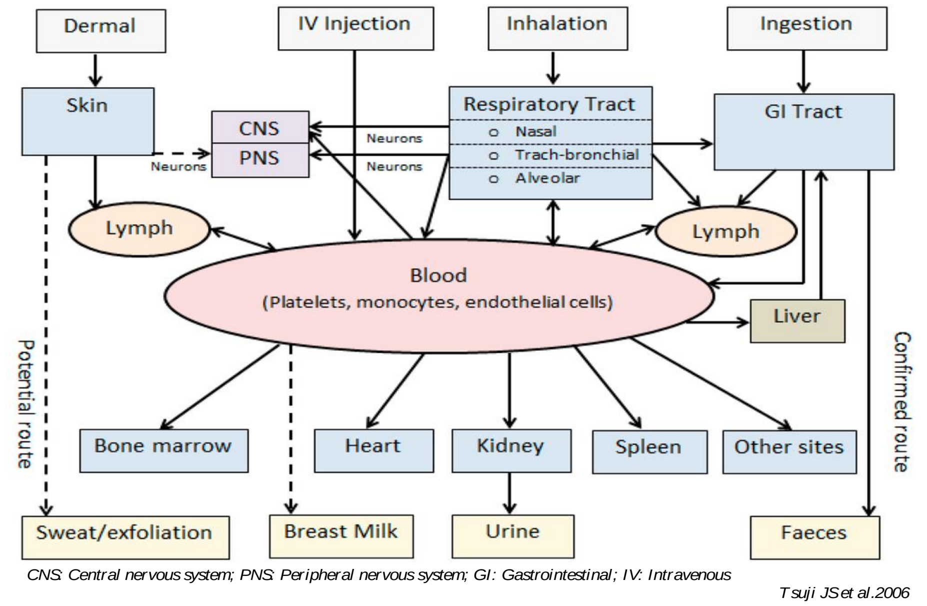

Figure 2. Nanoparticle Exposure Routes

NMs can reach to very deep areas in human body because of its Nano-dimensions and can have potential biological effects (Table 2,3) on workers which can be different according to nanomaterial properties. Possible biological effects mean significantly dangerous effects on workers which needs more studies to have final conclusive results and all of nanomaterials should be handled with conisderation of its special potential effects.

Although there are studies for nanotechnological approach of occupational health and safety, epidemiological, vivo / in vitro and toxicological studies for the harmful effects and safe use of nanomaterials are very limited and there is a lack of knowledge on these issues in terms of human health (NSTC/NSET, 2016).

Thinking of that long term harmful efects will apear in the years after exposure, to take precautions and control measures for nanomaterials possible effects have to be considered seriously. Potential dangerous effects and exposure routes to health of workers have to be a part of risk management and risk assesment prosess in the whole process of nanomaterials including designing. Medical surveys and medical screening should encompass detection of any effects of its harms in the working area. Nanomaterials can have different characteristics such as; surface properties, compositions, solubility properties and agglomeration. That characteristic variability gives nanomaterials to have spesific properties and production advantages but also can have different ways of effect on health [Table 2 (BAKAND, S; HAYES, A., 2016)].

Nanoparticle reactivity depending on surface area is also an significant factor for its health effects. If there is smaller dimensions, then it has more reactivity. If the dimensions are divided; then the volume/surface area ratio increases. This is also true for the same mass concentration of material and particle reactivity with biological tissue will increase as size decreases. Aerosol particles can also absorb surface gas molecules. Therefore, particle surface area should be measured to determine exposure assessments (Stone, Vicki, et al., 2017).

Table 2. Nanomaterial Properties and Possible Biological Effects

Nanomaterial Properties	Potential Biological Effects
Size/size distribution (aerodynamic, hydrodynamic)	Crossing cell membranes and tissue
	Cellular injury
	Breakdown in defense mechanisms and phagocytosis impairment
	Migration to other organs
	Transportation of other environmental pollutants
Surface properties Surface area/mass ratio	Increased reactivity
	Increased toxicity

Table 2. Nanomaterial Properties and Possible Biological Effects (Continuation)

Nanomaterial Properties	Potential Biological Effects
Chemical Composition Surface Characteristics	ROS generation
	Oxidative stress
	Inflammation
	Cytokine production
	Glutathione depletion
	Mitochondrial exhaustion
	Cellular injury
	DNA, protein damage
Insolubility or low water solubility	Bioaccumulation inside living systems such as tissues, human cells and lungs
	Potential long-term effects
Agglomeration/aggregation	Interruption of cellular processes
	Cellular injury

Studies for nanomaterials potential health effects imply that a harmless nanomaterial to human health is not yet available but effects emerging in time and long term effects are currently unknown to evaluate potential occupational illness types. Currently there is no defined occupational illness legally or in any manuals for workers with nanomaterial exposures.

