

A Comprehensive Study on Engineered Nanomaterials and its Applications

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Abstract

Technological improvements have been made possible by the NMs' tunable physical, chemical, and biological properties, which outperform bulk materials. Size, composition, shape, and provenance all play a role in determining the classification of natural materials (NMs). For each classification, predicting the unique qualities of NM improves its worth. Toxicological concerns are certain to arise as NM production and industrial use expand. Accordingly, the purpose of this study is to examine the nanoscale properties of both synthetic and naturally occurring NPs and NSMs and to identify specific knowledge gaps relevant to risk assessment of NPs and NSMs in the environment. NPs and NSMs, both naturally occurring and synthesised, and their harmful effects on mammalian cells and tissues are discussed in detail, as are their origins and categorization systems. Toxic reactions to NPs and NSMs are also explored, as well as the restrictions put in place by various countries to mitigate the associated hazards.

Keywords: Engineered nanomaterials, nanotoxicity; oxidative stress; nanoscience; nanotechnology.

Introduction

Nanoparticles (NPs) and nanostructured materials (NSMs) are an active area of study and a techno-economic industry that is expanding rapidly in a wide range of application domains.

Because of their tunable physicochemical properties such as melting point, wettability, electrical and thermal conductivity, catalytic activity, light absorption and scattering, NPs and NSMs have gained prominence in technological advancements, resulting in improved performance over their bulk counterparts. A nanometer (nm) is a unit of length in the International System of Units (SI). In principle, NMs are characterised as materials with a length of 1–1000 nm in at least one dimension; nevertheless, they are most usually defined as having a diameter of 1–100 nm.

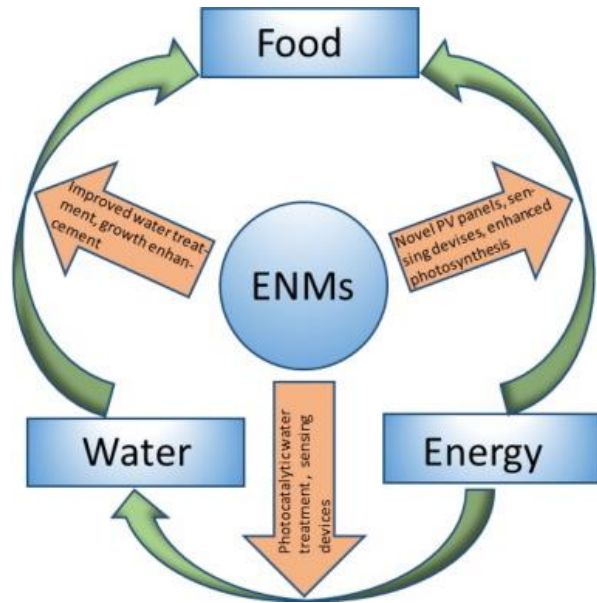
NMs are specifically mentioned in numerous pieces of law in the European Union (EU) and the United States (US) today. However, there is no single widely accepted definition of NMs. Different organisations have different definitions of NMs [1]. "NMs can exhibit distinct features dissimilar to the equivalent chemical component in a larger dimension," according to the Environmental Protection Agency (EPA) [2]. NMs are also defined by the US Food and Drug Administration (USFDA) as "materials with at least one dimension in the range of roughly 1 to 100 nm and exhibit dimensiondependent phenomena" [3]. Similarly, the International Organization for Standardization (ISO) defines NMs as "materials with any outward nanoscale dimension or with any internal nanoscale surface structure" [4]. This ISO definition has been used to define nanofibers, nanoplates, nanowires, quantum dots, and other related terminology [5]. According to the EU Commission [6,] a nanomaterial is "a manmade or natural material that possesses unbound, aggregated, or agglomerated particles with exterior diameters ranging from 1 to 100 nm." Recently, the British Standards Institution [7] recommended the following definitions for commonly used scientific terms:

Nanoscale: A size range of approximately 1 to 1000 nm.

- **Nanoscience:** The science and study of matter at the nanoscale, focusing on their size- and structure-dependent properties and comparing the emergence of individual atoms or molecules or bulk material-related distinctions.
- **Nanotechnology:** The manipulation and control of matter on a nanoscale scale through the use of scientific knowledge in a variety of industrial and biomedical applications.
- **Nanomaterial:** A material with internal or external nanoscale structures.
- **Nano-object:** A material with one or more nanoscale dimensions on the periphery.
- **Nanoparticle:** A nanoparticle is a tiny item with three exterior dimensions. When the lengths of the longest and shortest axes of a nano-object are varied, the terms nanorod or nanoplate are used instead of nanoparticle (NP).
- **Nanofiber:** When a nanomaterial has two identical outer nanoscale dimensions and a third bigger dimension, it is referred to as a nanofiber.
- **Nanocomposite:** Multiphase structure containing at least one nanoscale phase.
- **Nanostructure:** Composition of nanoscale constituent parts that are interlinked.
- **Nanostructured materials:** Those that have an internal or external nanostructure.

The use of disparate definitions across countries obstructs regulatory efforts by causing legal uncertainty over the application of regulatory procedures to identical NMs. As a result, the

requirement to meet divergent viewpoints is a significant impediment to adopting a unified international definition for NMs.



What are the different types of nanomaterials?

There are four main categories of contemporary NPs and NSMs that can be broken down into (the references refer to recent reviews on these different categories of NMs).

In general, these NMs are carbon-based and can be found in hollow tubes, ellipsoids, or even spheres. It's not just carbon nanotubes, carbon nanofibrillar and graphene (Gr) that make up the carbon-based NMs family.

