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Prospect of nanotechnology: A brief review

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Nanotechnology has offered a great improvement in science, engineering, medicine, biomedical engineering, food technology, packing technologies, clothes, robotics, and computing from the beginning of twenty-first century. As the maximum potential of scientific discovery always contains some good and bad effects in human civilization, nanotechnology is not an exception among them. The major drawbacks consist of economic disruption and possible threats to security, privacy, health, and environmental hazards, etc. The advancements and benefits of nanotechnology are discussed along with different drawbacks in health-related problems due to their extensive application in medicine, food, agriculture, etc., are summarized. Besides, it highlights the social-economic disruption due to rapid use of nanotechnology. The nanopollution, not only affects human beings but also influences the existence of other living beings like microorganisms, animals and plants, which are also briefly reviewed. The safety and security of nanotechnological developments, current policies, regulation status, challenges and future trends using nanomaterials in humans are demonstrated. In conclusion, while nanotechnology offers more efficient power sources, faster and modern kinds of computers and life-saving medical treatments but some negative issues and limitations are prominent due to their toxicity. Finally, rapid research on nanotechnology bounds to think twice before any advanced technological applicationson its safety and security aspect will revolutionize the whole world in near future.

Keywords: Progress in nanotechnology, nanotoxicity, nanopollution, human health, safety.

Introduction

Nanoscience are the emerging field in modern technology with numerous applications in biomedical and manufacturing of new smart materials[1]. In the last two decades' nanotechnology integrates with the mechanical and electronic engineering to develop micro/nano-electromechanical systems (MEMS/NEMS) devices, which have diverse applications in different fields of science and engineering. These devices are potentially applicable for different sensing, actuating as well as biomedical analysis purposes[2]. Recently quantum dots have acquired much attention in biological fields owing to its unique size, tunable light absorption and emission properties[3]. Further, biocompatible nanomaterials have many applications in biomedical purposes such as orthopedic, cardiovascular, contact lenses, catheter, prosthetic replacement, etc.[4,5]. Past three decades, extensive research has been carried out to develop nanomedicine and nanoscience based biomedical sensor and instruments[6,7]. Metallic nanoparticles have unique optical, electrical and biological properties, that have attracted significant attention in applications, like catalysis, ultrasensitive chemical and biological sensors, bio-imaging, targeted drug delivery and fabrication[8–15]. It also comprise of large surface area to volume ratio, unique quantum size, having excellent magnetic properties, heat conductivity additionally to some catalytic and antimicrobial properties[16]. Nanoparticles are often synthesized via various chemical and physical routes like chemical reduction[17–19], photochemical reduction[20–24], electrochemical reduction[25,26], heat evaporation[27,28], etc. A series of reducing agents like sodium or potassium borohydrate, hydrazine and salts of tartrate, or organic ones like sodium citrate, vitamin-C, or amino acids are used to get oxidized. Several studies have reported shape and size dependency of silver nanoparticles formation on capping agents like dendrimer[29], chitosan[30], ionic liquid[31], and poly(vinylpyrrolidone) PVP[32]. These capping agents control the nanoparticle growth via reaction confinement within the matrix or through preferential adsorption on specific crystal facets. But, these approaches are costly and hazardous, with the involvement of toxic, non-environment-friendly agents. Hence, evaluation of the risk of these nanoparticles to human health becomes critical. Multiple studies have shown the increase of leukocytes number, neutrophils, in the lungs and bronchoalveolar lavages during airway exposure of nanoparticles in *in vivo* models of inflammation. The neutrophil counts act as biomarkers for inflammation. Therefore, selection of a synthesis route that minimizes the toxicity and increases the stability of nanoparticle leads to enhanced biomedical applications of silver and gold nanoparticles. The development of better experimental procedures for the synthesis of nanoparticles employing variety of chemical compositions and controlled polydispersity offers considerable advancement[33]. Methods of nanoparticle fabrication through different physical and chemical process as mentioned above have their demerits as they produce enormous environmental contaminations and unsafe byproducts. Thus, there's a necessity for "green chemistry" that ensures clean, non-toxic, and environment-friendly nanoparticles production[34]. Nowadays nanomaterials are produced by industries for commercial applications with enormous benefits. While there lies an enormous potential of nanomaterials for fulfilling human requirements, sidewise it also correspond to potential risks to human health[35].

