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Engineered nanoparticles (ENPs): Unexplored potential and limitations

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The rapid growing industry of global economic importance is exploring the novel material synthesized at the nanoscale. Engineered nanoparticles (ENPs) have been manufactured with specific shape, size, surface properties and unique functionalities such as catalytic behaviour, increased strength, improved thermal and electrical conductivity. These advancements have opened the door to new applications in biomedicine, nanoenergetic materials and functional nanocomposites including cancer therapy, drug delivery, tissue engineering, regenerative medicine, biomolecule detection, and antimicrobial activities. In cancer therapies, nanoparticulate delivery systems allow ENPs greater penetration of therapeutic and diagnostic substances within the body while posing fewer risks than conventional cancer therapies. Evidences suggested that ENPs offer some substantial danger to the environment by its toxicological effects when they are exposed to the environment, which leads to the chronic issues of nanopollution. The aquatic environment is at the greatest risk from ENPs, as it serves as a sink for nearly all environmental contaminants. Despite these challenges, ENPs holds promise to in different field as well as minimize environmental pollution, by employing the innovative environmental remediation methods. There are gaps in understanding the fate of ENPs in the environment hence more stringent and critical research is the need of the hour. It also call for the advancement of tools and techniques that can accurately quantify and analyze the uptake of ENPs into biological systems. This review includes the different types of ENPs their sources and physiochemical characteristics and the ultimate fate of these ENPs in the environment.

Keywords: Engineered nanoparticles (ENPs), Nanoelectronics, Nanoenergetic materials, Nanopollution

Introduction

The pioneering acknowledgement of the nano-world and its potential to be manipulated at molecular and atomic scales developed over half a century ago[1]. Nanoparticles are particles with all three dimensions on the nanoscale (1-100 nm). Nanoparticles have been around since the beginning of time. However, interest in nanoparticles has risen over the last two decades. This is especially true for Engineered nanoparticles (ENPs), which are nanoparticles that are prepared to have specific characteristics so as to be used for specific purposes[2-3]. ENPs are currently being used, or are being investigated and developed for use, in a wide range of applications across multiple technology sectors. ENPs with specific shape, size, and surface properties deliver unique functionalities such as catalytic behaviour, increased strength, improved thermal and electrical conductivity, and controlled release of host molecules. These breakthroughs have paved the way for applications in biomedicine, nanoenergetic materials, and functional nanocomposites. Despite the fact that nanotechnology is still in its infancy, many workers are currently exposed to ENPs in research and manufacturing operations. Various research studies and evaluations have shown that nanoparticles have greater biological activity than larger particles of the same material. At the same time, significant toxicity has been observed in laboratory animals exposed to some types of nanoparticles so there is a need to study control measures to prevent occupational disease or damage[4]. Few investigations have been conducted to determine the toxicity of these ENPs after exposure, either directly or indirectly. The true extent of their toxicity to ecosystems and human health requires further study. Many questions have still to be answered and one of the most important question is what precisely has to be measured in regards to the ENPs toxicity. There is a pressing need for interdisciplinary cooperation amongst professionals in different scientific fields to create novel ideas and technology. Though reports of toxicity from nanoscale component exposure in living systems using cell lines & incubation periods are increasing, the observed toxicity is physiologically somewhat irrelevant due to the lack of a precise understanding of the mechanism, the number of varying conditions, and the cell lines[5].

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One of the most important areas where further study is needed is our limited understanding of how nanoparticles interact with the natural world. The ENPs have essential applications in research, engineering, medicine, medical surgery, foods, packaging, clothing, robotics, and computers. The most significant disadvantages include economic upheaval and dangers to security, privacy, health, and the environment. Because of the extensive use of medicine, food, and agriculture, among other things, significant downsides of ENPs emerge in human health. Some of the ENPs destroy harmful bacteria inside the body, while others kill healthy bacteria and live human cells. ENPs of various chemicals are utilised in mobile phone SIM cards and sunscreens. Because of their tiny size, inhaling these ENPs negatively influences human health. The inhalation causes severe lung damage and may even be deadly[6]. The ENPs are of utmost importance but at the same time they have various ecotoxicological effects in aquatic as well as terrestrial ecosystems. Studies of the ENPs' fate and impact in the environment are becoming highly significant due to existing discharges to the environment, which is likely to increase further due to dramatically increase in industry. The known toxicity of ENPs, and the enormous gaps in our knowledge make risk assessment and management difficult.[7]

Nanotechnology and nanoparticles

Nanotechnology is a branch of science concerned with the design, manufacture, and application of structures, devices, or systems created by manipulating atoms and molecules at the nanoscale, with dimensions of the order of nanometers or less and these structures are known as nanoparticles. Because of the demand and use of nanoparticles in many fields such as industry, agriculture, business, medicine, and public health, nanotechnology has piqued the public's attention[8]. Nanoparticle toxicity studies employing various cell lines and incubation durations are increasingly being reported. To adequately identify the possibility of human exposure, much more research is required to investigate the stability of these matrices in various test systems[9].