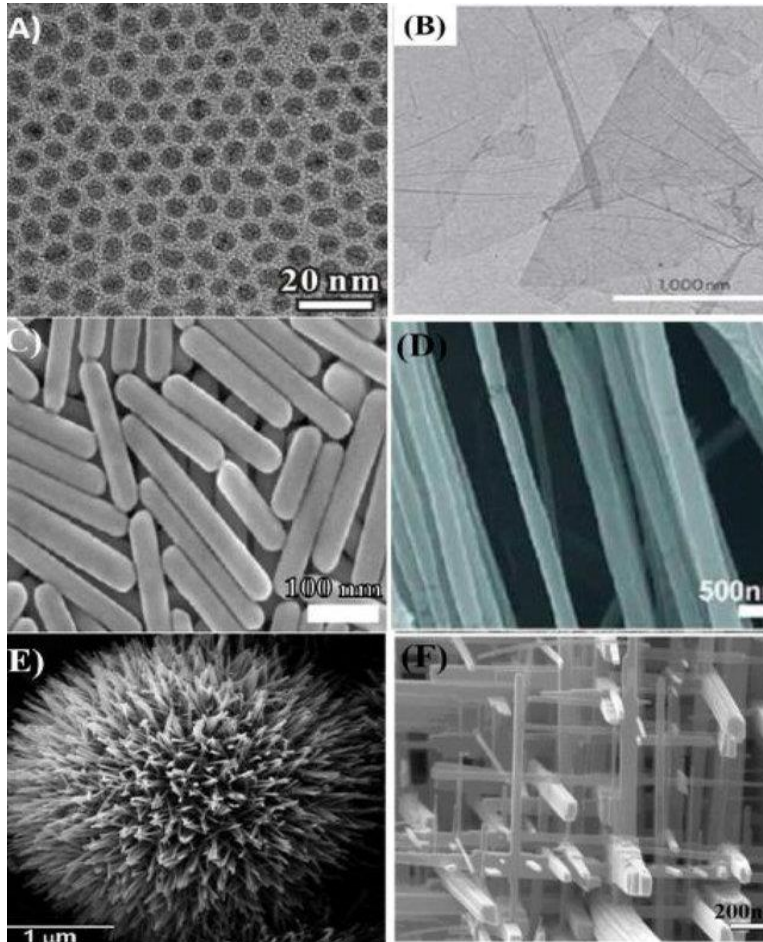
For the manufacturing of various carbon-based materials (excluding carbon black), laser ablation, arc discharge, and chemical vapour deposition (CVD) are the most important processes [8].

Metal and metal oxide NPs, as well as NSMs, are examples of inorganic nanomaterials. Metal NPs, such as Au or Ag, metal oxide NPs, such as TiO₂ and ZnO NPs, and semiconductor NPs, such as silicon and ceramics, can all be generated from these NMs.

Included in this category are organic-based nanomaterials, omitting carbon-based or inorganic NMs. Dendrimers, micelles, liposomes, and polymer NPs can be formed by utilising noncovalent (weak) interactions for the self-assembly and design of molecules.

(iv) Nanomaterials based on composites: It is possible to mix two or more NPs with larger or bulk-type materials (e.g., hybrid nanofibers) or more complex structures (e.g., metalorganic frameworks) to form composite NMs with one phase on the nanoscale dimension. Any combination of carbon, metal, or organic-based NMs with any type of metal, ceramic, or

polymer bulk materials can be used to create composite materials. Figure 1 shows the numerous morphologies of NMs that can be produced according on the desired qualities.



Nanomaterials with different morphologies:

(A) nonporous Pd NPs (0D) [9,10], copyright Zhang et al.; licensee Springer, 2012, (B) Graphene nanosheets (2D) [11], copyright 2012, Springer Nature, (C) Ag nanorods (1D) [12], copyright 2011, American Chemical Society, (D) polyethylene oxide nanofibers (1D) [13], copyright 2010, American Chemical Society, (E) urchin-like ZnO nanowires (3D), reproduced from [14] with permission from The Royal Society of Chemistry, (F) WO₃ nanowire network (3D) [15], copyright 2005 Wiley-VCH.

Nanomaterials classified according to their dimensions

The nanoscale manufacture of conventional items is currently assisting and will continue to assist multiple countries' economic development. Numerous NPs and NSMs have been described, and many more are expected to emerge in the future. As a result, the time has come for their classification. Gleiter et al. [16] pioneered the concept of NM classification. NMs were

categorised in this section according to their crystalline structure and chemical content. However, the Gleiter approach was incomplete since it did not account for the dimensionality of the NPs and NSMs [17]. Pokropivny and Skorokhod created a new classification method for NMs in 2007 that incorporated recently produced composites such as 0D, 1D, 2D, and 3D NMs, as seen in Figure 1 [18]. This classification is largely dependent on the electron motion in the NMs' dimensions. For instance, in 0D NMs, electrons are imprisoned in a dimensionless environment, whereas in 1D NMs, electrons can flow along the x-axis, which is less than 100 nm in length. Similarly, electrons travel along the x-y and x, y, z axes in 2D and 3D NMs, respectively.

The capacity to forecast the qualities of natural products (NMs) dictates their categorization value. The properties of NMs are largely dependent on the grain boundaries, as indicated in Gleiter's classification idea of "grain boundary engineering."

Thus, grain boundary engineering will increase the typical inner size effects, such as melting point lowering and diffusion amplification. Pokropivny and Skorokhod argued that the features of NMs are ascribed to the shape and diameter of the particles, in accordance with the "surface engineering" idea, thereby classifying NMs. Thus, these considerations emphasise particle shape and dimension engineering, as well as grain boundary engineering, in order to broaden the applicability of NSMs [18].

The classification of nanomaterials based on their origin.

NPs and NSMs can also be categorised as natural or synthetic depending on their origin, in addition to their dimensions and materials.

Nanomaterials can be found in nature in the form of both biological and manmade sources. Natural resources can be used to produce artificial surfaces with unique micro and nanoscale templates and features that can be used in technology applications. The Earth's spheres (i.e., the hydrosphere, atmosphere, lithosphere, and even the biosphere) contain naturally occurring NMs, regardless of human activity. Nature-made NMs (NMs) are present in all of Earth's physical spheres: the atmosphere, the hydrosphere, the lithosphere, and the biosphere.

By mechanical grinding, engine exhaust and smoke, or by synthesis of synthetic nanomaterials (iii), synthetic nanomaterials can be created. Engineered nanomaterials (NMs) are increasingly being used in consumer items and industrial applications, which has prompted the question of risk assessment methodologies in recent years. In order to predict the behaviour and fate of manufactured NMs in various environmental media, these risk assessment methodologies are useful. Is it possible to predict their behaviour based on current knowledge or do they exhibit specific environmental-related behaviours that are separate from natural organisms? Engineered NMs are now made from a variety of sources, all of which are linked to their prospective applications.