In recent times, eco-friendly approaches have been developed to engineer stable nanoparticles with intelligible morphology and configured constricted sizes[36]. Additionally, owing to the high demand for precious metals like silver and gold and their oxides is of great significance and interest[37,38]. Bio-inspired synthesis of nanoparticles is an advanced, cost-effective, environment-friendly approach over chemical and physical methods, without any inclusion of high pressure, energy, temperature, and toxic chemicals[39]. For example, plant leaf extract is used for the biosynthesis of silver and gold nanoparticles for pharmaceutical and biomedical applications, without employing any toxic chemicals in the synthesis protocols[40]. Eco-friendly acceptable reducing and capping agents are considered to be an effective one for "green" synthesis nanoparticles[41]. The fabrication process also necessitates the use of non-toxic solvents to make eco-friendly. Generally in this technique, microwave retains a constant temperature of the solvent systems. In conventional extraction techniques hexane, ethanol and water are used for the collection of bioactive molecules[42]. But hexane and ethanol are immensely problematic due to their instability as well as environmental and health hazards[43]. To overcome this problem, researchers developed the supercritical fluid (SCF) extraction technology to avoid toxic organic solvents in green technology. SCF possesses physical properties intermediate between CO_2 gas and a liquid at a temperature and pressure above of its critical point. Supercritical CO_2 is non-polar, non-toxic, non-flammable, and has low critical temperature. In this regard, nanomaterials, including metal nanoparticles, carbon nanotubes, quantum dots, and other active nanomaterials can be used to develop biosensors against a broad spectrum of microorganisms for the formulation of a new generation of antimicrobial agents. Among noble metals, silver (Ag) and gold (Au) nanoparticles synthesis via marine algae are used as a broad-spectrum antimicrobial agent towards a variety of pathogens in the biomedical field[44]. Many microorganisms are used for the synthesis of nanoparticles such as cyanobacteria, eukaryotic algae, and fungi. Biosynthesis of nanoparticles by plant extracts are better source in comparison to the various biological processes often considered as eco-friendly substitutes of chemical and physical methods[1,5]. Seaweeds with rich in organic and inorganic is used widely in agriculture, pharmaceutical, biomedical, and nutraceutical industries for consisting high amount of vitamins and minerals[45,46]. Among several genera of microalgae, *Spirulina platensis* is blue-green algae of the cyanobacteria family grown in temperate water in the whole world. A blue-green algae has served as food with high protein content and nutritional value from ancient times[47]. The algae produce novel and potentially useful bioactive compounds[48,49]. The bioactive materials have gained significant attention in recent years and have been used considerably in the development of new pharmaceutical products, food products, renewable bio-energy and biomedical applications[50–52]. However, antibiotic resistance is a global issue that lowers these drugs' effectiveness via genetic mutation or gene acquisition. Therefore, new classes of antibiotics with novel structural diversity are required to battle this trend. Now food preservation is dealing with severe concern of microorganisms mediated spoilage along with fall in quality and nutrition worldwide[53]. Recently, nanoparticles are used in various industries like electronics, aerospace, cosmetics, textile, and even in food. Consequently, the chance of human exposure to nanoparticles is rising, heading towards the time when nanoparticles will eventually be present in blood circulation interacting with immune blood cells.

Advantages and growth of nanotechnology

Recently, research and development in nanotechnology have seen exponential growth due to advantages in different fields like drug delivery, cell imaging, material improvement, medical devices for diagnosis and treatment. More powerful computers are being designed using nonmaterial having faster in speed and consuming very less power, long-life batteries.

The term nanocomputers framed in several ways, using mechanical, electronic, biochemical, or quantum nanotechnology. Circuits consisting of carbon nanotubes can maintain the computer system more advance. Carbon nanotubes are also commercially used in sports equipment, with light weight and high strength. Nanoparticles in fabrics improve the water-resistance, stain resistance, and flame resistance, without putting on extra weight, stiffness, or thickness of the fabric[54]. Nanoparticles are used in medical products for dermal, oral or inhalation applications. Tiny insize, corresponds to higher surface area of nanomaterials offering greater strength, stability, chemical, physical, and biological activity. The carbon-based nanomaterials (fullerenes and nanotubes) are employed in thin films, coatings, and electronics. The metal-based nanomaterials (nanosilver, nanogold) and metal oxides (titanium dioxide (TiO_2)) are useful for food, cosmetics, and drug-related products. The dendrimers are nano-polymers, an ideal candidate for drug delivery. Composites such as nanoclays are formed with a combination of nanoparticle with other particles. Many beverage bottles are made up of plastics with nanoclays. The nanoclay reinforcement increases penetration resistance to oxygen, carbon dioxide, moisture and thus increases shelf life and thus nanoclays are also being used in packaging. It helps to improve vehicle fuel efficiency and corrosion resistance by using diamond-like-nanocomposite (DLN) materials that are lighter, stronger, and high chemical resistant[55,56]. The DLN film exhibits biocompatibility in nature, which have potential applications as a coating material for biomedical purpose. Few nanoparticles are also used in water filter technology that can remove heavy metals, kill viruses and bacteria. These cost-effective, portable water-treatment systems are ideal for the improvement of drinking water quality in developing countries. Now a day, most sunscreens also contain nanoparticles for effective absorption of light including the more dangerous ultraviolet range and pass the other wavelengths, which is healthy for skin. Recently, nanosensors are able to detect a toxic chemical at very low levels, for example, single molecule detection, out of billions of molecules[57,58]. In medical science, the detection of single biomolecules has tremendous applications for DNA/RNA sequencing and disease analysis. The nanobiosensors can be used to precisely identify particular cells or substances in the body for different diagnostics purposes. Current research is focused on preparing the smaller, highly sensitive and cost-efficient biosensors. The new biosensors are updated to even detect odors specific diseases for medical diagnosis, pollutant detection, and gas leaks for environmental protection.

