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ISAR Journal of Multidisciplinary Research and Studies
Abbriviate Tittle- ISAR J Mul Res Stud
ISSN (Online)- 2583-9705
https://isarpublisher.com/journal/isarjmrs

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Applications and the Risks of Nanoparticles in the Healthcare Sector and Industries

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Article History
Received: 18.11.2023
Accepted: 23.11.2023
Published: 01.12.2023

Abstract: *This review paper is focused on the application of nanoparticles in the health sectors, and industries and the risks of nanomaterials in workers and employers in workplaces. Nanotechnology is a facilitating science and new technology that mainly changes matters at a nanosized scale. Nanotechnology and sciences are used for disease diagnosis and screening, drug delivery systems, and health monitoring. Nanoparticles have a great significant purpose in novel drug development due to their very small size and large surface area. As it is broadly used in the industries and health sectors, there is a great risk of exposure in the workers to the nanomaterial in their workplaces through skin contact, inhalation, or ingestion and particularly in powder form can cause the risk of explosion especially particulate nanometer, whereas non-nano sized same substances that not have this effects. The workers and employers should be aware of the potential hazards of nanomaterials in their workplaces, and employers should be taken their appropriate measures to control the exposure, especially in a developing country like Africa*.

Keywords: Nanotechnology, Nanoparticles, Healthcare, Drug delivering, Nanomaterials.

1. INTRODUCTION

A new and dynamically developed science is nanotechnology which has great applications in the medicinal fields such as drug delivery systems, disease diagnosis, and health monitoring. Nanotechnology is not considered a tiny science and should not view as a single technique that means it covers a broad range of structures and huge products. Nanotechnology is producing a new and sophisticated nanosized material and also that design the application of the materials at the molecular and atomic scale [1]. Particles with very smaller than one micron and nanoparticles are particles with at least one dimension smaller than one micron and theoretically as small as atomic and molecular length scales (~0.2 nm) besides they have a shape of regular crystalline and amorphous based structure also their surfaces may act as carriers for liquid droplets or gases which are generally nanoparticles. Nanoparticles have original physical and chemical features of bulk material due to their enormous surface-to-volume ratio, greater interaction, immovability, bioaction, bioaccessibility, and ordered particle size, ordered the discharge of medications, site-definite directing, and ordered arrival of capsules [2].

Characteristics of nanomaterials are generally combined into the high surface also in bulk materials. Physicochemical and biological properties can be developing with the matter in the nanoscale. Nanoparticle levels such as bioavailability improvement, drug distribution that may be varied from body parts like brain, liver, lungs, and other body parts in delivering system in which can be increasing the efficiency and safer of drugs [3]. The challenge of modern medicine that the entire drug dose not absorbed by the patient body and therefore, drugs can be ensured to the specific area in the body with greater accuracy and precision as well as it can be formulated with the active components better permeates cell membranes, reducing the required dose by the scientists using nanotechnology. However, there is little knowledge about the risk of nanomaterial by the worker and employers in the workplace, especially in the developing country. The services of healthcare can be varying in locations that include clinics, hospitals, and mobile emergency centers and homes.

1.1 Properties of a Nanomaterial at the Nanoscale

Particles that have a diameter smaller than about one hundred nanometers (100 nm) can be considered nanoparticles. Nanoparticles in other word defined as nano-objects and it has all three dimensions in the range of 1-100 nm [4]. It includes nanofibres and nanotubes, composite materials, and nanostructured surfaces. As shown in **Fig. 1**, in most cases, nanoparticles show that different physical and chemical, as well as biological features, also thus acts differently with the materials of the same rough structure of the molecular composition of matter. Nanomaterials have a high fixed surface or interface area and they are more reactive than the same thicker arrangements with the same mass as many reactions of biological and chemical reactions that take place at the material surfaces. Because nanomaterials are much small in size, they easily move through the biological systems in the body and have a high ability to across or penetrate the cell membrane in the cell tissues that were taken by the cell-like lung, brain, and other cell tissue and therefore they cause unexpected and unusual exposure [5].

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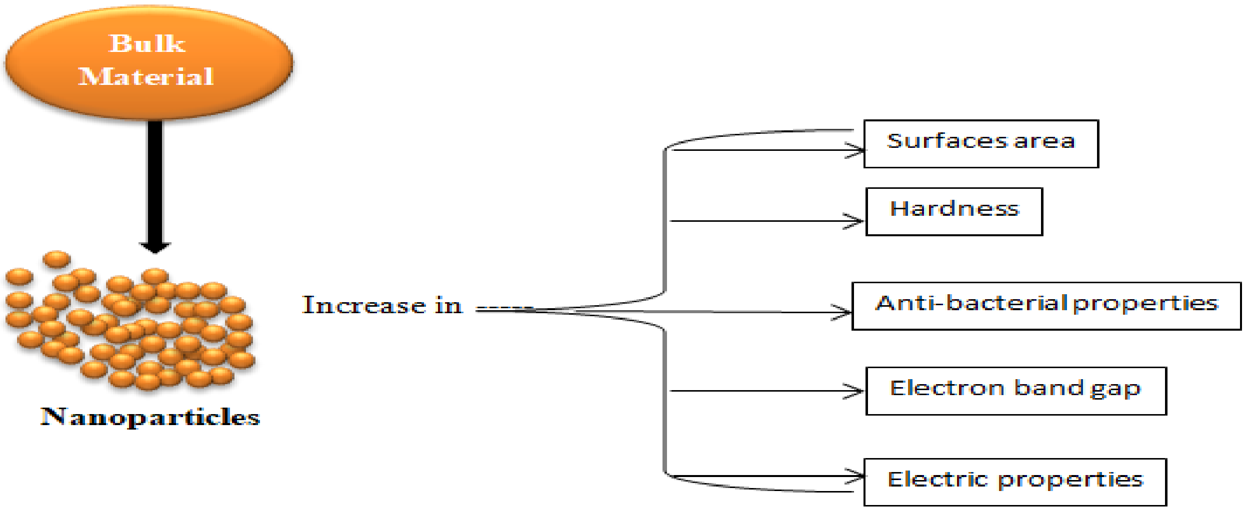

Fig. 1: Bulk materials cannot be implemented in most fluid products unless made very small [6]

For the surface of nanoparticles, metal ions, minor molecules, and polymers most important to functionalized. As shown in **Table 1,** a broad range of material properties can be selectively adjusted by structuring at the nanoscale.

Table 1: Some changeable properties of nanomaterial **[7]**

Properties	**Examples**
Catalytic	✓ Due to the higher ratio of surface-to-volume, catalytic efficiency is high
Electrical	✓ Increase in metallic resistance ✓ Increase in ceramic and magnetic nanocomposite electrical conductivity
Magnetic	✓ Magnetic coactivity and superparamagnetic behavior increase
Mechanical	✓ The hardness and toughness of metals and alloys increased ✓ The ductility and superplasticity of ceramics improved
Optical	✓ The spectral properties of optical absorption and fluorescence are shifted ✓ Quantum efficiency of semiconductor crystals increase
Biological	✓ The biocompatibility is improved ✓ Permeability is increased in membranes, blood-brain barrier

1.1.1 Catalytic properties

Every nanoparticle will have a precise extraordinary surface area to volume ratio. This means for catalyzing the reaction of the percentage of atoms that available on the surface of the particles with the inverse of the radius of the particles [8].