Nanomaterials' history and development

The incorporation of natural asbestos nanofibers into ceramic matrixes has been used by humans for more than 4,500 years [2]. More than 4,000 years ago, the Ancient Egyptians used synthetic

chemical processes to produce PbS nanoparticles for hair colour. Like "Egyptian blue," a sintered mixture of nanometer-sized glass and quartz was employed by the Egyptians in the 3rd century BC to make and use a synthetic colour. It is a complex blend of $\text{CaCuSi}_4\text{O}_{10}$ and SiO_2 that gives Egyptian blue its colour (both glass and quartz). Throughout the Roman Empire's historic territories, including Egypt, Mesopotamia, and Greece, Egyptian blue was used extensively for ornamental purposes during archaeological investigations. [5] Chemical methods for producing metallic NPs date to the 14th and 13th century BC, when Egyptian and Mesopotamian civilizations were first creating glass with metals.

It is possible that these are the first examples of synthetic NMs being used in a real-world context. Frattesina di Rovigo (Italy) has unearthed red glass from the late Bronze Age (1200–1000 BC) that is coloured by the surface plasmon excitation of Cu NPs. Cu NPs and cuprous oxide (cuprite Cu_2O) have also been found in Celtic red enamels from the 400–100 BC period [7]. However, the most well-known example of early metallic NPs use is a Roman glass pane. During the 4th century BC, the Lycurgus Cups are a Roman glass cup composed of dichroic glass that changes colour depending on the direction of the light. The Lycurgus Cups have been found to contain Ag–Au alloy NPs, with a 7:3 ratio, as well as roughly 10% Cu [9]. [Gold and silver nanoparticles (Au and Ag NPs) were later used to generate the red and yellow stained glass prevalent in mediaeval churches. Mesopotamians began decorating their ceramics with metallic brilliance around the 9th century [2]. Due to the presence of discrete Ag and/or Cu NPs in the outermost glaze layers, these decorations have amazing optical characteristics. Metal nanoparticles that exhibit iridescent vivid green and blue colours under specific lighting circumstances can be found in these ornaments. There is a double layer of 5–10 nm-thick silver nanoparticles (Ag NPs) on the outer layer of these ceramics and larger ones (5–20 nm) on the inner layer. Interference effects were noticed because the spacing between two layers was found to be constant at roughly 430 nm. The phase shift is caused by the scattering of light from the second layer by the first layer. This wavelength-dependent phase shift results in a distinct scattering wavelength. Later, red glass was produced all over the world using this method. The famed Satsuma glass in Japan was made using a similar method in the mid-19th century. In order to enhance the Satsuma glass with a ruby colour, Cu NPs were used. Natural NM has been used in clay minerals of a few nanometers in thickness since antiquity. Clay was used to bleach wool and clothing in Cyprus as far back as 5000 BC [1].

A colloidal Au NP solution was synthesised by Michael Faraday in 1857, which was the first scientific description of the creation of NPs and sparked the scientific history of NMs. The optical properties of Au colloids, he found, differed significantly from those of their bulk counterparts. This may have been one of the earliest reports of quantum size effects being observed and documented. Later, Mie (1908) explained why metal colloids come in a variety of hues. The use of SiO_2 NPs as an alternative to carbon black for rubber reinforcing was first developed in the 1940s.

As reinforcement for construction or safety sensors, today's manufactured NMs can significantly improve bulk material properties such as strength, conductivity, durability, and weight. They can also provide useful properties such as the ability to self-heal, self-clean, resist freezing, and be antibacterial. There are numerous advantages to using nanoparticles (NPs), but the most common use of NPs is to enhance the aesthetics and functionality of materials. As a result, the commercial usage of NMs is usually restricted to bulk utilisation of passive NMs embedded in non-inert (polymer or cement) composites.

Antibacterial technology with the trade name Silver Nano™ was introduced in 2003 by Samsung, which uses ionic Ag NPs in its washing machines, air conditioning, refrigeration and vacuum cleaners [4]. There are numerous applications for NPs and NSMs in the automotive industry, including tyre fillers, body fillers, and clear layers for heated, mist and ice-free window panes [5]. For metallic and non-metallic paint finishes, Mercedes-Benz introduced an NP-based clear coat in series production by the end of 2003. The coating boosts the shine and scratch resistance. Ferrofluids, or ultrastable suspensions of tiny magnetic NPs with superparamagnetic characteristics, are a type of liquid magnet [36]. In the presence of a magnetic field, macroscopically magnetized liquid will be aligned in the direction of the magnetic field [7]. Earth-based astronomical telescopes with adaptive optics and magnetic mirrors that can change shape thanks to ferrofluids have been the subject of recent research [8,9]. The commercial usage of TiO₂ NPs in solar cells that can be dye-sensitized is well established. To highlight Logitech's first major commercial use of dye-sensitized solar cells, the company unveiled an external iPad keyboard powered by light in summer 2012. It was in 2005 when Abraxane™ was developed, marketed, and released in the pharmaceutical market as a human serum albumin NP material containing paclitaxel. Nanotechnology-based consumer products were commercially available in more than 20 countries in 2014 [2].

Nanomaterials' origins

According to their source, nanomaterials can be divided into three categories: For example, engine exhaust particles and welding fumes contain nanoparticles, and so do forest fires and other naturally occurring processes, such as combustion. In addition to incidental nanomaterials, there are engineered nanomaterials and naturally produced nanomaterials, the latter of which can be found throughout nature. There are, however, many instances where the boundary between naturally occurring, accidental, and artificial NPs is muddled. Incidental NMs, for example, can be classified as a subclass of natural NMs in some situations.

As the building blocks of all living and non-living organisms, atoms make up molecules. Numerous natural processes have resulted in the creation of complex NSM and NPs that are essential to life on Earth. There is a constant supply of naturally occurring NMs in groundwater, surface water, seas, continental soil, and atmosphere. For one thing, engineered NMs can be purposefully developed to utilise innovative traits that emerge from their small size, which is one of the key differences between incidental and engineered NMs in terms of morphology. This

means we've been in direct contact with metal NPs for a long time, and that macroscale items are also a possible source of accidental nanoparticles in the environment.

Nanomaterials that happen to be in the environment.