Nanoparticles in pharmaceutical products facilitate improved absorption within the human body along with easy delivery, often in association with medical devices. For example, magnetite, a metal oxide has great potential applications in nanomedicine. Nanoparticles can assist targeted delivery of chemotherapy drugs to specific cells, i.e. cancer cells. Superparamagnetic iron oxide nanoparticles (SPIONs) and ultra-small superparamagnetic iron oxide (USPIO) have also proved its significance for targeted drug delivery[59]. Nanoparticles can improve the water-solubility of weakly soluble drugs. It can increase drug half-life, modify pharmacokinetics, perk up bioavailability, diminish drug metabolism, assist to controlled and targeted drug delivery, and also combined drug delivery[60–64]. According to the data by the International Agency for Research on Cancer (IARC), estimates nearly 13.1 million deaths due to cancer by 2030. It is obvious that the low survival rate occurs not because of scarcity of potent, natural, or synthetic antitumor agents but owing to inadequate drug delivery systems. This develops the requirement of technology advancement to need to develop carriers and delivery systems, capable of targeted and efficient delivery of the chemotherapeutic agents without unwanted systemic side effects[65]. The solid lipid nanoparticles and nano-emulsions are the most employed lipid-based drug delivery particles. However, nanosilver based commercial products are capturing market.

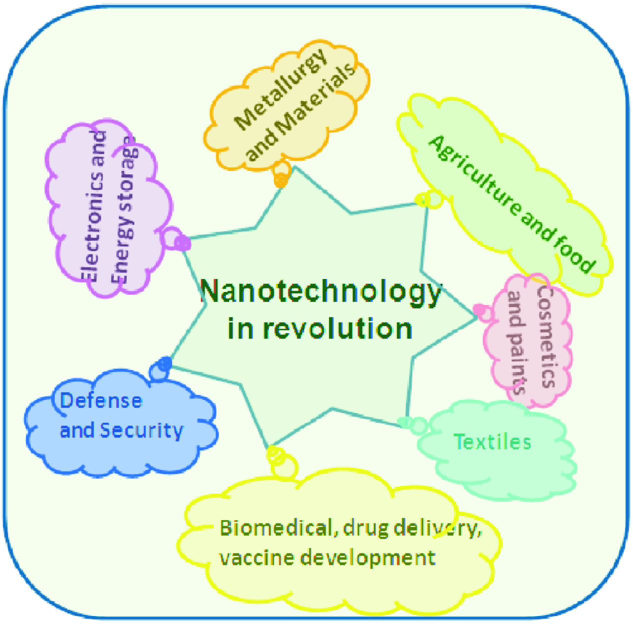

Fig. 1. Technological tsunami due to nanotechnology.

The newly developed nanomaterials for theranostics are being employed alone or in association with "classical" drugs, e.g. cytostatic drugs, or antibiotics. Theranostics is a combined term for nanomaterials with diagnostic and therapeutic properties[64]. Fig. 1 shows Technological tsunami occurs due to nanotechnology in the fields of energy storage, defense and security, metallurgy and materials, electronics, optical engineering and microelectromechanical systems (MEMS), biomedicine and drug delivery, agriculture, food science, cosmetics and paints, textile, etc.[66]. According to Zion market research analysis in 2017[67], there is a rapid increase

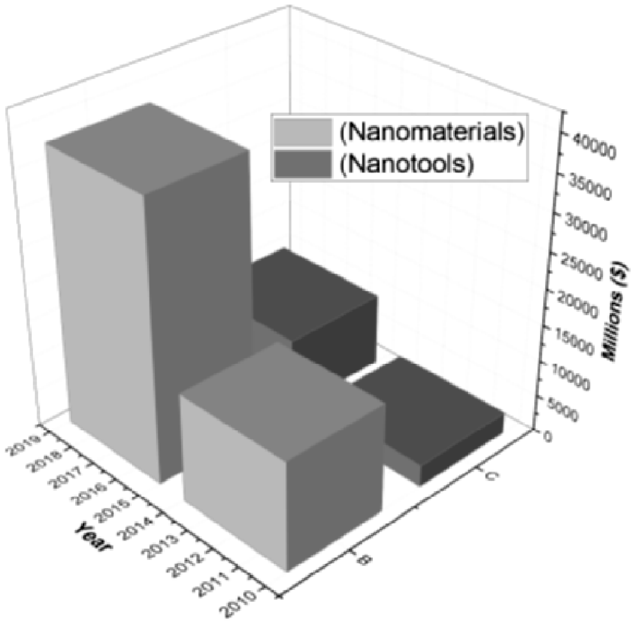

Fig. 2. Global nanotechnology review for nanomaterials, nonotools and nanodevices market from 2011 to 2017 (in Million USD).

of global nanomaterials market volume (in kilo tons) and revenue (in USD Billion), which is estimated from 2014 to 2022, is shown in Fig. 2(a). Other statistical surveys from two different agencies (see Fig. 2(b) and Fig. 2(c) (BCC research)) also confirmed the rapid increase of global nanotechnology market of nanomaterials, nanotools and nanodevices, etc.[68,69]. Some important key points are summarized below about the advantages and growth of nanotechnology. The key benefits of nanotechnology are:

(i) Reduction of size of any material, machine or equipment.