1.1.2 Optical properties

The valuable properties of nanoparticles are optical properties in which its application includes the optical detector, solar cell, photo-electrochemistry, photo-catalysis, imaging, laser, biomedicine, and sensor [9]. Diameters of particles that less than 10 nm are quantum dots which are a nanoparticle subset. The small sizes of the particle that affect the intrinsic bandgap of the semiconductor are semiconductor nanoparticles which are quantum dots. The bonding and antibonding configuration of the crystal lattice causes valence and conduction band in the semiconductor [8]. As shown in **Fig. 2**, the parameters like shape, size, doping, and surfaces of the nanomaterial affect the photosensitive characteristics [9].

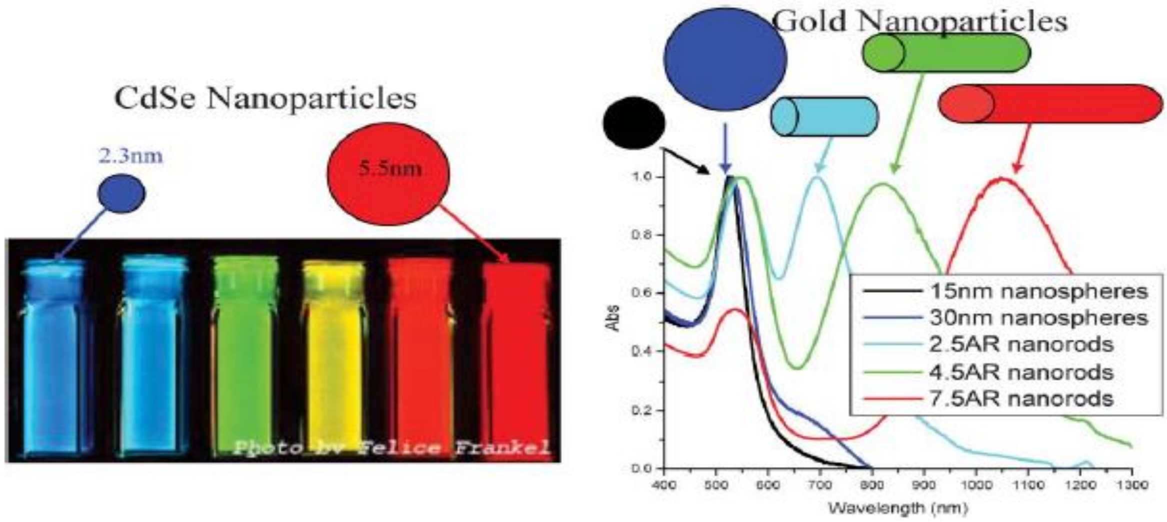

Fig. 2: Fluorescence emission of (CdSe) ZnS quantum dots of various sizes and absorption bands of numerous sizes and shapes of gold nanoparticles [9].

1.1.3 Electrical properties

Electrical properties are the most important characteristics of nanoparticles. Nanoparticles have notable electrical, quantum effect, and lattice characteristics due to their very small size and great symmetrical structure. Nanoparticles can act as metals. They can carry a current which is 100 times greater than metals and semiconductors or insulators and this very important to make materials with high temperature [10, 11].

1.1.4 Mechanical properties

Nanoparticle characteristics mainly differ from the individual atoms, molecules, and wholesale materials. Various mechanical parameters may be surveyed to identify the mechanical nature of nanoparticles, for example, hardness, stress, elasticity, strain, abrasion, and linkage [12, 13]. The most important characteristics of the nanoparticle are a mechanical property that studies the bulk metallic and ceramic materials, the influence of grain size, superplasticity, the influence of porosity, filled polymer composites, particle-filled polymers, and polymer-based nanocomposites filled with platelets, carbon nanotube-based mixtures [9].

1.1.5 Magnetic properties

The most important characteristic of nanoparticles is their magnetic behavior which is of great interest for investigators from a diverse range of disciplines for instance catalysis of heterogeneous and homogeneous, attractive fluid, biomedicine, and data storing magnetic resonance image (MRI). When the size of nanoparticles is < critical value i.e. 10-20 nm, it is the best performance [12, 14]. Nonmagnetic metals like bulk gold and platinum at nanosize can act as magnetic properties. The surfaces of atoms are different from the bulk materials and also can be modified by collaboration with chemical samples [9].

2. Methods of Nanoparticles Synthesis

Several materials are used to synthesize nanoparticles, such as organic compounds like polysaccharides, protein molecules, and polymers. Nanoparticles can be manufactured in different ways, but out of many types, there are two most common methods. Based on the **fig.3**, the production of nanoparticles can be generalized from top-down and bottom–up methods [15]. The first is the top-down or breakdown method of synthesis, in which the solid sample is broken up by external forces and the second, is the bottom-up or build-up method, in which atoms transform or molecules condense.

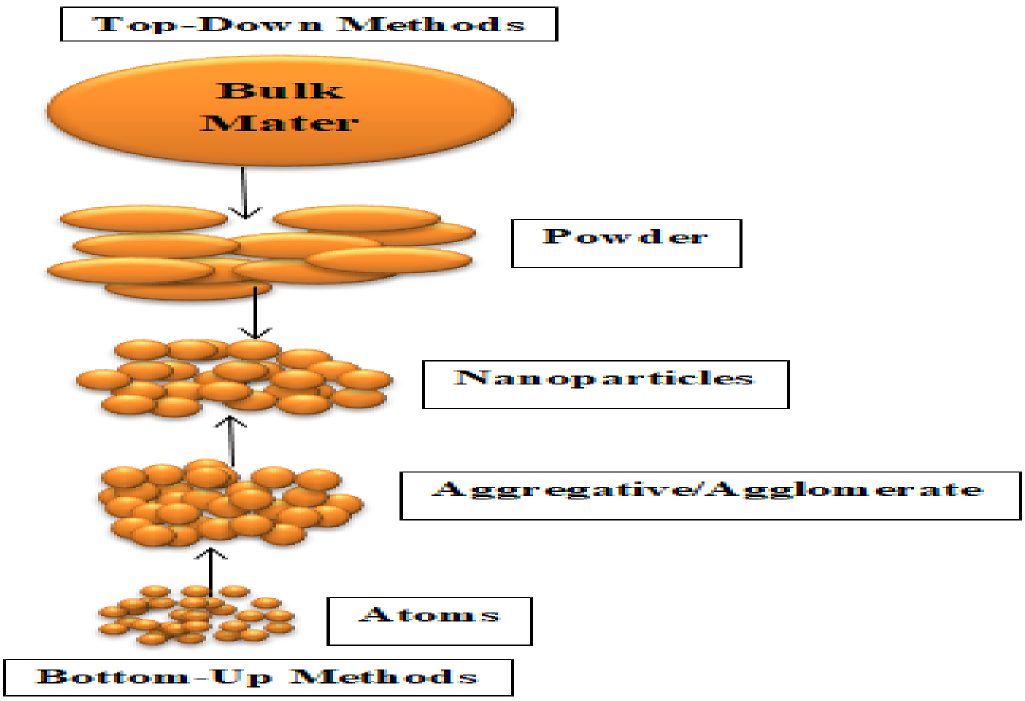

Fig. 3: The two methodologies of nanoparticles production [15]

2.1 Top-down method

From **Fig.4**, we can observe that larger materials undergo a process by removing matter until only the nanometric dimensions are reached. However, this approach requires the use of grinding; lithography, etching, and engineering precision are the most common techniques [3]. It includes the structural decomposition of the coarser-grained structure as the result of this severe flexible deformation. It is a more popular method because it uses inexpensive equipment; it is simpler and suitable for producing amorphous or nanocrystalline alloy particles, elemental or compound powders [3].