Natural NPs are produced by a variety of processes, including photochemical reactions, volcanic eruptions, and forest fires. The natural shedding of animal and plant skin and hair also contributes to the composition of NP. Nanoparticulate matter (NPM) is a type of particle matter that is produced by natural phenomena such as dust storms, volcanic eruptions, and forest fires. Similarly, human activities such as transportation, industrial operations, and the burning of charcoal all contribute to the development of synthetic NPs.

Human activity accounts for only 10% of the total aerosols in the atmosphere, whereas natural aerosols make up 90% of the total [3].

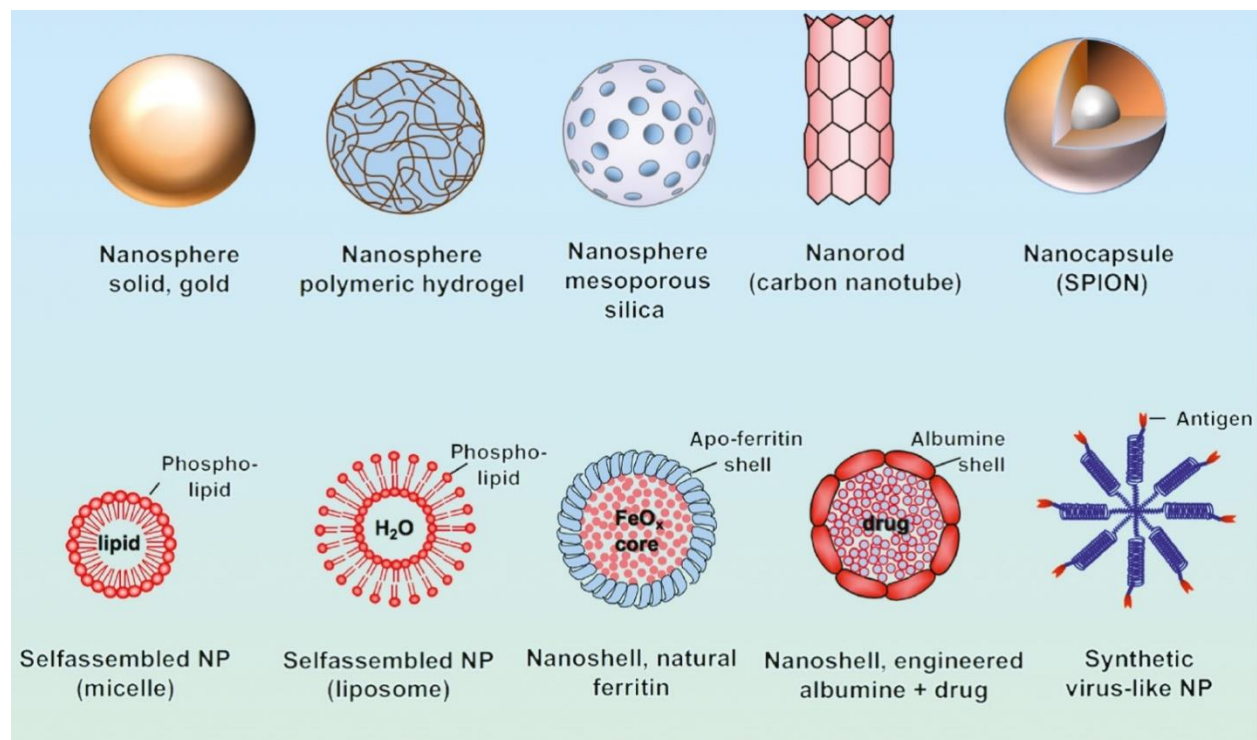
Storms of dust and cosmic dust: The Eagle Nebula stars, which are 6500 light years from Earth, are born with a disk-like cloud with the possibility to form solar systems accompanied by dust and gas (mainly hydrogen) [4]. Astronomical observations (particularly infrared spectroscopy) and direct "stardust" research during space missions and meteorite collections indicated that the major components of stardust are a diverse range of carbide, oxide, nitride, silicate, carbon, and organic-based NMs [4]. Diamond of a few nanometers in diameter has been found in the Murchison meteorite, which is an excellent example of nanoparticulate genesis in planetary system objects other than stars [5]. Various sorts of NMs exist throughout the universe, which are mixed, sorted, and transformed into various forms. Electromagnetic radiation, pressure gradients, extreme temperatures, physical collisions, and shock waves all contribute to the energising and formation of NPs in space [4]. This results in the greatest variety of nanoscale materials with different re-equilibration/phase mixing and isomerization across the chemical spectrum [19].

In desert and terrestrial areas, dust storms are the primary source of NPs. According to satellite photos, dust storms in one place can transport nano and micro-sized minerals and anthropogenic pollutants thousands of kilometres away from their source. About half of the atmospheric aerosol particles emitted by dust storms in deserts are in the 100–200 nm range [16,17]. Buseck and Posfai conducted an exhaustive analysis of the effects of aerosol particles on the environment and climate. They stated that the extensive dispersion of aerosols across oceans has a significant impact on life, particularly species at the bottom of the food chain [18]. Another study by Al-Dabbous and Prashant Kumar discovered the occurrence of 5–1000 nm range airborne NPs during summertime and dust events in Kuwait's busy roadside (terrestrial) [19].

Asthma and emphysema are two common health disorders in humans induced by dust particles in the air [10,11]. Metal-containing dust NPs have the potential to harm lung tissues by creating reactive oxygen species [43]. According to a case study, dust storms in the Gobi Desert severely disrupt the quality of air in Asia and North America during the spring season [12,13]. Shi et al.

(2009) recently showed (through simulated cloud processing) that dust storms contribute to the formation of Fe NPs in clouds, which causes pH changes and affects the atmospheric, mineralogical, physical, and chemical aspects of the Saharan desert region [14-17]. Figure 2 depicts aggregated NPs in a dust storm location during and after a dust storm.

Cosmic dust is a collection of extraterrestrial dust particles that occur in large quantities on the nanoscale in space. Many meteorites and extraterrestrial materials have been discovered to include natural NMs, which were thoroughly mentioned in the review "Nanotechnology: nature's gift or scientists' brainchild?" [19]. Cosmic dust poses a serious threat to astronauts and aeronautic sensors [18]. Lunar dust is smaller than conventional terrestrial dust, with an abundance of sub-micrometer particles..