Nanotechnology has affected various fields of utility services, including consumer items, health care, transportation, energy, and agriculture, to fulfil society's ever-increasing requirements. Nanotechnologies enable the creation and manipulation of minute objects as small as one billionth of a meter in size (the nanometer). The indiscriminate and unregulated usage of nanoparticles has the potential to endanger humanity. The noble hope is that the industry and certain developed and developing nations are looking into the issues[10].

Nanotechnology synthesized several disciplines that have resulted in revolutionary processes and products that have revolutionized many facets of contemporary life. This technique rose to popularity in India primarily to give a significant infusion of cash for research to meet pressing social fundamental requirements such as water purification and health care. However, a wide variety of ethical difficulties such as privacy, value conflicts, responsibility, intellectual property rights, non-discrimination, equality, hype, self-replication, and Cyborgs may result in permanent societal calamities. We need to develop a clear set of regulations or guidelines that will help avoid or at least mitigate the negative consequences of Nanoscience's fast ramifications. Because of their ease of availability and simplicity, many stakeholders in India are adopting various nano goods without considering the hazards. Even the government was unconcerned until the recent initiation of the Nano mission (2007) by the Department of Science and Technology (DST). There are no specific rules in India to govern risk assessment, management, and communication. It has prompted the emergence of a new area of ethics known as 'Nanoethics'.

Types of nanoparticles

Nanomaterials differ in dimensions, shapes, sizes, compositions, porosity, phases, and uniformity, several classifications have been developed. A lot of nanomaterials have been described, and many more will be developed. In terms of origin, nanomaterials can be divided into naturally occurring, incidental, bioinspired, and engineered nanomaterials[11] (Fig. 1). Natural nanomaterials and living organisms have co-evolved in a harmonious manner as part of the Earth system. However, the increased use of incidental, engineered, or anthropogenic nanomaterials has shifted this balance.

1) *Natural nanoparticles:* these nanoparticles and nanostructured materials are created through natural biogeochemical or mechanical processes, with no connection to anthropogenic activities or processes. Foraminifera (single cell protists) and virus (capsid) structures, wax crystals that coat lotus or

nasturtium leaves, spider and silk spider mites, blue tarantula hues, gecko foot spatulas, some butterfly wing scales, natural colloids (milk, blood), horny materials (claws, skin, feathers, hair), nacre, corals, and human bone matrix are some examples of natural nanoparticles. Crystal growth produces natural inorganic nanomaterials. Clays, for example, exhibit complex nanostructures due to anisotropy in their crystal structure. Furthermore, volcanic activity may result in the formation of opals, which, due to their nanoscale structure, are an example of naturally occurring photonic crystals. Forest fires (combustion materials), volcanic ash, ocean spray, radon gas decline, and weathering of metal- or anion-containing rocks and acid mine drainage sites are all natural sources of nanomaterials[12].

2) *Incidental nanoparticles:* these nanoparticles and nanostructured materials are produced inadvertently as a result of direct or indirect human influences or anthropogenic (*e.g.*, mechanical or industrial) processes such as vehicle exhaust gases, welding gases, solid fuel heating (home heaters), and combustion during cooking. Incidental atmospheric nanomaterials formed inadvertently during a deliberate procedure may cause an increase in air pollution. Forest fires produce a diverse range of nanomaterials such as pigments, fumed silica and cement *etc*. Incidental nanomaterials have significant environmental consequences and should be weighed against engineered nanomaterials[13].

3) *Bioinspired nanoparticles:* These are nanomaterials that have been engineered to mimic the properties of natural nanomaterials or living matter. Many bioinspired nanomaterials with specific functions can be fabricated using advanced nanofabrication technologies by modulating their structures. Chameleons, for example, can quickly change their colours from camouflaged to highly visible when fighting or courting. This colour shift is primarily caused by actively tuning the lattice of guanine nanocrystals within iridophore cells[14]. Mechanochromic elastomers that mimic the photonic structure of chameleon iridophore cells have been developed[15].