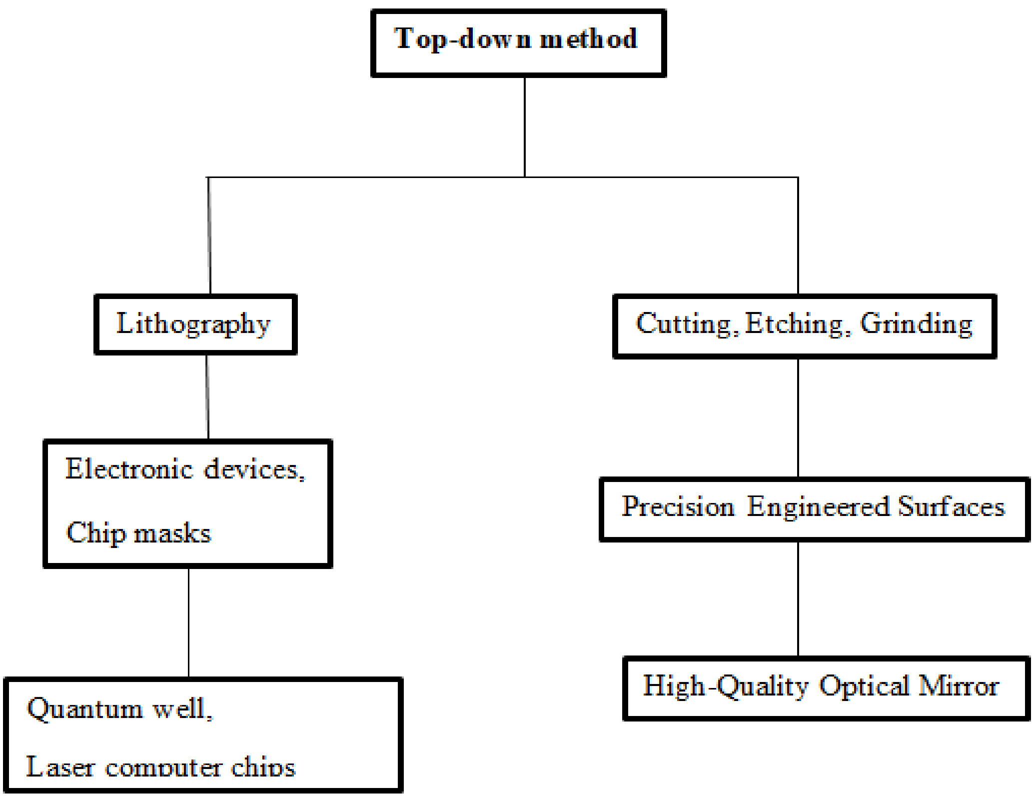

Fig.4: The top-down method of nanoparticles preparation [3]

The top-down method further categorized in to dry method and wet method. There is an increase in the surface energy in the grain refining of particles that causes an increase in particle aggregation. The solid sample is ground by different methods such as shock, friction, and compression using a hammer mill, a roller mill, ball mill, and tumbling mill in the dry grinding method. However, the solid sample is ground by using a vibratory ball mill, a tumbling ball mill, a planetary ball mill, and a son. In the wet processing method, the condensation of nanoparticles is easily prevented than in dry methods as the result can obtain highly spread nanoparticles [10].

2.1 Bottom-up method

This method starts from a very small unit of materials, individual molecules, or even atoms, and assembles these building-block units into larger structures–clearly the domain of chemistry [16]. Limiting the concentration is one of the ways used for controlling the size of the nanoparticles as well as this methodology can be influenced by on the standard of super-saturation to control particle dimension [17]. This method can be carried out in three ways, such as chemical synthesis, self-assembly, and positional assembly [18].

As shown in **Fig. 5**, the bottom-up methods use chemical, electrical as well as physical forces to form a nanomaterial atom-by-atom or molecule-by-molecule by starting with component materials (often gases or liquids) [3, 19].

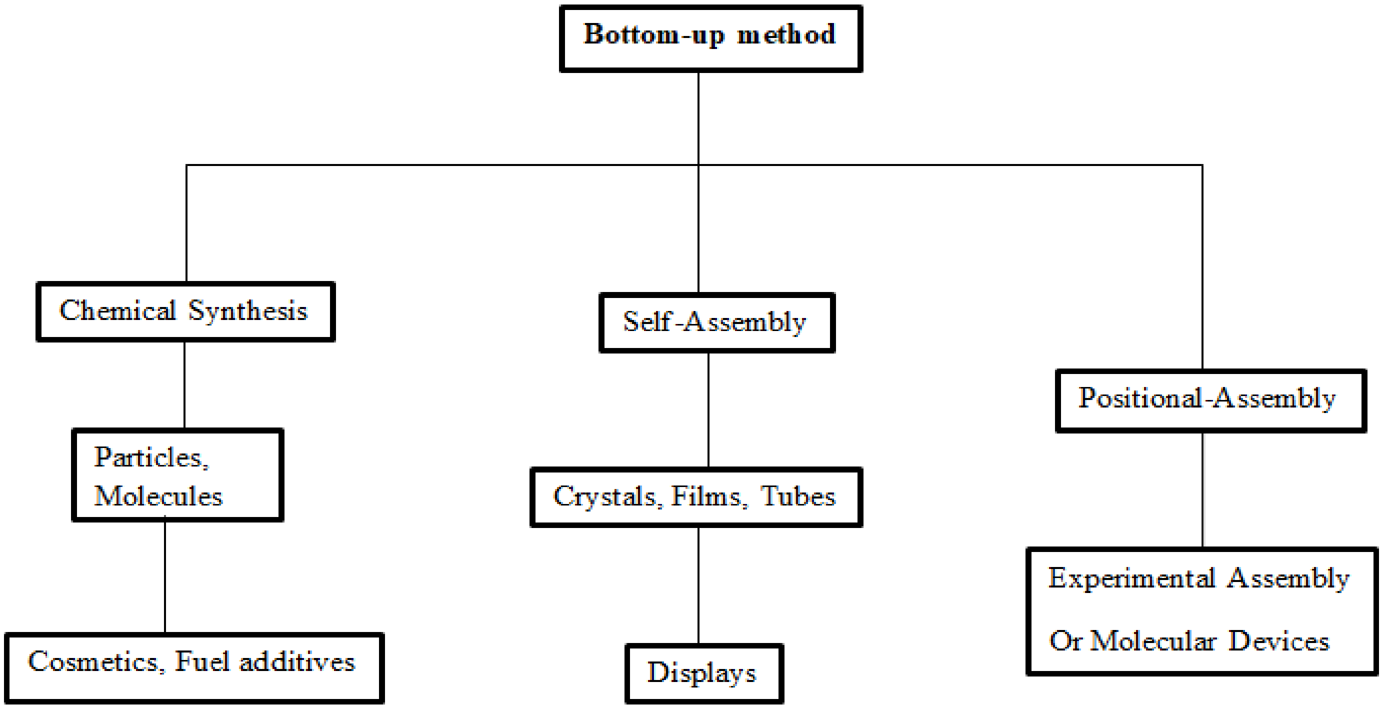

Fig.5: The bottom-up method of nanoparticles preparation [3]