Electrostatic attraction may cause astronauts' space suits to get contaminated with lunar dust that contains a few magnetic nanoparticles (NPs) [59,60]. By becoming airborne, they've been known to irritate the lungs and eyes of Apollo astronauts [11]. Lunar compounds have been shown to cause pneumoconiosis and fibrosis in rats when ingested intracranially [12]. By accumulating on the solar panels of exploration robots, dust particles on Mars can harm the sensors, communication, and movement of the robots, causing them to malfunction. As a result of long-term exposure to cosmic dust, astronauts who frequently travel into space are at an elevated risk of developing respiratory disease. Spacesuits and airlocks can also be damaged and mechanically broken down by dust particles [14].

As a result of volcanoes erupting, a large number of aerosols and tiny particles with diameters ranging from micrometres to several nanometers are released into the atmosphere. During a single volcanic eruption, 30 106 tonnes of NPs can be released into the atmosphere in the form of ash. It is the stratosphere and troposphere, the lowest atmospheric levels, where the released NPs land. However, NPs will have a substantial impact within a particular distance of the volcano (10 km).

Volcanic eruptions in the 1980s sent bismuth oxide NPs into the stratosphere, according to Rietmeijer and Mackinnon [18]. The sunlight is obstructed and scattered by volcanic ash, which has a negative impact on the activities of humans, animals, and plants. Particles emitted by volcanic eruptions may contain heavy metals that are harmful to people. When inhaled in large quantities, volcanic ash particles can cause short-term irritations such as nosebleeds and sore throats as well as long-term disorders such as podocinids [10–12] and Kaposi's sarcoma [13,14]. Because of the absorption of soil micro- or nanoparticles through skin contact with the ground, fluid retention is generated in lower limbs. Similar to cancer and the human herpes virus infection that affects the blood and lymph arteries of Kaposi's sarcoma, the disease. [13] NPs enter the body, causing the problem.

Fires in the forest and the evaporation of ocean water It is lightning and human activity that are the most common causes of forest and grass fires around the world today. As these forest fires burn, ash and smoke are generated, which can travel long distances and impair the standard of ambient air quality [10]. It has been found that Asian brown clouds carry and deposit enormous quantities of black carbon and soot over the Himalayas glaciers. Glacier melting is accelerated due to greater absorption of sun's heat by these accumulated particles [16,17]. Nanoparticulate can be seen in the smoke.

These micro and nano-sized particles can cause respiratory issues in humans and animals when they travel via smoke and ash in forest fires [18-20]. Patients with pre-existing cardiovascular problems can be worsened by smoking containing very minute particles [13]. Smoke inhalation is also claimed to be responsible for 75% of fire-related deaths [14]. Aerosolized sea salt is another type of naturally occurring NP that is produced by water evaporation and the upwards ejection of water droplets produced by waves into the atmosphere.

Natural precipitation and temperature change are the most common mechanisms for producing these salt aerosols, which can range from 100 nm to a few micrometres in diameter. CaCO₃ NPs in Lake Michigan have been linked to weather and temperature fluctuations [11]. Microorganisms and contaminants may be transported via these sea salt aerosols, increasing the risk of disease and death in plants, animals, and people.

Nanomaterials created by scientific means

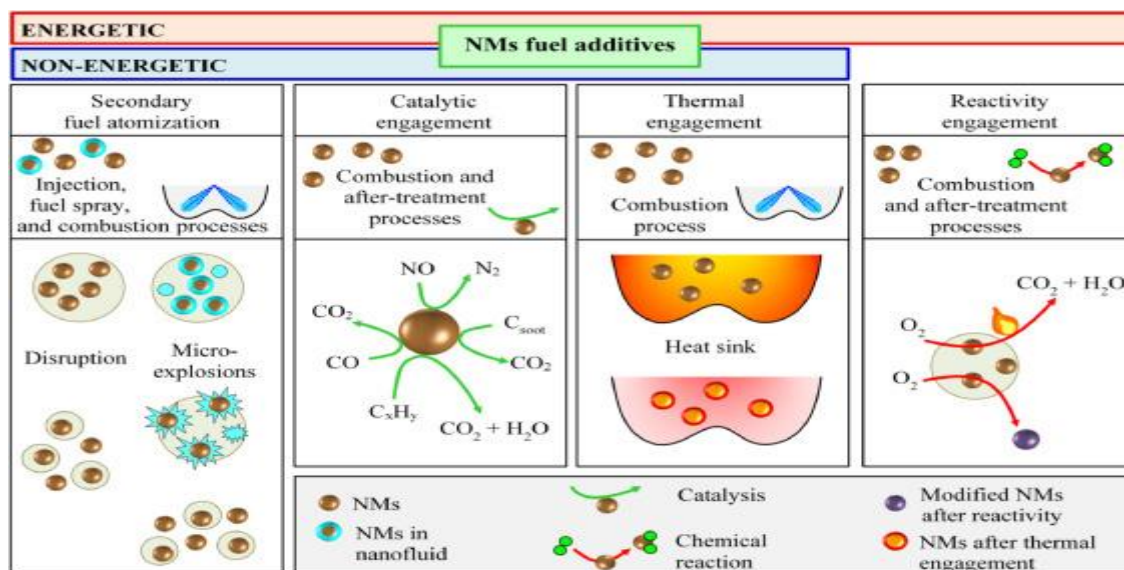
Anthropogenic activities that lead to the development of NP include simple combustion in cooking, cars, power generation using fuel oil and coal [3], aviation engines, chemical manufacturing, welding, ore refinement and smelting [14].

The presence of nanomaterials (NMs) in commercial cosmetics, athletic goods, sunscreen, and toothpaste is well documented. In other words, these novel types of nanoparticles (NPs) could have harmful environmental and human health repercussions.

Fuel- and engine-generated nanoparticles:

The primary source of air micro- and nanoparticles in cosmopolitan cities and towns is automotive exhaust [8]. As far as automotive exhaust goes, diesel engines emit particles ranging from 20 to 130 nanometers in diameter, while gasoline engines release particles ranging from 20 to 60 nanometers in diameter. In the combustion of fuel and gas, CNTs and fibres are released as by-products [11]. Diesel-generated carbon NPs make up more than 90% of the carbon NPs in the atmosphere [12].