4) *Engineered nanoparticles (ENPs):* these are nanoparticles and nanostructured materials designed for specific applications based on their dimensions and properties (*e.g.*, nanostructured medical implants)[16-17]. Aerosol (fumed silica) produced in the 1940s was used to create the first commercial nanomaterials. In this case, the first silica nanospheres were created in the 1960s using aqueous solutions. Natural and incidental nanoparticles can have regular or irregular shapes. Engineered nanoparticles typically have regular shapes such as rings, spheres, tubes, and so on. Engineered carbon nanostructures with a more regular shape and structure than carbon soot (Incidental nanomaterial) such as fullerenes, carbon nanotubes, and graphene[13].

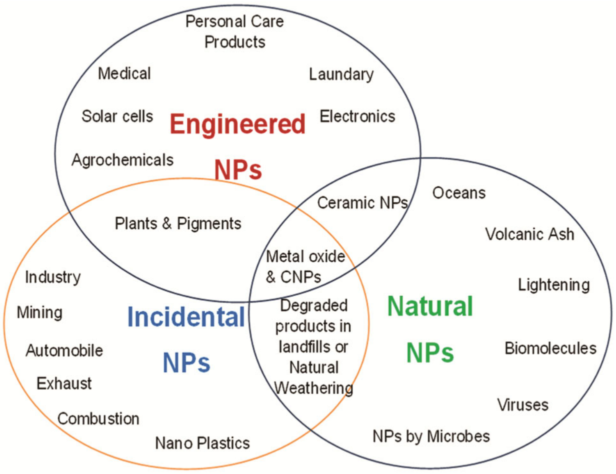

Fig. 1 — Types of Nanoparticles and their source of origin

5) *Anthropogenic nanoparticles:* Both incidental and engineered nanomaterials are referred to by this term. The intentional and unintentional release of anthropogenic nanomaterials into the environment is becoming a major public concern[13].

Applications of engineered nanoparticles (ENPs)

Nanotechnology and the development of ENPs have revolutionised the fields of medicine and given physicians a hope in combating diseases for which there are currently no specific drugs. ENPs have potential applications in many areas of medicine and biology. Several groups have synthesised and characterised various types of ENPs for this purpose[18]. These ENPs have applications in various fields of science and technology viz., electronics, textile, food, biomedicine, energy and agriculture etc.(Fig. 2A). Some of these applications are discussed below:

1) ENPs in electronics

Nanotechnology has aided in the removal of barriers and the abrogation of constraints in the field of electronics. Nanoelectronics is the use of nanotechnology in electronic devices, particularly transistors. Nantero Inc. announced in November

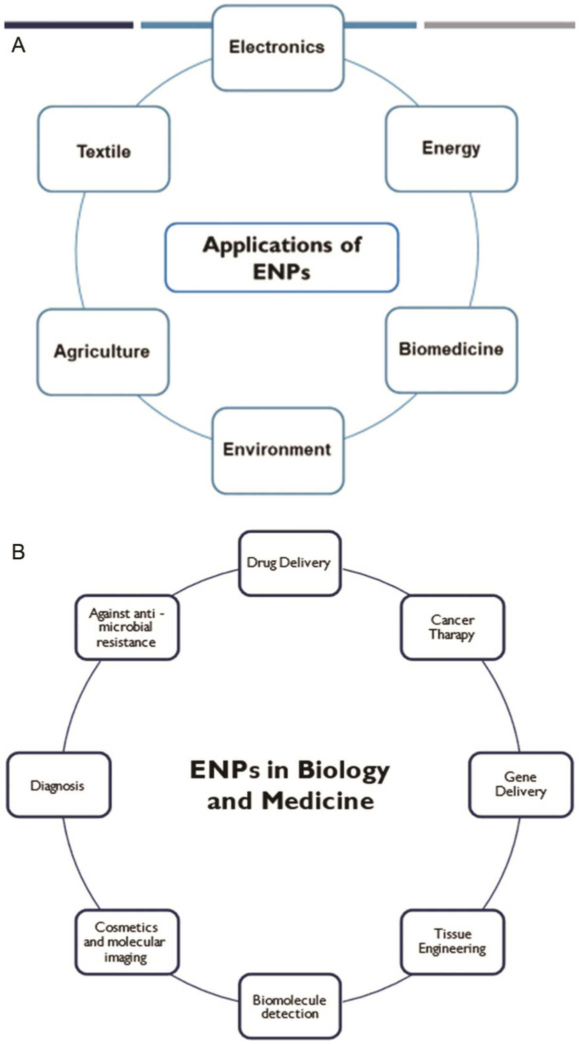

Fig. 2 — Applications of ENPs in (A) Various fields; and (B) Biology and Medicine