The bottom-up method can be further divided into the gaseous phase and liquid phase method. In the gaseous phase approach, there is a chemical and physical vapor deposition method that involves a chemical reaction and uses cooling of the evaporated material respectively. Organic impurity occurrences are lower in the gaseous phase method than in the liquid phase method. Mainly, nanoparticles are prepared by the liquid phase method, and they can be subdivided into liquid-liquid and sedimentation methods. In the liquid-liquid method, nanoparticles are produced in various shapes and sizes by the chemical reduction of metal ions [10].

3. Applications and Risks of Nanomaterials in the Healthcare Sector and Industry

3.1 Applications of Nanomaterials in the Healthcare Sector

Nanotechnologies have basic inventions that contribute to human health and environmental safety in different ways, like cleaning drinking water, increasing efficiency of energy conversion, and energy storage. Nanomaterials can circulate through blood vessels in the body by moving in and out of the vessels, and they can interact with biomolecules on the cell surface and inside cells in various areas of the human body by entering cells [20]. Due to their very small size, nanoparticles have the potential to penetrate certain protective cell membranes in the body, so they can be used as carriers for targeted drug delivery. As a result, nanomaterials can easily circulate through the blood vessels and have a high ability to penetrate the cell membrane, have a high potential to detect diseases and prevent diseases in new ways. As shown in **Table 2**, the physical and chemical properties of the nanomaterial generally allow us to monitor, prevent, and diagnose diseases, such as cancer, cardiovascular diseases, and neurodegenerative and psychiatric diseases, diabetes, and infectious diseases [21].

Table 2: Applications of some of the types of nanomaterials in the health sector.

Type of nanomaterial	Applications in healthcare
Metallic particles (e.g. iron (III) oxide, gold or silver))	- Hyperthermia cancer treatment - Selective magnetic bioseparations - Covered with antibodies to cell-specific antigens, for departure from the surrounding matrix - Membrane transport studies - Drug delivery - Magnetic Resonance Imaging contrast agent [22]
Silver nanoparticles	- Anti-microbial agent - Incorporated into a wide range of medical devices, including bone cement, surgical instruments, surgical masks [22]
Gold shell nanoparticles	- Improve solubility of drugs - Permit further conjugation [22]
Carbon nanomaterials [fullerenes and carbon nanotubes (CNTs)]	- Buckyballs' (football-shaped structures made of 60 carbon atoms) are used in drug delivery systems to support the optimal transport and release of medicines to the right target inside the body [22, 23] - Coatings for prosthetics and surgical implants - Functionalized CNTs: ✓ for therapeutic delivery ✓ for biomedical applications such as vascular stents and neuron growth and neuron growth and regeneration ✓ gene therapy, as a strand of DNA, can be bonded to a nanotube
Quantum dots	- Tag multiple biomolecules to monitor complex cellular changes and events associated with diseases - Optics technology [22, 24] - Disease diagnosis and screening technologies
Dendrimers	- Polymerized macromolecules—highly branched structures with interior nanocavities or channels with properties different from those on the exterior - Used as a transporter for a diversity of drugs (e.g. anti-cancer, anti-viral, anti-bacterial, etc.) with the capacity to improve solubility and bioavailability of poorly soluble drugs [22]
Lipid-based nanoparticles	- Can fuse with the cell membrane and deliver molecules inside the cells
Ceramic nanoparticles	- Inorganic systems used as drug vehicles (if porous and biocompatible); used in cosmetic applications (zinc oxide, titanium dioxide) [22]
Nanotubes, nanowires, magnetic nanoparticles	- Disease diagnosis and screening technologies, including 'lab on a chip [22, 24]

Nanoparticles have a great ability to deliver drugs in the optimal amount range, resulting in increasing the therapeutic efficiency of the drugs and weakened side effects which have more interest in every branch of medicine [12, 25]. Polymers and hydrophilic nanoparticles can be used to deliver the drug to the targeted part of the body and minimize the side effects [12].

3.2 Applications of Nanomaterial in the Industries

Today, industrial development, therefore, considers nanoparticles as an extended toolbox containing traditionally difficultly to realize properties. **Fig. 6** shows how nanomaterials can be used in a variety of industries, including food processing and drinking, agricultural areas, textile industries, and so on [7]. Nanoparticles can have different applications in mechanical industries, particularly in lubricants, coating, and adhesive applications as shown by their mechanical properties. When nanoparticles are inserted into metals and polymer matrix, the tribological properties at the nanoscale can be controlled to increase mechanical strength. Nanoparticles can improve low friction and wear in the lubricated contact area because of their rolling mode [12, 13].