As a result, vehicular pollution is a major source of urban air pollution [3]. The danger posed by exhaust fumes from motor vehicles is directly related to the particle combination it contains [4]. Anthropogenic carbon nanotubes have recently been identified in the broncho-alveolar lavage fluids of asthmatic Parisian children, particularly in small particulate matter. Carcinogenicity and neoplasia have been shown to be linked to the existence of carbon nanotubes in the lungs by the results of this study. Car exhaust samples from Paris, air samples from the US, a spider web sample in India, and ice core samples from Antarctica were all found to contain carbon nanotubes, according to the study's findings. Diesel exhaust contains benzo[a]pyrene, a polynuclear aromatic hydrocarbon and a carcinogen, which makes it more dangerous than gas engine exhaust [16]. Some of the health issues associated with excessive exhaust exposure in densely populated cities include cardiovascular mortality, paediatric malignancies, myocardial infarction, and proinflammatory, prothrombotic, and hemolytic responses.



Cigarette smoking and building destruction is both anthropogenic activities that contribute to the dispersion of NPs into the atmosphere. Cigarette smoke comprises a complex mix of over

100,000 chemical components in the form of nanoparticles (NPs) ranging in size from 10 to 700 nm [2]. Similarly, when larger buildings are demolished, nano- and microparticulates smaller than 10 m are discharged into the atmosphere [3]. Lead, glass, respirable asbestos fibres, and other harmful particles from home products, in addition to building debris, are released as nanosized particles surrounding the site of building demolition [3]. Cigarette smoking has been linked to chronic respiratory illness, cardiovascular disease, pancreatic cancer [4], genetic changes [5], middle ear disease, and asthma exacerbation [4]. It is worth noting that the risks of myocardial infarction linked with inhaled NPs can be reversed after smoking cessation [6]. The dangers of demolition particles, as well as their long-term impacts on humans, are still unknown. However, respiratory symptoms such as coughing and bronchial hyperactivity were observed among firemen who participated in the World Trade Center rescue mission on September 11, 2001 [7]. This suggests that considerable research should be conducted among demolition workers to discover the negative effects of dissipated particles.

Nanoparticles in biomedical and healthcare products: NMs are used as antioxidants and antireflectants in cosmetics and sunscreens [8, 9]. Most NPs utilised in commercial applications are designed NPs created using physical [10], chemical [11], and biological [12] processes. The possibility of designed NPs detaching and creating health problems is reduced because they are attached to a hard surface [4]. NPs have been widely used in commercial items ranging from personal care products to paints, in addition to cosmetics [3].

Titanium oxide NPs with diameters more than 100 nm are commonly used as a white pigment in cosmetic lotions and sunscreens [4]. Ag NPs have also been employed in a variety of applications such as air sanitizing sprays, wet wipes, food storage containers, shampoos, and toothpastes [5]. Several NPs are being researched and evaluated as personal care product additions. Despite the growing popularity of items using various types of nanomaterials, the dangers they pose to humans are mostly unclear.

Extensive research found that Ag NPs were more harmful to human and animal cells than asbestos [9-10] because of their size, shape, and dosage-dependent cytotoxicity. The harmful consequences of other NPs found in consumer products are unknown and under investigation.

Nanomaterials generated naturally

Nanoparticles and nanostructures are found in living species ranging from microorganisms such as bacteria, algae, and viruses to sophisticated organisms such as plants, insects, birds, mammals, and people. Recent advancements in nanomaterial visualisation technology aid in detecting the morphology of these spontaneously generated NMs, leading to a better knowledge of these organisms. The understanding of the nanostructures found in microbes is critical for the future usage of these organisms in beneficial healthcare applications.

Insects contain nanostructures that form as a result of an evolutionary process, allowing them to survive in severe living environments. Plants also use the nutrients in the soil and water to grow, resulting in the buildup of these biominerals in nano-form. Animals and small insects use

nanostructures to shield themselves from predatory animals and in their lightweight wings via nanowax coats.

Similarly, humans have organs that are essentially made up of nanostructures, such as bones. Antibodies, enzymes, and other secretions that are extremely important to human function have been discovered to be in the nanometer range. It should also be mentioned that genetic material (DNA or RNA), which is essential for cell creation and function in all living cells, is a nanostructure. This clearly demonstrates that nanostructures are the fundamental building blocks for all life forms on Earth. The sections that follow will attempt to list the nanostructures found in living beings.

Nano-organisms: Nanoscale creatures, colloquially referred to as nano-organisms, are ubiquitous in our environment and even within our bodies. The term "nano-organisms" refers to naturally occurring nanomaterials that encompass a diverse spectrum of species, such as nanobacteria and viruses, as well as fungus, algae, and yeast that can make nanoparticles.

Viruses are the biggest structurally defined molecular assemblages known to date. They can exist as a non-living crystal or as a live organism inside host cells. They are regarded as dangerous in general because they induce disease in bacteria [1], plants [2], animals [3], and people [4]. Molecular biology advances have increased the possibilities of genetically tailoring viruses for use as catalysts and bioscaffolds. Nanoscale, monodispersity, different morphologies, selective permeability to smaller molecules, compositional control via genome alteration, self-assembly and polyvalence, rapid growth, and resistance to pH and temperature are all characteristics that distinguish viruses from other NMs [5,6]. As illustrated in Figure 4A, viral NPs can be created by extracting the genetic material from viruses and repurposing them as "nanocargoes" for targeted medication delivery. Saunders et al. [18] described the proteolytic synthesis of viral NPs using RNA-depleted cowpea mosaic virus. Nanocages or protein capsids were employed to encapsulate medicines, genes, enzymes, or proteins for biocompatibility and bioavailability during targeted delivery [18]. Recent research has concentrated on the use of viral NPs as conjugation templates to generate new nanostructures and cages for drug encapsulation [19,10,11,12]. Plant viruses have been shown to be harmless to human cells at the concentrations required for effective medication administration [13,14]. Aspects of nanobacteria and nanobes: Bacteria will typically bind to soluble, poisonous heavy metals and precipitate them to their surface, forming metal nanoparticles. These are referred to as nanobacteria, and they are extremely beneficial in the production of low-toxicity nanoparticles [17].