2006 that it had developed and received patents for the process of producing semiconductors using carbon nanotubes on silicon wafers[19]. Nantero is working on a high density nonvolatile random access memory chip known as NRAM (Nanotube-based/Nonvolatile random access memory).Carbon nanotubes are used as active memory elements in conventional semiconductor technology. NRAM is expected to eventually replace DRAM (dynamic RAM), SRAM (static RAM), flash memory, and hard disc storage[20].

2) ENPs in energy

Nanoparticles and nanocomposites are finding new uses in sustainable energy research. $Cu_2Sn_3S_7$ nanoparticles can be used as a light-absorbing layer for thin-film solar cells. This material, created through the powder, baking, sulphur, and sintering (PBSS) process, has a wider energy band gap and higher carrier concentration and mobility. Also, ZnO needle-shaped nanoparticles can be used to fabricate dye-sensitized solar cells. In this example, ZnO was deposited on a fluorine-doped tin oxide (FTO) glass to form the working electrode, with a platinized FTO glass serving as the counter electrode. As the authors demonstrate, this system produced high power conversion efficiency and improved electron transport[21].

ENPs in biology and medicine

Aluminum NPs (AlNPs), copper NPs (CuNPs), copper oxide NPs (CuONPs), gold NPs (AuNPs), silver NPs (AgNPs), magnesium oxide NPs (MgONPs), and carbon-based NPs have all been synthesised, characterised, and tested for biological activity. Furthermore, advances in DNA nanotechnology and the preparation of various DNA-based NPs have had a significant impact in the fields of medicine and biology, such as drug delivery and the preparation of biosensors/biochips[22]. Various organic ENPs with biological activity have been identified, including quaternary ammonium compounds, chitosan, polysiloxanes, and triclosan[23]. ENPs have various applications in Biology and Medicine (Fig. 2B) such as:

- **ENPs in cancer treatment**: Cancer treatments that are most commonly and widely used include surgical removal of an abnormal tissue, chemotherapy, biotherapy, radiation therapy alone or in combination with two or more different therapies. Although conventional cancer therapies have improved patient survival, they have limitations such as non-specific drug distribution, aqueous insolubility of drugs, and multidrug resistance[24-25]. In addition to overcoming the limitations of conventional chemotherapies, the development of ENPs has provided significant benefit and interest in cancer therapy[26-27]. ENPs have a number of advantages, including improved hydrophobic drug solubility, increased circulation time, the ability to carry larger drug payloads, reduced non-specific uptake, prevention of undesirable side effects, enhanced intracellular penetration, specific anticancer drug targeting, and use in cancer imaging[28-29].

- **ENPs in tissue engineering and regenerative medicine**: The advancement of biomaterials has resulted in the evolution of advanced medical technology known as tissue engineering (TE) and regenerative medicine (RM), which has revolutionised the field of medicine. Several research groups have investigated various types of biological nanomaterials, such as ENPs, nanotubes, nanofibers, and fabricated nano-devices with dimensions less than 100 nm and potential applications in cell growth and tissue regeneration. Biological nanomaterials investigated in TE and RM must be capable of eliciting a variety of cell-to-cell interactions, including attachment, adhesion, multiplication, and differentiation. As a result, the selection of biomaterials is the most important factor in the success of the TE approach [30]. Several different nano composite materials based on polyester have been developed for use in medical applications. Natural polymeric substances such as silk, starch [31]and collagen [32] have been studied for their significant medical applications.

- **ENPs in biomolecule detection**: Nanoscience and nano-biotechnological research advancements in recent years have centred on the use of nanotechnology in biomolecular detection. ENPs have played an important role in the detection of biomolecules. They have specifically replaced traditional molecular techniques and improved the sensitivity and accuracy of identification[33]. When observed in biosensing devices, thermal, optical, physical, and electrochemical techniques have undoubtedly improved in recognising molecules in solution. NPs are widely used in the development of new sophisticated sensing devices and assays that can improve nucleic acid and protein identification[34].