Each type of nanoparticle must be considered unique and must undergo a specific toxicological investigation regardless of the traditional toxicological tests performed on the chemical species, which is included in its composition. Action mechanisms, biological effects and exposure routes of Nps [Table 3(MIRABILE, Marco, et al., 2014)] should give new perspective for testing and measuring methods and new methods should be designed in accordance with them. Specific medical screening methods in working area should be designed to eliminate the risks.

Table 3. NMs Mechanisms of Action

Nanomaterials		Mechanisms of Action
Carbon Nanotubes	SWCNTs	Decrease in the cellular adhesion and cell proliferation, induction of apoptosis. Oxidative stress and DNA damage.
	MWCNTs	Cell penetration and reduction in cell viability and IL-8 release. ROS generation. Inflammation, lung fibrosis and granuloma and development of mesothelioma.
Fullerenes		Considered less toxic than CNTs. ROS production. Induction of DNA damage, mutagenicity and induction of chromosome aberrations and micronuclei.
Metal and Metal Oxide Nps	TiO2, ZnO, SiO2 and FexOx	Induction of DNA damage through ROS production and inflammatory response.
	Al2O3	ROS production. Pro-inflammatory response.
	TiO2	ROS and SCE induction, increased micronucleus frequency and lung carcinoma. Glutathione depletion and oxidative stress as a result of photo activity and redox properties. Membrane disruption.
	ZnO	ROS production. Dissolution and release of toxic cations. Lysosomal damage. Inflammation.
	Ag	Dissolution and Ag+ release, inhibition of respiratory enzymes and ATP production. ROS production. Disruption of membrane integrity and transport processes.
	Ag and Co	Enhanced expression and phosphorylation of p53, DNA breakages and chromosome aberrations.
	CdSe	Dissolution and release of toxic Cd and Se ions.
	Fe3O4	Liberation of toxic Fe2, Interference on the electronic and/or ion transport activity in the cell membrane.
	CuO	Induction of DNA damage and oxidative stress.
Quantum Dots		Penetration into the cell nucleus through membrane and induction of breakages in DNA chain. Activation of p53 and chromatinic condensation. Decreased cyto-genotoxicity due to ZnS.

3. NANOPARTICLE EXPOSURE ASSESSMENT

To be realize and determine for potential health effects and to make an exposure assesment in workers, test and measurement is a critical issue at this point and is also a keystone for effective risk management. The advised test methods to evaluate acute and chronic toxicity, sensitiveness, reproductive toxicity, geno toxicity and carcinogenicity were issued by OECD and these methods included four sub groups; occupational epidemiology, vivo methods, vitro methods, methods to determine physicochemical properties (Kaluza, S., et al., 2012).

4. PROTECTION AND NANO EXPOSURE LIMITS IN OCCUPATIONAL HEALTH

The results of various studies on nanomaterials have only established occupational exposure limits [Table 4 (VAN BROEKHUIZEN, Pieter, et al.,2012)] for some NMs and protection against harms from NM in a pre-determined 8 hour time-weighted average (TWA) may be provided by these occupational exposure limits. However, This is not sufficient for all, Nanomaterials and Nanomaterial components can be used in chemical Labaratories, Pharmacy firms, medical offices, hospitals, construction companies, etc. The people in the working area and especialy workers should check whether handled material and chemical is nanomaterial and for harmfull effects of it they are to be trained before by employer or authorized personel. Exposure limits is a way to ensure not having any harmfull effects in the short and long terms for workers. Therefore, they have a key role in terms of occupational illness and sometimes could be a prediction asset for occupational illness if there is an excessive exposure of nanomaterial in the working area.