The first bacteria to be employed to synthesise Ag NPs was *Pseudomonas stutzeri* A259 [18]. Subsequently, numerous metal NPs, including gold [19,10], alloy NPs [11,14], nonmagnetic oxide NPs [13–17], and metal sulphide quantum dots, including CdS [18,19] and ZnS [10], were produced utilising various bacteria strains. Apart from bacteria, actinomycetes such as *Thermomonospora sp.* and *Rhodococcus sp.* are also employed to synthesise NPs [11]. This bacteria-mediated NP production was found to be extremely beneficial in a nanomedicine

application because it reduced the possibility of cellular toxicity [12]. However, the key disadvantages of these NPs are that they take longer to synthesise, are difficult to filter, and yield fewer NPs than chemical synthesis [13].

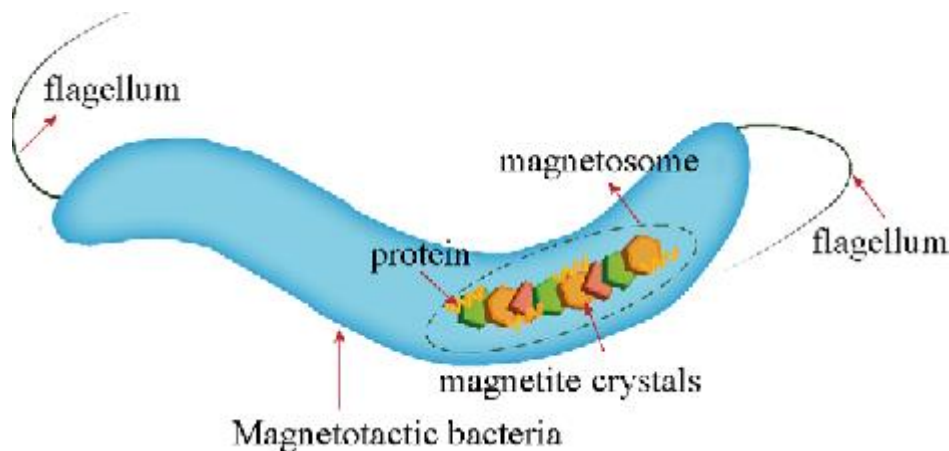
Because they are discovered during off-shore petroleum prospecting on Triassic and Jurassic sandstones in Western Australia [14], novel nanoorganisms, also known as nanobes, are attracting the attention of nanotechnology experts worldwide. These nanobes are formed of individual cells with diameters ranging from 20 to 150 nm that are composed of carbon, oxygen, nitrogen, DNA, a membrane-bound structure with a dense cytoplasm and nuclear region, as well as mineral components, comparable to actinomycetes and fungi in structure. In addition to their small size, which is much below the range regarded to be feasible for autonomous life on Earth, nanobes are also notable for the fact that they were recently discovered in the martian meteorite ALH84001 [15].

Magnetotactic bacteria: Magnetotactic bacteria are extremely beneficial in the production of magnetic oxide nanoparticles (NPs), which have unique properties such as superparamagnetism, high coercive force, and micro configuration, and can be used for biological separation and in biomedicine fields [12]. For the most part, magnetic hyperthermia, magnetic resonance imaging (MRI), DNA analysis, and gene therapy are used to treat cancer using magnetotactic bacteria [16,17]. Magnetotactic bacteria are used to synthesise biocompatible magnetite (Fe_3O_4), iron oxide (Fe_2O_3), iron sulphides (Fe_2O_3), and maghemite (Fe_2O_3), all of which are useful in cancer treatment [18]. Furthermore, magnetotactic bacteria were used to make surface-distributed magnetic iron-sulfide particles [19], 12 nm magnetic octahedral NPs [10], modified iron NPs [161], and superparamagnetic NPs [12,13]. It has been proposed that Bacterial Magnetic Particles (BacMPs) [14] produced by bacteria can operate as a bio-needle in compass, allowing bacteria to migrate under the influence of the Earth's geomagnetic field as well as oxygen gradients in aquatic environments, as illustrated in Figure [15]. *Vibrio*, cocci, spirilla, rod-shape, ovoid, and multicellular bacteria are among the morphologies that have been shown to have distinct properties in terms of producing NPs [14-17]. In recent years, there has been much discussion on the mechanism of neutron capture (NP formation), and exposing the mechanism will aid in the future development of magnetotactic-bacteria-based neutron capture.

Algae, fungi, yeast, and bacterial spores are examples of microorganisms. Phytochelatin-coated CdS by *Phaeodactylum tricorutum* [19] and nanocomposite and nanoporous structures by coccoliths and diatoms [19] are all produced by algae such as *Chlorella vulgaris* [168]. Algae such as *Chlorella vulgaris* also contribute to the development of Ag NPs [18]. As a result of the limited number of researches that have been conducted, the putative pathways for algae-mediated nanoparticle production are yet unknown [10]. Similar to this, fungi have been used in the synthesis of nanoparticles, and the literature has suggested that they are suitable candidates for the synthesis of metallic and metal sulphide nanoparticles, as illustrated. Fungi have a range

of enzymes and are relatively easy to handle, which allows for the production of NPs of varied sizes and forms in a straightforward manner. It has been observed that the fungus *Fusarium oxysporum* and *Verticillium* sp. have been shown to aid in the synthesis of Au, Ag, and Au–Ag alloy NPs [11,12,13] as well as other metals. It has been discovered that the fungus *Fusarium oxysporum* contains enzymes that aid in the creation of CdS quantum dots [14] and that it is a source of sulphate reductases [11, 14], as well as in the formation of zirconium particles [15]. As illustrated in Figure, yeasts such as *Candida glabrata*, *Torulopsis* sp., *Schizosaccharomyces pombe*, and MKY3 (which is a yeast strain with Ag tolerance) were also employed in the production of NPs such as CdS quantum dots [16,17], PbS nanocrystals [18], and Ag NPs [19], among others. The nanoscale spores of bacteria such as *Bacillus anthracis* have been discovered to be capable of causing food contamination and infectious diseases [10].

In a similar vein, recent review articles [13,11-14] give a list of autotrophic plants and heterotrophic bacteria that contribute to the creation of Ag NPs, as well as probable nucleation mechanisms. This list aids in the identification of the critical factor that causes nanoparticle nucleation to occur. This finding will be used in the development of nanometer-sized targeted medications that can prevent the growth of these hazardous bacteria at an early stage in their development.