- **ENPs as antimicrobial agents**: Antimicrobial resistance in microorganisms is a current global challenge that poses a significant risk to patients infected with pathogenic microbes[35]. The number of drug-resistant bacteria, such as methicillin resistant *Staphylococcus aureus* (MRSA) and vancomycin resistant *Enterococci*, is increasing, posing a challenge to medical practitioners. Recent advances in nanobiotechnology have made it possible to synthesise nano-range molecules with incredible applications in biomedicine and therapeutics. Furthermore, these nanoscale nanocomposites have outstanding antimicrobial properties against a variety of resistant microbes. As a result, ENPs' antimicrobial properties can be used as alternatives in the treatment of drug-resistant microbes in the medical field[35-36]. Several inorganic NPs, including silver ENPs (AgNPs), have antimicrobial activity against a wide range of microbes[37].

Limitations of ENPs

Medical imaging, textile fabrics, tissue engineering, nanocomposites, bioremediation, and biomedicine are just some of the industrial and biotech applications that hold great promise for the future of nanomaterials and nanoproducts. Their effects on living systems are unclear. However, they are likely to be negative. The rise of nano wastes is one of the most pressing concerns facing the waste management industry, yet the efficiency and capacity of existing systems to deal with them have yet to be determined. Nanowastes are byproducts of making ENPs and nano products in laboratories and factories. Sustainable development in nanotechnology requires the careful administration of nano waste streams. Waste management as we know it may need to be rethought in light of nanowaste[38]. Nanowaste is mostly a collection of ENPs that are discharged into the environment. Even when inert substances such as gold are constructed, nanomaterials become very active at the nanoscale scale. It may float smoothly through the air and easily infiltrate animal and plant cells, generating unclear consequences[39]. These ENPs have dangerous effects on the ecosystems when they got released untreated to the environment. This can be understood by understanding the life cycle of an ENP (Fig. 3).

- **Nano enabled products**: ENPs may be released into water resources when nano-enabled products (NEPs) are used. The rising commercialization of NEPs increases the possibility of environmental exposure. The research looked at the release and properties of ENPs from six commercial items. Long and angular $nTiO_2$, nAg, and nZnO were formed when ENPs discharged into aqueous environments were associated with cation (Ag^+ and Zn^{2+}) and coating agents (Si and Al). The material kind and quality of the receiving water affected the total concentration. It was shown that the amount of ENPs injected into NEPs at the outset is directly related to the pace at which the ENPs are released. Each of the three factors—receiving the quality of the water, ENM loci within the product, and product matrix composition—affected the amount and characteristics of ENPs released by the product. It is not yet possible to quantify the dangers of nano pollution to human health in the environment.

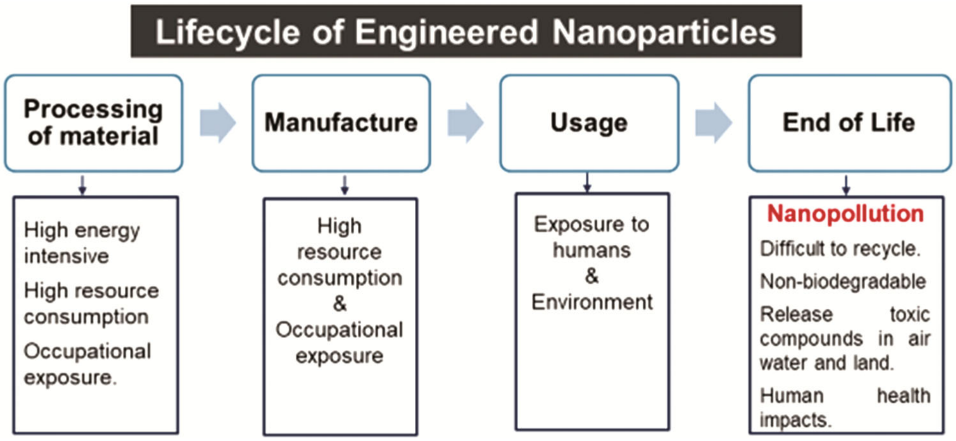

Fig. 3 — Life cycle of ENPs

Reducing the production of ENPs and other preventative measures may lessen their impact on the environment (safety-by-design principle). All affected the amount and characteristics of the ENPs released by the product while lighting conditions had no influence[40].