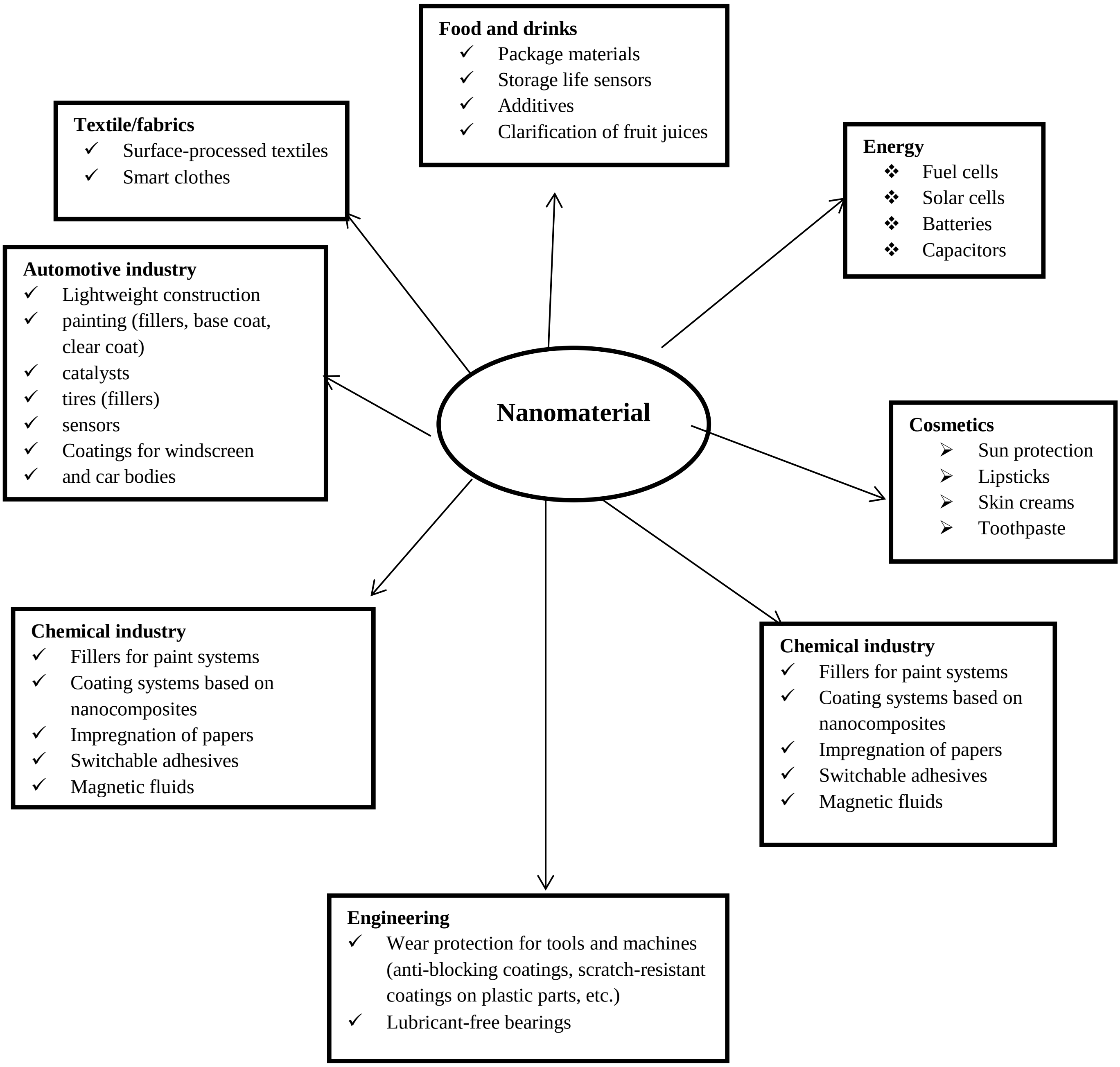

Fig.6: Overview on applications of nanomaterial-based products in different areas [7]

Nanotechnology can be used to develop textile characteristics, for instance fabric softness, toughness, breathability, water repellency, fire retardant, anti-microbial characteristics, and the like in fibers, yarns, and fabrics, and nanoparticles and nanomaterials are being used for water and wastewater treatment [26].

3.3 Risks of Nanomaterials in the Healthcare Sector and Industries

Workers may be exposed to nanoparticles during the manufacturing of these materials, transportation of these materials, formulation of these materials into products, and handling of these materials. The nano-scale materials have a high frequency of exposure to the worker due to higher concentrations and high surface area. Special attention is required in the workplace. The study concluded that occupational exposures of Nanomaterials are most likely to happen during handling and bagging of the materials and there is a high risk of dermal uptake [**27**].

Parts of the human body, like the skin, lungs, and gastrointestinal region directly or indirectly interact with the environment. Nanoparticles may be discharged to the surroundings throughout fabrication, usage, additional treating, and removal. Due to their unique shape, small size, composition distribution, reactivity, and morphology of nanoparticles are estimated to affect their toxicity, creating their toxicity assessment complex as well as they may stay in the human environment and the body for a longer period compared to their larger corresponding item [**28].** Not all nanoparticles produce adverse health effects and the effects or toxicity of nanoparticles depend on several factors, including morphology, size, shape, aggregation, crystallinity, etc. Some of the main effects of nanoparticles found in the lung include cell tissue damage, inflammation, chronic toxicity, oxidative stress, cytotoxicity, and tumor formation, among other things, while nanomaterials also affect the cardiovascular system [**24**]. As illustrated in **Fig. 7**, nanomaterials can enter the human body through several pathways, potentially posing a risk to occupational health:

- The most common method is inhalation, in which exposure to airborne nanomaterials at work can deposit in the lungs and respiratory tract. As the result of inhalation, they can cross to blood vessels and reach various body organs and tissues as well as reach the brain through the olfactory [**29, 30**].
- As shown in **Fig. 7,** nanoparticles can enter the body through the ingestion transfer from hand to mouth from the contaminated surface or by contaminated food or water ingestion as well as nanomaterials also ingested as the result of inhalation of nanoparticles [**29, 30].**
- Nanomaterials have a high potential to penetrate dermal organs. As a result, they can enter the body in this way and to less extent damage the skin surface [**31**].
- Nanomaterials can enter into the blood circulatory systems that are related to blood clots, heart diseases, arrhythmia, and cardiac death, etc. [**32].**