(ii) Reduction of amount of energy and resource.

(iii) Helps to clean up the existing nano-pollution.

(iv) Able to secure economy once it can be fully implemented.

(v) Can alter the basic of technology for human, in its matured phase.

(vi) Early stage detection of some diseases.

(vii) Improvement of the drug therapeutic index by increasing efficacy and/or reducing toxicities.

(viii) Targeted delivery of drugs in tissue-, cell- or organelle-specific manner.

(ix) Enabling sustained or stimulus-triggered drug release.

(x) More sensitive cancer diagnosis and imaging.

(xi) Better pharmaceutical properties like stability, solubility, and half-life of drug molecules.

(xii) Approaches to develop synthetic vaccines.

Limitations of nanotechnology

Nanomaterials are being employed in different industries and everyday life. Therefore, the interplay of nanomaterials and human surroundings is worth scientific exploration. Nanomaterials with several benefits can be toxic in nature. Various studies also confer with the above-mentioned effects, indicating the potential toxicological effects on human environment[60]. Different toxic and hazardous effects of nanotechnology are briefly discussed below.

Potential routes for nanomaterials to enter into human body:

Nanomaterials can enter into human body in various ways. Potential routes nanomaterials entry into human body are ingestion, inhalation and skin absorption[70]. Many nanomaterials are employed in drug transport or cell imaging via intravenous entry to the human body. In the body, nanomaterials are translocated throughout the body by blood circulation. For the purpose, the nanoparticles must fulfill the requirement of permeability across the barrier of blood vessel wall. Absorption through the skin serves as an alternate route of entry for nanoparticles inside a human body. The skin is the largest organ of the human body, provides a large surface area for interactions with the external environment. TiO_2 nanoparticles can take either route for entry i.e. the lungs or gastrointestinal tract. Nanomaterials can enter into the body through skin due to various reasons, such as use of medicine, cosmetics, ointments and use of clothes containing nanomaterials, occupational contact in industry etc. Soaps, shampoos, toothpaste, hair gels, creams, and some cosmetics containing the nanosilver, which can enter into the body through skin. Cream or solution containing silver nanoparticles is used for treatment of wounds, burns, etc. to prevent infections and damaged skin and the size of nanoparticles drive the penetrating ability in cell. The smaller the nanoparticle, has a greater penetrating ability. The inhaled particulate matter gets accumulate in human respiratory tract, while one major portion of those inhaled particles gets deposited in the lungs. Nanoparticles also have the potential to travel across the placenta in pregnant women to the fetus along with other organs i.e. brain, liver, spleen and induce lung inflammation and heart disease[70]. The pulmonary inflammation is due to the inhalation of nano-sized urban particulate matter appear due to the oxidative stress, imposed by these particles in the cells[60,71,72]. The first reported nanoparticle is nano-silver, which can damage DNA molecules. Silver nanoparticles have the most harmful effects on the most sensitive biological groups[60,73–76]. This nanoparticle can penetrate into blood through the skin. Silver binds with the thiol group of some proteins. If silver complexes with thiol groups are located near-skin region, it gets readily available to get reduced either by visible or UV light into metallic nanosilver particles. This results in immobilization of silver nanoparticles in the skin. Further, the effect of nano copper-induced renal proximal tubule necrosis in kidneys has been reported by Liao and Liu[77].

Toxicity of nanomaterials:

Greater the human exposure of nanomaterials presents in environment, greater is the harmful effect on human health. The assessment of the cytotoxicity of nanomaterials assists in proper elucidation of their biological activity. Gerloff *et al.*[78] reported the cytotoxicity of various nanoparticles such as zinc oxide (ZnO), SiO_2, and TiO_2 on human Caco-2 cells. Shen *et al.*[79] showed the human immune cells are prone to toxicity due to ZnO nanoparticles[80]. The ZnO nanoparticles damage mitochondrial and cell membranes in rat kidney ultimately leading to nephrotoxicity[80]. Generally, nanomaterial toxicity mechanism comprises reactive oxygen species formation and genotoxicity. But as described earlier, toxicity of ZnO nanoparticles particularly affects immune cells. Various nanomaterials with their diverse sizes alter mitochondrial function. For example, ZnO nanoparticles generate Zn^{2+} ions, which disrupts charge balance in electron transport chain in the mitochondria and therefore triggers reactive oxygen species generation. Nanosilver particle has a genotoxic effect. Nanosilver (~20 nm) has a genotoxic effect on human liver HepG2 and colon Caco2 cells. It has also increased mitochondrial injury as well as loss of double-stranded DNA helix in both cell types[81]. TiO_2 nanoparticles inhalation, resulted in pulmonary overload in rats and mice with inflammation[82,83]. The cytotoxic and genotoxic effects of TiO_2 nanoparticles on human lung have been reported by Jugan *et al.*[84]. TiO_2 nanoparticles are genotoxic and it can induce pathological damage of the liver, kidney, spleen, and brain. Du *et al.* reported cardiovascular toxicity of silica nanoparticles in rats[85]. The surface coating of quantum dots causes toxicity to the skin cells including cytotoxicity and immunotoxicity[86]. Nanosilver is used in wound dressings, affects both keratinocytes and fibroblasts. Fibroblasts show higher sensitivity towards nanosilver than by keratinocytes. Again, iron oxide nanoparticles rapidly get endocytosis on cultured human fibroblasts and interrupt the function. Citrate/gold nanoparticles have shown toxicity on human dermal fibroblasts[87]. Carbon nanotubes have high toxicity and produce harmful effects on human. The nanoparticles can penetrate into the lungs, then reached blood and act as barrier for the circulation of blood into brain. They can also enter inside other organs like bone marrow, lymph nodes, spleen, or heart. Sometimes, nanoparticles can incite inflammation along with oxidant and antioxidant activities, oxidative stress, and change in mitochondrial distribution. These effects depend on the type of nanoparticles and their concentrations[69]. Copper nano particles (diameter 40 nm and 60 nm) have harmful effect on brain cell at low concentration. It activated the proliferation of the endothelial cells in brain capillaries. Ag nanoparticles (25, 40, or 80 nm) influenced the blood-brain barrier, causing a proinflammatory reaction, which might induce a brain inflammation with neurotoxic effect. Smaller Ag nanoparticles (25 nm and 40 nm diameter) can induce cytotoxic effect at a greater rate compared to larger nanoparticles. Nanoparticles also have harmful effects on the brain cell of the mouse and rat. The high concentration of nanoparticles can affect brain blood fluxes, with consequent cerebral edema. Pathogenic effects of Ag-nanoparticles (25, 40, and 80 nm diameter), Cu-nanoparticles (40 and 60 nm) and Au-nanoparticles (3 and 5 nm) on the blood-brain barrier of pig have been reported[88]. Silver nanoparticles (45 nm) influenced the acetylcholine activity via nitric oxide generation; it induces hyperactivity of rat tracheal smooth muscle[89]. It is also reported that Ag-nanoparticles (25 nm) produced an oxidative stress after the injection into the mouse. The nanoparticles were aggregated in the kidneys, lungs, spleen red pulp and in the nasal airway, with no observable morphological changes apart from nasal cavity[90].

Very few cells do not undergo morphological changes after withstanding the air-liquid interface culture for an extended duration. Au-nanoparticles (5 nm and 15 nm diameter) penetrated into the mouse fibroblasts, where they remained stocked. Only the presence of 5 nm Ag-nanoparticles disrupted cytoskeleton resulting in narrowing and contraction of cells. Many engineered nanomaterials, such as TiO_2, magnetite iron, CeO_2, carbon black, SWCNTs, and MWCNTs, also might cause different levels of inflammatory reactions, including enhanced pro-inflammatory cytokines expression, target inflammation-related genes, and micro-granulomas formation[91,92]. The intra-tracheal administration of MWCNTs with variable length and iron content in hypertensive rats Led to the lung inflammation with increased blood pressure and lesions in abdominal arteries along with accumulation in multiple organs i.e. liver, kidneys, and spleen post 7 days and 30 days exposure[93]. Maneewatttanapinyo *et al.* studied acute toxicity of colloidal silver nanoparticles administered in laboratory mice and observed neither any mortality any acute toxicity symptoms after a limited dose of 5.000 mg/kg post 14 days of oral administration. No differences could be observed in among groups after hematological and biochemical assessment and the histopathological study. The instillation of silver nanoparticles at the concentration of 5.000 ppm developed a transient eye irritation for 24 h. The application of these nanomaterials on skin did not produce any micro or macroscopic toxicity[94]. The schematic mechanism of silver nanoparticles toxicity in human body is shown in Fig. 3[95]. Liver and spleen are maximum exposed organs to nanomaterials owing to the prevalence of phagocytic cells in the reticuloendothelial system. Also, the organs with high blood flow such as kidneys and lungs can be affected.

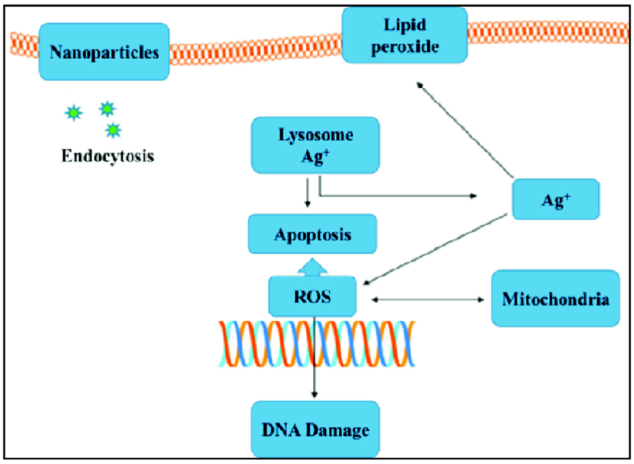

Fig. 3. Mechanism of silver nanoparticles toxicity (Abbreviations: NPs – nanoparticles; ROS – reactive oxygen species; Ag^+ – silver ions) Redrawn from[95].