- **Nanomaterials:** ENP-containing pollutants emitted by domestic, industrial, and medical items are developing as a new environmental danger. NPs have been proven in recent research to have a considerable impact on plant growth, development, and physiology. Reactive oxygen species (ROS) production in response to NPs interactions has been documented across plant species. Secondary metabolites may protect plants against herbivores and harmful bacteria by acting as Phytoalexins/ Phytoanticipins, as signals for symbiotic plant associations with helpful microbes, and as allergenic agents to protect crops from rhizosphere competition. However, the impact of NPs on plant secondary metabolism remains unknown. Changes in plant secondary metabolism caused by NPs might impact plant interaction with their surroundings and growth and production. Because many phytomedicines exhibit their positive effects via additive or synergistic activities of numerous chemicals acting on single or multiple target sites, the presence of NPs in the environment may impact the pharmacological characteristics of medicinal plants[41].

- **Nanopollution**:Nanopollution has been linked to neurodegeneration, heavy metal deposition, and beta-amyloid plaques in the brain. Air pollution consists of nano pollutants of various sizes that may enter the system and cause sickness. The impact of nano pollutants, rats were exposed to various particle sizes for 0.5, 1, 3, and 10 months, and their brain tissues were examined. Spectroscopy demonstrated the buildup of some heavy metals in the rat brain[42]. It alsohas negative impact on aquatic life leading to biomagnification. Tottori University researchers revealed how carbon nanotubes (CNT) penetrate the circulation within minutes of breathing. This example shows how nanomaterials' size, shape, and surface charge influence their behavior in living organisms[43]. Finally, all of these micro contaminants enter the ecosystem through drainage to the soil. It is vital to have remedies for nano pollution and treatment to restore the ecosystem to its original state[43]. Nanopollutants (NPTLs) have lately sparked worldwide concern owing to their potential damage to the environment and human health. To date, knowledge of the incidence, fate, and toxicity of NPLTs in the environment is limited[44].

Environmental impact of ENPs

ENPs may have a significant role in their adverse effects on human health. Although their release into the atmosphere is widely studied, little is known about the ecological destiny of ENPs[45].

- Metal-based ENPs

Magnetic combustion as friction derived nanoparticles[45] in air pollution are distinguished by the abundance of iron-rich particles that condense or oxidise after airborne discharge. The production of nanoparticles, exceptionally demonstrably inert iron-oxide nanoparticles for nanomedicine, gives information on their cytotoxicity, metabolism, biodistribution, and cellular absorption[46].

- Carbon-nanotubes

Anthropogenic carbon- nanotubes (CNTs) and other carbon-based nanoparticles have been found in the alveolar macrophages of Parisian youngsters[45]. Carbon nanotubes have been revealed to be present and historical atmospheric aggressors, and these nanomaterials may reach the human lungs. Another research found carbon nanotubes in the lungs of World Trade Center victims. However, the test specimens were only discovered using lower magnification transmission electron microscopy (TEM)[46]. It might be incorrect since pulmonary surfactant filaments are similar to filamentous Single walled carbon- nanotube (SWCNT) bundles. Anthropogenic carbon nanotubes are difficult to detect in both outdoor and indoor air. Particulate matter, including CNTs, may be recognized in biological specimens utilising a restricted number of methods that are seldom employed in clinics[45]. Specific techniques for identifying synthetic carbon nanotubes have been developed and may readily be adapted to fulfil the detection requirement of anthropogenic carbon nanotubes. The production of sophisticated nanomaterials is thriving, and research into airborne nanoparticle identification is plentiful; yet, information on the prevalence of anthropogenic carbon nanotubes in the outdoor and interior air is still limited. Consequently, practical clinical research needs user-friendly approaches for detecting airborne carbon nanoparticles.

The impact of nanotechnology on the environment can be described in two main aspects: Innovation in Nanotechnologies helpful to improve the environment, another aspect is the type of pollution that Nano technological materials might cause if released into the environment.

Conclusion

The introduction of nanotechnology and its related fields transformed the field of medicine. The development of ENPs represents an exciting, dependable, and promising advancement in medicine and biology. These ENPs have also added a plethora of beneficial developments in engineering and technology. The various fields of textile, food, electronics and energy have been advanced by the use of nanotechnology. However, ENPs interactions with different biological and cellular systems confer toxicity to them which requires cautious manipulation of engineered nanomaterials. There is urgent need to develop laws, policies and guidelines for safely managing different aspects of nanomaterials.

Conflict of interest

All authors declare no conflict of interest.

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