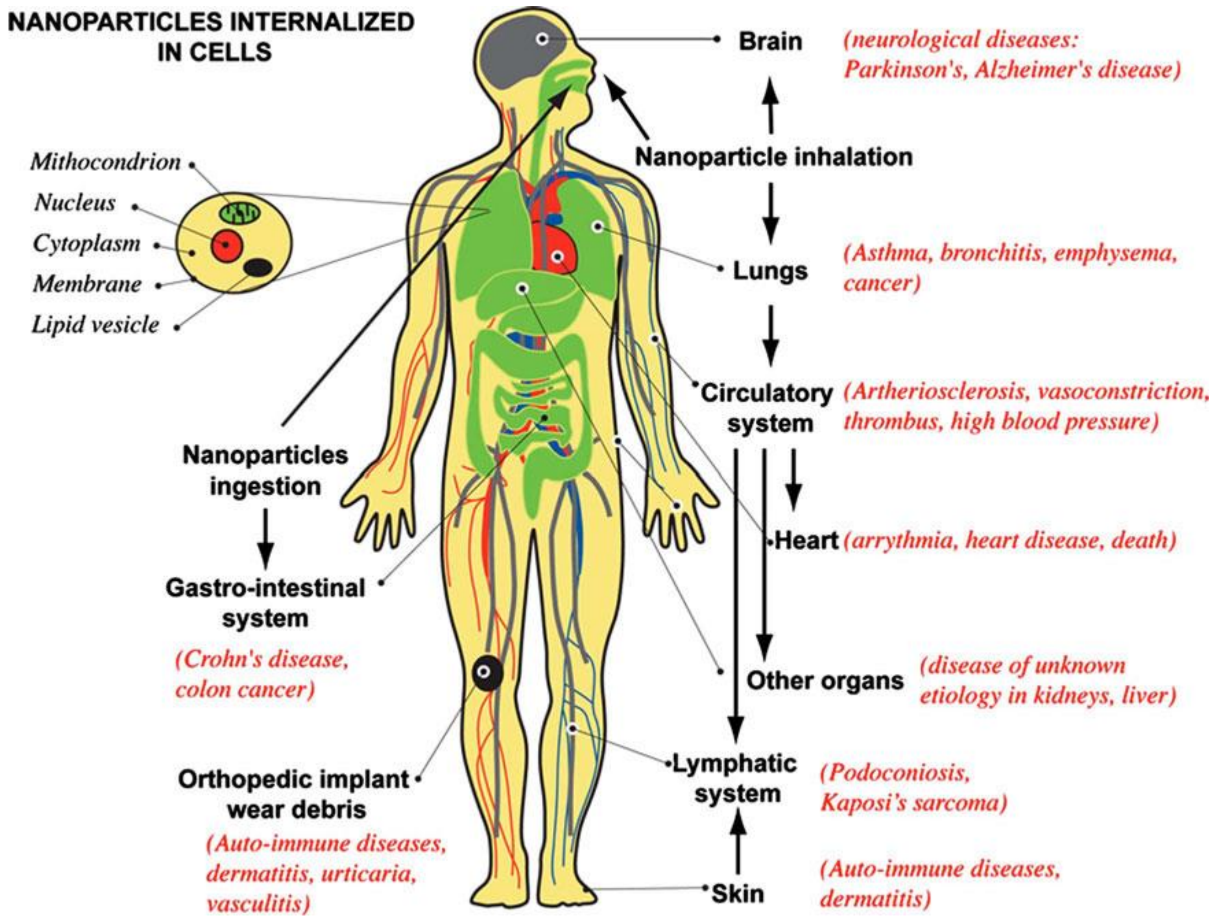

Fig. 7: Diagrams of the human body with paths of exposure to nanoparticles, affected body parts, and related diseases from epidemiological studies [**32**].

In standard atmospheric environments, nanoparticles can form agglomerates or aggregates greater than 100 nm, so changing their nano-specific characteristics. However, nanoparticles can be released from softly assured groups, and definite environments, they can be discharged from further toughly assured aggregates. Just before determine whether this be situated promising, research should be conducted into lung fluid subsequently inhalation of agglomerates or else entire sum [24, 33]. Nanomaterials found in the form of agglomerates of as entire sum should be agglomerates as well as entire sum containing nanomaterials should be taken into consideration in the workplace risk assessment. As shown in the **Fig. 8**, after inhalations or ingestion of nanoparticles, they simple distributed throughout the body by the blood circulation that cab causes to different illness and metabolism disorder.

Some environments that exposure to nanomaterials in healthcare can occur during [29]:

- Extra disposal of nano drugs from patients
- Spills of nanomaterials
- Handling of items containing nanomaterials
- Consumption of food and beverages that are contaminated with nano-drugs and
- Cleaning and maintenance of areas where nano-drugs are handled.

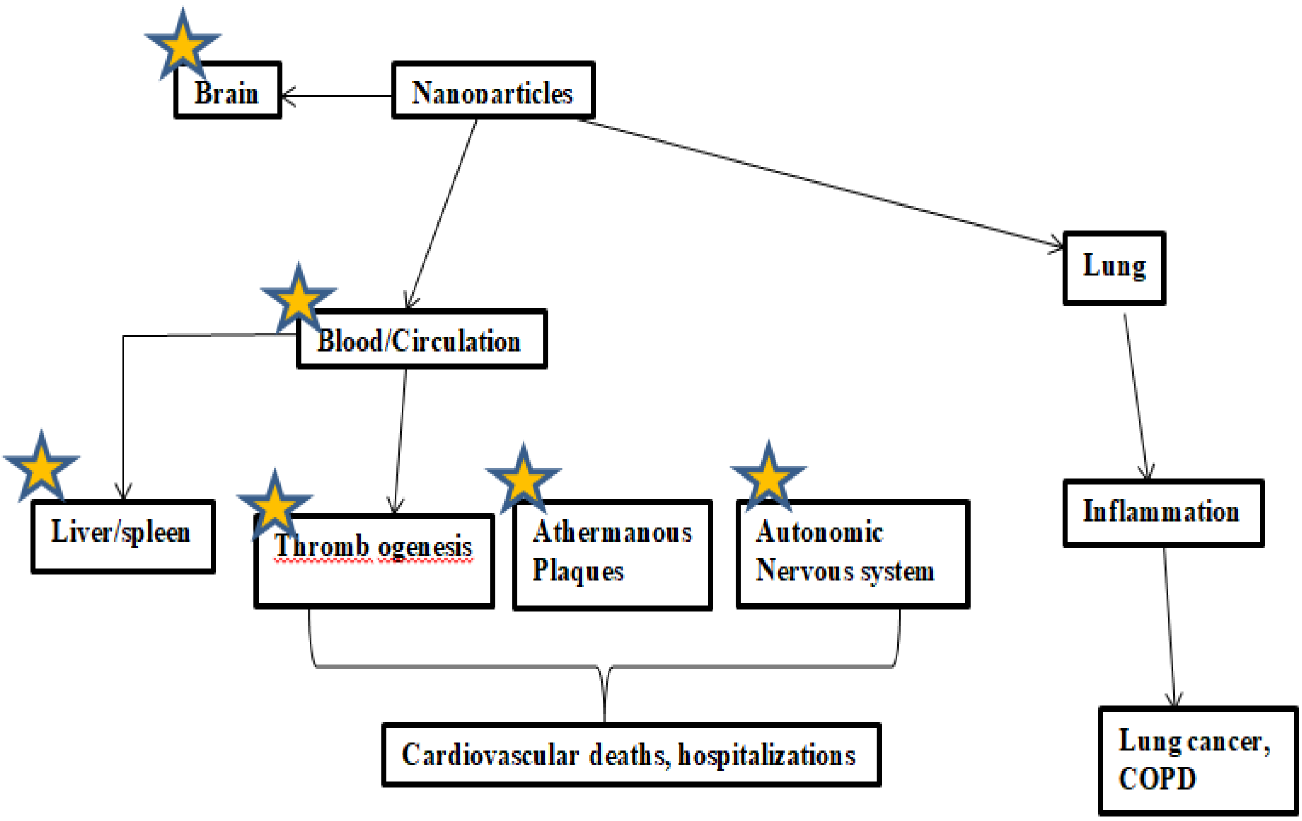

Fig. 8: Summary of potential human effects of nanoparticles [29]

3.3.1 Risk Assessment of Nanomaterials

Knowledge of the identity of the toxicity or risks of the products besides the exposure levels at the different workstations is considered by way of hazard valuation [34]. Exposure to nanomaterials is becoming one of the most significant risks in the workplace [35], especially for developing countries like African countries. The risks and occupational exposures of workers or employers to nanoparticles are caused by a severe lack of knowledge in these critical areas for assessing danger or risk, particularly in African countries [34]. In general, to control the risk and exposure of nanomaterials, there are three approaches, such as engineering techniques, administrative means, and individual protective equipment [36].

Employers should measure worker contact to nanomaterials to find the control actions desired and conclude if the controls used are active in decreasing exposures by [34]:

- Detecting and describing processes and job tasks where workers may be exposed to nanomaterials;
- Identifying the physical state of the nanomaterials (dust, powder, spray, or droplets)

- Determining paths or methods of contact (breath, membrane interaction, or digestion) of particulates, slurries, suspensions, or solutions of nanomaterials;
- Determining what extra controls may be needed based on the exposure valuation results as well as evaluating the effectiveness of controls already in place.