Health hazards in human:

In spite of having many benefits and uses the nanomaterials may cause health hazards to humans owing to very small size. The large absorption surface of lung, the thinner air-blood barrier, and comparatively less inactivation of enzymes leads to faster entry for particles into the systemic blood circulation at higher drug concentrations. Additionally, intentional uptake, exposure of particles carried by the wind from the environment, and nanoparticles released at manufacturing units may also cause health hazards for human. Usually, the biological effects of nanomaterials are based on their size, composition, shape and also on their electronic, magnetic, optical, and mechanical properties. Presently, the influence of nanotechnology on human health and environment is still controlled. Most of the studies assessed the outcomes of unintentional and accidental exposure (inhalation, medical procedures, or accidental ingestion) and focused on local effects only[66,67]. Though, along with introducing nanomaterial-based biomedical procedures, it is mandatory to analyze their toxicity at a systemic level. Centuries before, Paracelsus said, “everything is a poison, and nothing is a poison, it is only a matter of a dose”. For nanomaterials, it is applicable in both the aspects of dose and particle size[68]. There is a huge demand for the use of nanomaterials in various applications, ranging from diagnostic technology, bioimaging, to gene/drug delivery[96–98]. Therefore, intended or unintended human exposure to nanomaterials is unavoidable and has greater prospects of exposure in the future. Therefore, a branch of science is developing, named “nanotoxicology”, the study of toxicity of nanomaterials. Nanotoxicology assess the role and safety of nanomaterials on human health. Several anthropogenic sources like power plants, internal combustion engines and other thermo-degradation reactions also generate nanoparticles and therefore develop the need to assess them as well[69].

Hazards in nanomedicine:

The nanomaterials represent a variety of biomedical applications, however, there is some potential risks factor related to the toxic issue. For example, cytotoxicity, genotoxicity, oxidative stress and inflammation have been reported on *in vitro* and *in vivo* models for testing nanoparticles. The difference in the size of nanomaterial and bulk comes with the differences in properties and toxicity as well. Nanomaterials are tremendously beneficial yet can be toxic. Ag, ZnO, or CuO nanoparticles are frequently used as bactericides[79]. But waste disposal in the environment can also negatively affect non-target organisms.

Hazards in medical instrumentation:

Nanomaterials are involved in medical interventions like prevention, diagnosis, and treatment of diseases. With development of science and technology, more accurate and multi functional medical diagnostic equipment are being fabricated for easy and safe operation. The ‘lab-on-a-chip’ technology facilitates instantaneous point-of-care testing, enhancing the standards of medical care. Nanomaterial based thin films on implant surfaces improve the wear and resist infection. But until now, these medical nanodevices are not 100% hazard free due to manufacturing processes, not following guidelines of nanotoxicity and also operating without the assessment of long term effects of nanotoxicity.

Hazards in food product:

Nanotechnology is used to produce advanced food products and smart packaging technology[99–101]. In this way, the possibility of direct exposure of nanomaterials with human beings is enhanced and different types of long-term or short-term toxicity may occur[102,103]. Nanoparticles and diamond-like nanocomposite (DLN) thin films are used in food packaging to reduce UV exposure and prolonged shelf life. Due to very few articles being reported in this area, further research is needed to fully explore the potential use of these nanoparticles for food products and medical treatments.

Environmental nanopollution and its effect in society:

Environment conservation is a challenging task. Its vastness and complexity make this even more difficult. As the production of nanomaterials is growing multiple issues concerning nanotechnology arise as environmental pollution and industrial exposure. Nanoparticles serve as pollutants in diesel exhaust or welding fumes, presenting new toxicological mechanisms[104,105]. It also makes us face pollution in macro, micro, and nano-scale. New branches of electronics are also creating new sources of occupational exposure hazard. The circumstances produce new challenges for both classical toxicology and nanotoxicology. Though nanotechnology is improving the living standard, simultaneous increase in water and air pollution has also occurred. As the origin of this pollution lies in nanomaterials hence termed as “nanopollution”. Nanopollution is extremely lethal to both underwater flora and fauna and organisms living on soil. The pollutants can enter in human body in multiple ways. Cellular mechanisms can get affected by nanomaterial toxicity, which mainly comprises reactive oxygen species generation and genotoxicity[105,106]. The nanoparticle's exposure on humans can occur unintentionally by environmental particles (e.g. air pollution) and deliberately because of a diversity of consumer products, cosmetics, and medical products containing nanoparticles. The release of nanoparticles during the manufacturing process may result in exposure on workers via dermal, oral, and inhalation routes. Exposure to air pollutants, such as ultrafine particles, is known to cause inflammatory air-way diseases and also cardiovascular problems in humans[107]. Pope *et al.*[108] stated that even very very low amount of ambient nanoparticle exposure, have a momentous consequence on mortality. To decrease nanopollution, scientists and researchers used nanotechnology to develop nanofilters, which can eliminate almost all airborne particles[109].