Table 4. Proposals for Occupational Exposure Limits (OELs), Recommended Exposure Limits(RELs), Derived No Effect Levels (DNELs) for specific NPs

Substance		OEL or REL (mg m3)	DNE (mg m3)
MWCNT (Baytubes)	8-h TWA	0.05	
MWCNT (10–20 nm/5–15 µm) Scenario NOAEC pulmonary effects	Short-term inhalation		201
	Chronic inhalation		33.5
MWCNT (10–20 nm/5–15 µm) Scenario LOAEC immune effects	Short-term inhalation		4
	Chronic inhalation		0.67
MWCNT (Nanocyl)	8-h TWA	0.0025	
CNT (SWCNT and MWCNT)	8-h TWA	0.007	
Fullerenes	Short-term inhalation		44.4
	Chronic inhalation		0.27
Fullerene		~0.8	
Ag (18–19 nm)	DNEL-lung scenario 1		0.33
	DNEL-lung scenario 2		0.098
	DNEL-liver		0.67
TiO2 (21 nm)	Chronic inhalation		17
TiO2 (10–100 nm; REL)	10 h day−1, 40 h week−1	0.3	
TiO2 P25 (primary size 21 nm)	TWA 8 h day−1, 5 day week−1	1.2	

Van Broekhuizen, Schulte, et al. 2012

If nanomaterials are easly dispersible (powder, sprey, etc.) or not isolated, threats from health and safety to workers is much bigger. Employees or authorized personell should be given training about nanomaterials such as; nanomaterial identity and prosses, exposure assessment results, determining engineering and management controls and identifying Personel Protective Equipment (PPE), usage and limitations of PPE’s, emergency protocols for nanomaterial spills or release.

OSHA (Occupationla Safety and Health Agency) refers to NOISH (National Institute for Ocuppational Health and Safety) recomendations for exposure limits (REL) and refers that time weighted awarage (TWA) for carbon fibres and respirable carbon nanotubes should not exceed 1.0 (µg/m3) in 8 hours working time. While OSHA recommends that TiO2 particles in nanodimensions should not exceed 0.3 mg/m3, NOISH recomends exposure limits of 2.4 mg/m3 for ultrafine TiO2 particles (>100nm) (OSHA, N. 2013).

In addidtion, criteria levels for nanomaterials were determined by the British Standart Institution in four different classifications;

• Criteria for insoluble nanomaterials is 0.066 Å ~ occupational exposure limit (OEL) have been suggested as mass concentration versus microstructural mass (1 Angström (Å), = 0.1 nm). The 0.066 factor is consistent with the potential difference between nanoscale and micro-scale TiO2 as defined by the US-American National Institute for Occupational Safety and Health.

• The criteria for fiber nanomaterials have been suggested as 0.01 fiber / ml. This level is derived from the current limit value determined during asbestos disposal in U.K.

• 0.5 Å to OEL for high-dissolution nanomaterials.

• For the CMAR (carcinogenic, mutagenic, asthmatic repeat) nanomaterials, a range of 0.1 Å to OEL was determined (OSHA, N. 2013).

In Turkey, there is Regulation for "Health and Safety Measures in Working with Chemical Substances" determining TWA's for chemicals (Regulation, "Health and Safety Measures in Working with Chemical Substances" (2013). However If a chemical become more smaller then its original size, it could be more reactive and there is not any determined regulation regarding nano-specific TWA's in Turkey yet.

5. RESULTS AND CONCLUSION

Nanomaterial exposure of workers and other people is an unexplored and compelling subject. Findings from laboratory studies indicate that exposure of workers to nanomaterials results in adverse health outcomes and have possible adverse results that may become as a occupational illness in the future. Studies based on experimental tools (cell and tissue studies) indicate for a specific bio-reactivity of nanoparticles. It is associated with the high chemical surface reactivity because of nano dimensions. Furthermore, nanoparticles present potential hazards to humans. However, there are no sufficient data for appropriate and definite conclusive methodology to evaluate completely and appropriately nanomaterial effects on human health.

An appropriate risk management, risk assessment and toxicity assessment are needed to protect employees. Inhalation exposure, dermal and potential routes of exposure to nanoparticles should be assessed. In this context employers are responsible for creating a safe and healthy working environment. Likelihood of exposure to nanomaterials and its potential health effects is not only a threath in the working environment but also in the environment of people and users.

Different exposure limits are recommended in the studies. Exposure limits should be elaborated more specifically according to the process used for the chemicals, particulates, powders and the substances and for their sizes. This, of course, will be possible over time as the studies to be done and the results of the studies be brought together.

Even if some of the potential damage to human health is revealed by studies, the name of the occupational diseases that may arise due to nanomaterial has not been addressed yet. To mention an occupational illness existance, it should be clinically proven that is a result of an exposure of any specific nanomaterial in the working area within required exposure times. In this context, more epidemiological, vivo / in vitro and toxicological studies are needed to shed light on. Targeted research with standart test methots would make easier for toxicity analysis. Occupational illness is also requires some legal considerations. It can be said that directly or indirectly new legislations on possible occupational diseases will take place or nedded in the regulation of countries for public health.

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