3.3.2 Prevention

Companies must guarantee that each worker receives acceptable and occasionally repeated health and welfare information and training. Therefore, the obligatory workshop risk assessment and the hierarchy of regulator actions like elimination, substitution, technical procedures at source, organizational actions, and individual caring apparatus (PPE) set in these employees' safety directives also apply to workplaces in the healthcare sector and nanomaterials [37]. There are many types of limitations related to the nanoparticles at the workplaces that are carried out:-

1. Knowledge of the hazardous properties of nanomaterials;
2. To identify the source of emission and nanomaterials, the availability of methods and devices
3. The user chains down when the nanoparticles or products containing the nanomaterials are used or processed that nanomaterials present in the mixture or articles.

Generally, there are some methods that employers may use to reduce the potential of nanoparticles at the workstation [38].

a. Personal Protective Equipment (PPE)

It is the last mark of protection in the hierarchy of contact regulators which provides employees with proper individual protective apparatus such as respirators [29, 39] gloves as well as protecting wear. The investigation is ongoing interested in the suitable choice of lab-coat material as it is related to nanoparticle penetration.

1. Respirators

Local ventilation systems cannot be sufficient in the activities that relate to airborne nanomaterials, for instance, milling of bridges or implants that contain nanomaterials, grinding, sanding. As a result, respiratory protection such as gas mask respiratory, dust masks, filtering face-piece respiratory, and powered air-purifying respirators [39] must be used.

2. Gloves

Most of the time gloves are used in the chemical hazards and in the health sectors which are effects from the synthetic polymer formed to protect from the nanomaterials [40]. For particular nanomaterials, the effectiveness of the glove depends on its form in the workplaces which is tested with the supplier of the glove. The actual flow rate of the nanomaterial in the glove depends on the width plus usage of two pairs of gloves recommended at the same times [41].

3. Protective clothing

Best prevent the method of dermal contact to nanoparticles; there is no guide to the choice of other wear.

b. Engineering Controls

Most workplaces in the healthcare sector cannot have a methodological system for protecting or reducing exposure to nanomaterials, for instance, closed systems that create a physical barrier between a person and the nanoparticles due to the nature of the work [42]. This controlling method has used the application of nanotechnology that is similar to those that are currently used in controlling aerosols (gases, dust, chemical vapors, etc.) found in other laboratory applications and/or processes [43].

c. Elimination and substitution

As with all other hazardous materials, the appropriate measure of elimination and substitution must be given priority over other prevention measures to prevent workers from exposure to nanoparticles. If the nanoparticles are possessed, workers should be eliminated or substituted by other less toxic or hazardous ingredients. Organizational controls, which are policies and procedures, are one method for reducing and preventing worker exposure to nanomaterials or risk [44].

d. Administrative controls

One most important method to reduce and preventing of worker exposure to nanomaterial or risks is organizational controls which are policies and procedures [45]. These methods mainly include a nanoscale material hygiene plan; preparation, training in, and monitoring use of standard operating procedures; reduction of exposure time; modification of work practices; and good workplace and housekeeping practices. These also provide hand washing facilities and information that encourages the use of good hygiene practices. To clear out the nanomaterial spills, the appropriate procedure must be established and the surfaces would be decontaminated to minimize employee contact [38].

CONCLUSIONS

Nanotechnology and nanoparticles are a fast-growth or expanding and emerging interdisciplinary field of technology. Nanotechnology is a science that studies materials on a nano-dimensional scale that is completely different from the same substances with larger compositions or dimensions. Nanoparticles have many applications in other fields, not only in healthcare centers but his review is focused only on the application and risks of nanoparticles in the healthcare sector. The physicochemical properties of nanomaterials and health effects must give more attention at the workplaces especially in developing countries. In developing countries like Africa, the full information about the chemical and physical properties of nanomaterials is still not addressed or completed. The suitable hazard assessment and prevention systems must be improved and continue in these countries.

Conflicts of Interest

The author declares that there is no conflict of interest for this review.

Acknowledgments

The author acknowledges the Injibara University for his moral supporting.

Author Contributions:

Elmineh Tsegahun and Alemu Talema performed all the manuscript preparation, analyzed the data, and wrote the paper.

Funding

No funding has been received to conduct this study.

REFERENCES

1. Hagens, W.I., Oomen, A.G., de Jong, W.H., Cassee, F.R. and Sips, A.J., 2007. What do we (need to) know about the kinetic properties of nanoparticles in the body?. *Regulatory toxicology and pharmacology*, *49*(3), pp.217-229.
2. Ulhaq, Z.S., 2019. Brain aromatase modulates cardiac functions in embryonic zebrafish. *International Journal of veterinary science and medicine*, *7*(1), pp.31-34.
3. Zahin, N., Anwar, R., Tewari, D., Kabir, M.T., Sajid, A., Mathew, B., Uddin, M.S., Aleya, L., and Abdel-Daim, M.M., 2019. Nanoparticles and their biomedical applications in health and diseases: special focus on drug delivery. *Environmental Science and Pollution Research*, pp.1-18.
4. Santos, C.S., Gabriel, B., Blanchy, M., Menes, O., García, D., Blanco, M., Arconada, N. and Neto, V., 2015. Industrial applications of nanoparticles–a prospective overview. *Materials Today: Proceedings*, *2*(1), pp.456-465.
5. Lövestam, G., Rauscher, H., Roebben, G., Klüttgen, B.S., Gibson, N., Putaud, J.P. and Stamm, H., 2010. Considerations on a definition of nanomaterial for regulatory purposes. *Joint Research Centre (JRC) Reference Reports*, *80*, pp.00-41.
6. Stark, W.J., Stoessel, P.R., Wohlleben, W. and Hafner, A.J.C.S.R., 2015. Industrial applications of nanoparticles. *Chemical Society Reviews*, *44*(16), pp.5793-5805.
7. Nass, R., Remškar, M. and Žumer, M., 2004. *Industrial application of nanomaterials-Chances and risks: Technology analysis*. Future Technologies Division of VDI Technologiezentrum.
8. Christian, P., Von der Kammer, F., Baalousha, M. and Hofmann, T., 2008. Nanoparticles: structure, properties, preparation, and behavior in environmental media. *Ecotoxicology*, *17*(5), pp.326-343.
9. Alagarasi, A., 2013. Chapter-Introduction to Nanomaterials. *Indian Institute of Technology Madras*, pp.1-24.
10. Horikoshi, S.A.T.O.S.H.I. and Serpone, N.I.C.K., 2013. Introduction to nanoparticles. *Microwaves in nanoparticle synthesis: fundamentals and applications*, pp.1-24.
11. Kaluza, S., Balderhaar, J.K., Orthen, B., Honnert, B., Jankowska, E., Pietrowski, P., Rosell, M.G., Tanarro, C., Tejedor, J. and Zugasti, A., 2009. Literature Review-Workplace exposure to nanoparticles. *EU-OSHA-European Agency for Safety and Health at Work*.
12. Khan, I., Saeed, K. and Khan, I., 2019. Nanoparticles: Properties, applications, and toxicities. *Arabian journal of chemistry*, *12*(7), pp.908-931.
13. Guo, D., Xie, G. and Luo, J., 2013. Mechanical properties of nanoparticles: basics and applications. *Journal of Physics D: applied physics*, *47*(1), p.013001.
14. Reiss, G. and Hütten, A., 2005. Applications beyond data storage. *Nature Materials*, *4*(10), pp.725-726.
15. Roy, A. and Bhattacharya, J., 2015. *Nanotechnology in industrial wastewater treatment*. IWA Publishing.
16. Chemical Industry Vision 2020, Technology Partnership. Report of the US Chemical Industry Working Group 2003.
17. Christian, P., Von der Kammer, F., Baalousha, M. and Hofmann, T., 2008. Nanoparticles: structure, properties, preparation, and behavior in environmental media. *Ecotoxicology*, *17*(5), pp.326-343.
18. Pareek, V., Bhargava, A., Gupta, R., Jain, N. and Panwar, J., 2017. Synthesis and applications of noble metal nanoparticles: a review. *Advanced Science, Engineering and Medicine*, *9*(7), pp.527-544.
19. OECD, A., 2005. Opportunities and risks of Nanotechnologies. *The report in co-operation with the OECD International Futures Programme*
20. Lauterwasser, C., 2005. Opportunities and risks of Nanotechnologies. *The report in cooperation with the OECD Futures Programme. London/Ismaning*.
21. Filipponi, L. and Sutherland, D., 2010. –Overview of Nanomaterials. *NANOYOU Teachers Training Kit in Nanoscience and Nanotechnologies*, pp.18-46.
22. Leka, S., Van Wassenhove, W. and Jain, A., 2015. Is psychosocial risk prevention possible? Deconstructing common presumptions. *Safety Science*, *71*, pp.61-67.
23. Lauterwasser, C., 2005. Opportunities and risks of Nanotechnologies. *The report in cooperation with the OECD Futures Programme. London/Ismaning*.
24. Ellis, J.R., Nanomaterials and Their Potential in Therapy, 2012. Available at: http://www.mddionline.com/blog/devicetalk/nanomaterials-and-their-potential-therapy (accessed 20 October 2012)
25. Alexis, F., Pridgen, E., Molnar, L.K. and Farokhzad, O.C., 2008. Factors affecting the clearance and biodistribution of polymeric nanoparticles. *Molecular Pharmaceutics*, *5*(4), pp.505-515.