Economic and social disruption due to rapid use of nanotechnology:

As the speed of nanotechnology development is growing, as a consequence the job opportunities are decreasing, arising the problem of unemployment in fields like industrial sector, manufacturing, and traditional farming[110]. Nanotechnology-based devices and machines have replaced humans to furnish the job more rapidly and efficiently, which has pointed out the importance of manpower in the field of practical work. Increasing growth and instant performance of nanotechnology have compromised the worth of commodities like diamond and oil. As an alternative technology i.e. nanotechnology has a detrimental effect on the demand as substitutes have more efficiency and do not need fossil fuels. Diamonds are losing the worth due to greater availability from nanotechnology-based fabrication methods. Currently, manufacturing companies are equipped for the production of the bulk of these products at a molecular scale, followed by disintegration to create new components.

At present, nanotechnology involves high investment technologies; raising the cost daily. The high cost is the resultant of intricate molecular structure and processing charges of the product. The whole process makes it difficult for manufacturers to randomly produce dynamic products using nanotechnology. Currently, it is an unaffordable business owing to huge pricing of nanotechnology-based machines. Hence, nanotechnology can also bring financial risks as manufacturers have to invest large sum of money for setting up nanotech plants. The manufacturers have to face a huge loss if by any chance the manufactured products fail to satisfy the customers. Alternate options such as recovery of the original product or maintenance of the nanomaterials are also a costly and tedious affair. Further, nanotechnology does not leave any byproducts or residues, generally basis for the small industries, therefore creating huge risk of extinction for small scale industries. As an outcome, the quantity of sub-products of coal and petroleum is deteriorating. Another gigantic threat (like Covid-19 pandemic situation), which is born with the arrival of nanotechnology. It can make the easy accessibility of bio-chemical weapons or nano-bio engineered biological weapons. Nanotechnology is making these weapons more powerful and destructive. Unauthorized criminal bodies or corrupt politicians can steal the formulations and may reach these hazardous weapons easily and they can easily destroy our civilization[111].

Effect of nanotechnology on microorganisms, animals, and plants:

Some nanomaterials are not only hazardous to human beings but are also harmful to the existence of different microorganisms, animals, and plants. Man-made nanopollution is very much unsafe for living microorganisms, animals, and plants under the water or on the earth. As a result, many microorganism's families have completely disappeared from the world. Recently, due to rapid application of nanotechnology in the agriculture sector without proper nanotoxicological analysis, many plants are directly exposed to nanotoxicity and animals are indirectly exposed. Thus, in last two decades, a vast number of valuable plants and animals are completely disappeared from our world.

Key points about limitations of nanotechnology:

Some key points about limitations of nanotechnology are summarized below:

(i) Still at its infancy stage.

(ii) More research and developmental work need to be done.

(iii) Expensive technology till now.

(iv) Creates environmental nanopollution.

(v) Huge initial cost for implementation.

(vi) Resistance from culture perspective, activists, journalists and even within the government.

(vii) Knowledge limitation from many industries and misperception among many fields about its capabilities.

(viii) Nanomaterials are not regulated by the government.

(ix) Requirement of large investment and research but yield is still a limiting factor.

(x) Some nanoparticles may be toxic to humans.

(xi) Nanotechnology made weapons are more powerful and more destructiveby increasing the explosion potential.

(xii) Lack of employment in the fields of traditional farming, manufacturing, and industrial sector.

Safety and security of nanotechnological developments

Nanotechnology is an extensively expanding field. Researchers, scientists, and engineers are getting high success to produce nano-materials and take the advantages of improved properties, such as higher strength, lighter weight, increased electrical conductivity, and chemical reactivity with respect to their macro equivalents[112]. Human health concerns are also growing due to nanomaterials. The attempts of technological manipulations raise vocational risk to the workers in case of accidental exposures. Major cases of poisoning occur during coatings on the products. These micro or nano particles penetrate inside the brain, while in contact with humans and to lungs during inhalation. So it is matter of ethical issue. The problem can be addressed by using nanoscale materials to overcome the negative effects of micro or nano particles coatings in industry and health sectors. Academic and industry experts suggest that there exists ambiguity regarding the toxic effects of releasing nanoparticles into the environment. It is also noteworthy that, there is a lack of knowledge of nanoparticles interactions with humans and environment. Similar to most of the emerging technologies nanotechnology and nanochemistry industries have both benefits and challenges. To get maximum benefits the challenges must be overcome, managed and endured. Mesoporous silicates, alone or in combination with other inorganic or organic counterparts have been extensively explored for targeted drug delivery and cancer treatment. Even though the long-term toxicity of the nanoparticles is subjected to controversies and doubts, the use of gold and silver nanoparticles have provided more advantages in comparison to other actual alternatives (cytostatics). Consequently, there is a growing interest in developing *in vitro* assays for nanotoxicology study[113], it is strongly encouraged to use primary human cells as a source for *in vitro* study with nanoparticles since different origins of cancerous cell lines complicate data interpretation for human risk evaluation. Till now, the environmental effects and the toxicity of nanomaterials to organisms are in infancy state. The evaluation methods need to be cost-effective rapid, and quantity efficient.