26. Santos, C.S., Gabriel, B., Blanchy, M., Menes, O., García, D., Blanco, M., Arconada, N. and Neto, V., 2015. Industrial applications of nanoparticles–a prospective overview. *Materials Today: Proceedings*, *2*(1), pp.456-465.

27. Hristozov, D. and Malsch, I., 2009. Hazards and risks of engineered nanoparticles for the environment and human health. *Sustainability*, *1*(4), pp.1161-1194.

28. Sahu, S.C. and Hayes, A.W., 2017. Toxicity of nanomaterials found in the human environment: a literature review. *Toxicology Research and Application*, *1*, p.2397847317726352.

29. Murashov, V., 2009. Occupational exposure to nanomedical applications. *Wiley Interdisciplinary Reviews: Nanomedicine and Nanobiotechnology*, *1*(2), pp.203-213.

30. Hodson, L., Methner, M. and Zumwalde, R.D., 2009. Approaches to safe nanotechnology; managing the health and safety concerns associated with engineered nanomaterials...

31. Gratieri, T., Schaefer, U.F., Jing, L., Gao, M., Kostka, K.H., Lopez, R.F. and Schneider, M., 2010. Penetration of quantum dot particles through human skin. *Journal of biomedical nanotechnology*, *6*(5), pp.586-595.

32. Buzea, C., Pacheco, I.I. and Robbie, K., 2007. Nanomaterials and nanoparticles: sources and toxicity. *Biointerphases*, *2*(4), pp.MR17-MR71.

33. Haase, A., Rott, S., Mantion, A., Graf, P., Plendl, J., Thünemann, A.F., Meier, W.P., Taubert, A., Luch, A. and Reiser, G., 2012. Effects of silver nanoparticles on primary mixed neural cell cultures: uptake, oxidative stress, and acute calcium responses. *Toxicological Sciences*, *126*(2), pp.457-468.

34. Occupational Safety and Health Administration. "OSHA Fact Sheet: Working Safely with Nanomaterials." *URL: https://www. OSHA. gov/Publications/OSHA_FS-3634. pdf [retrieved 21 Nov. 2019]* (2017)

35. European Agency for Safety and Health at Work (EU-OSHA)., Previsiones de los expertos sobre los riesgos químicos emergentes en relación con la seguridad y la salud en el trabajo. Facts, 84, 2009

36. Ménard L, 2004. Principes généraux de maîtrise. Dans Manuel d'hygiène du travail. Du diagnostic à la maîtrise des facteurs de risque, Edited by Modulo-Griffon, Montréal, p 541-551

37. European Parliament and Council Directive 2004/37/EC on the protection of workers from the risks related to exposure to carcinogens or mutagens at work (Sixth individual Directive within the meaning of Article 16(1) Directive 89/391/EEC). Available at http://eurlex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:32004L0037R%2801%29: EN:HTML

38. OSHA Factsheet. Working Safely with Nanomaterials. Available at https://www.osha.gov › publications › OSHA_FS-3634

39. Yokel, R.A. and MacPhail, R.C., 2011. Engineered nanomaterials: exposures, hazards, and risk prevention. *Journal of Occupational Medicine and Toxicology*, *6*(1), pp.1 27.

40. Golanski, L., Guiot, A., Rouillon, F., Pocachard, J. and Tardif, F., 2009. Experimental evaluation of personal protection devices against graphite nanoaerosols: fibrous filter media, masks, protective clothing, and gloves. *Human & experimental toxicology*, *28*(6-7), pp.353 359.

41. Klenke, M., 2008. First results for safe procedures for handling nanoparticles. *Dissemination Report, Nanosafe*.

42. OSHWiki. Nanomaterials in the Healthcare Sector: Occupational Risks and Prevention,(2017).Available at https://oshwiki.eu/wiki/Nanomaterials_in_the_Healthcare_Sector:_Occupational_Ri ks_and Preven.

43. National Institutes of Health Office of Research Services Division of Occupational Health and Safety, Nanotechnology Safety and Health Program,(2014). Available at https://www.ors.od.nih.gov/sr/dohs/Documents/Nanotechnology%20Safety%20and%20Health%20 Program.pdf.

44. E-FACTS. Nanomaterials in the healthcare sector: occupational risks and prevention. Available at https://osha.europa.eu/en/tools-and-publications/publications/e-facts/e-fact-73-nanomaterials-in-the-healthcare-sector-occupational-risks-and-prevention.

45. Schulte P, Geraci C, Zumwalde R, Hoover M, Kuempel E: Occupational risk management of engineered nanoparticles. *J Occup Environ Hyg* 2008, 5: 239–249. 10.1080/15459620801907840.

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