Current policy and regulation status

The social implications of nanotechnology comprise of many fundamental aspects like ethics, privacy, environment, and security. Occasionally, the negative impacts on environment are too adverse to handle that the people simply give up. However, nanoscience researchers are still optimistic to see light of hope on the other side of the tunnel. Environmental clean-up is possible via design and manipulation of atomic and molecular scale of materials. It would develop cleaner energy production, energy efficiency, water treatment, and environmental remediation. Nanoscale fluid dynamics deciphers flow of nanoparticles in environment as a result of interactions with biological and environmental systems. Researchers are keen to understand the transportation of nanomaterials in association with environmental contaminants through groundwater systems. For food authenticity, safety, and traceability, every food company should need to use smart labels at stronger and innovative functional lightweight packaging. Now, each developed and developing countries have a separate policy and regulation for the use of nanotechnological products and applications. Explicit initiatives on nanotechnology must be needed to pledge that, the prospects provided by nanotechnology are not misused and research does not become bitty. The ambiguity, complication, and diversity of nanotechnology mean that any such initiative should not be a strictly predetermined closed program. Flexibility will be needed to stay side by side of development as they arise.

Challenges and future trends in using nanomaterials in humans

Nanotechnology-based production uses very little manpower, land, maintenance and it is cost-effective, high productivity with modest requirements of materials and energy. The extensively growing field offers scientists and engineers a great opportunity to manipulate or alter the materials at nanoscale to yield benefit of enhanced material characteristics like enhanced strength, lightweight, higher electrical conductivity, and chemical activity in comparison to their large-scale counterparts. However, for biomedical applications, the toxicity evaluation of nanomaterials should be performed. Broadly, detailed physicochemical characterization of nanomaterial should be performed before and during any toxicity study. Important properties that can control nanomaterial-induced toxicity, including size and shape of the nanomaterials, coating, chemical composition, crystal growth, nanomaterials purity, structure, surface area, surface chemistry, surface charge, agglomeration, and solubility should also be taken care. Measurements should be performed in full stable state of nanomaterials in the most relevant test medium, i.e. aggregation status and ion release from metallic nanomaterials. Various engineered materials should be tested for their multidisciplinary tiered toxicity using diverse models and experiments[114,115]. Therefore, the first step in the genotoxicity is an assessment of physicochemical properties of nanomaterials. The validation of the proposed tiered approaches is still waiting for future. The researchers are continuously trying to increase the relevant database with an increasing number of publications (papers, reviews, or even patents) every year[116], particularly market share of the nanotechnology products is also growing up to thousands of billions of Euros[117]. Balanced use of the nanotechnologies/nanomaterials must be arranged, to optimize the opportunities/risks factors. Further research related to the size and shape, capping agents, receptors immobilization onto the metal nanoparticles are still a matter of keen interest with high necessity. Surface plasmon resonance can be tuned by varying sizes, shape of the nanomaterials and different surface functionalization of both silver and gold nanoparticles can reduce the toxicity and enhance a variety of biomedical applications in future. For example, CNT toxicity can be reduced via functionalization, surface coating, and stimulation of the autophagic flux. The amino functionalization decreases the CNT toxicity to the cells[118], along with albumin coating for SWCNTs[119].

Conclusions

Nanoparticles can enter and get distributed around the human body very easily. After entering into human, it moves within the body and creates cellular toxicity. Then it attacks respiratory system, cardiovascular system, brain, skin, gut, and other organs. Again, some nanomaterials kill harmful bacteria within body and some of them kill good bacteria and live-cell of human body. Nanoparticles with different substances are used in SIM cards of cell phones or sunscreens. When these are used, free nanoparticles get released in the environment (air, water or soil). Engineering fields like civil and electronics also create new occupational health risks; making new potentially toxic nanomaterials. The toxicity of nanoparticles depends on their shape, size, and chemical composition. Centuries before, Paracelsus quoted, "everything is a poison, and nothing is a poison, it is only a matter of a dose". In regards to nanomaterials, the quotes hold value for both dose and particle size. The new interdisciplinary investigations explore the potentially harmful effects of these useful NPs and help in environmental preservation. Owing to smaller size the inhalation of nanomaterials imposes harmful effects on human health. The inhalation causes severe injury to the lungs and can also become fatal. The deterioration of lungs can be observed even after 60 s of nanoparticle inhalation. Therefore, for sustainable nanotechnology development, it is mandatory to evaluate and spread knowledge about the short term and long term exposure benefits and hazards for nanomaterials. To conclude, nanotechnology has the potential to impact society, both positively or negatively. Its consumers, producers and dealers include all the members of the society and all stakeholders; so we should collectively raise the voice in its various growth and commercialization phases. Currently, nanotechnology is in its infancy stage with a significant lack of awareness about its effects on humans and the environment. As civilization moves forward, the vital query is: how should we manage the risks and uncertainties of this emergent technology? Is anyhow COVID-19 pandemic situation manmade? If not, we can face such type of situations due to careless application of nanotechnology in different fields. However, all these limitations can be overcome itself by the rapid research on each such suspected fields of nanotechnology.

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