Plant nanoparticles and nanostructures

Natural fibres are cellular hierarchical bio-composites, and wood is made up of them. At the nanoscale, natural fibres are composites of cellulosic-fibrils. Nanometer-sized cellulosic fibres are 100–1000 nm long and contain both crystalline and amorphous segments in their most basic form. The fundamental hierarchical structure with nanofibrillar components is related to the unusual strength and exceptional performance attributes of diverse natural fibres such as wood [17]. Nanotechnology allows for the isolation of nanocellulose from natural sources, which necessitates a combination of mechanical, chemical, and other procedures. The cellulose

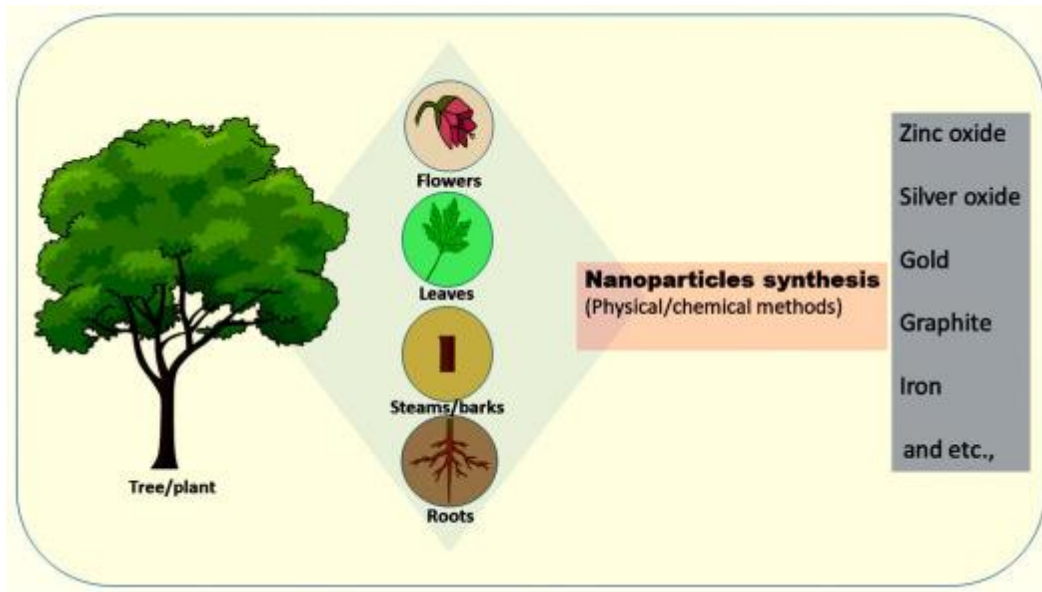
nanofibers that develop could have a variety of morphologies, including rod-like NPs (whiskers) or an entangled network (nanofibers) [18].

As shown in Figure 6, plant surfaces, particularly leaves, include nanostructures that are employed for a variety of reasons, including insect sliding [19], mechanical stability [10], increased visible light and damaging UV reflection and radiation absorption [11,12]. The most well-known nanostructure property in plants is superhydrophobicity, which helps lotus leaves self-clean and be super-wettable [193]. Stacks of nanostructures are thought to be responsible for the circular layer in plants and insects that permits them to float on water without sinking, according to many studies [19].

Many artificial superhydrophobic materials with self-cleaning capabilities have been created [19] with distinctive morphology and roughness [20] based on these studies using electrodeposition, photolithography, and colloidal systems [17-19]. Water treatment [20], wettability switchers [4,5], smart actuators [6], transparent coatings and electrodes [7-9] were among the uses for these superhydrophobic materials.

Insects with nanoparticles and nanostructures

Insect wing membranes are made up of 0.5 mm to 1 mm thick building components [12]. Insect wings are also constructed by a complex vein system that offers the entire wing structure exceptional stability [13-15]. The main architecture of insect wings is a long chain crystalline chitin polymer that provides membrane support and allows for bearing stresses on them during flight [16,17]. Resilin is a unique component found between the vein and wing connections that improves the flexibility of the wing [17-19]. The vascular system, together with their weightless wing substance, supported the routine and longer colonisation flights [20- 22]. Insect wing surfaces have a rough, highly structured structure made up of micro- and nanoscale characteristics that help to reduce mass and protect them from moisture and contaminants. In a review, Byun et al. [2] created a rigorous nomenclature to explain the structural features of insect cuticles. The review focuses on using SEM images to describe the structures and highlights different insect wing shapes. The phrases "Setae," "denticles," and "fractal" are commonly used to characterise the properties of wax crystals seen on wing surfaces. A denticle is organised with morphology spanning from smaller hemispherical to taller fractal; pillars are fine irregular nanoscale projections [2].



There are SEM photos and photographs of a wide variety of insect species and orders available. It has been discovered that the wings of wood termites (*Schedorhinotermes* sp.), cicada (*Meimunamicrodon*), and hornet (*Vespa* sp.) are all coated by a denticle layer. Both constructions [2- 6] have water contact angles (WCAs) of less than 150° , and so are not termed superhydrophobic. When it comes to insects, the wing of the grasshopper, the dragonfly, and the butterfly all had a WCA more than 150 degrees on their surface.

According to the research, superhydrophobic characteristics can be found in species with complex fractal and multilayer cuticle structures. [4] The hierarchical organisation of these structural kinds may increase the hydrophobicity of the surface. Butterflies are also known for their vibrant hues, which are due to their delicate wings. Nanostructures in multilayers, which act as diffraction gratings, generate interference, and hence iridescence, have been documented in the literature.

In animals and birds, nanoparticles and nanostructures

Variable-body-weight animals (insects from Kingdom Animalia) can attach to ceilings and move up and down vertical walls. As a result of the patterning on their surface and the substrate profile interacting, they have an effective mechanism for attaching to the legs of insects. A comprehensive microscopic examination reveals an extreme inverse scaling impact in these attachment devices. Submicrometric devices have been shown to ensure adhesion, whereas flies and beetles rely on micrometer-sized terminal setae. Adhesion causes the breaking of contacts into finer subcontacts, which explains the insect body weight to setae trend. It is possible that the natural adhesive system, which is based on this principle, may be used in actual applications in the future.

Insects' ability to walk on ceilings utilising their hairy attachment systems has been studied for over 300 years. [9] The insect's attachment process is explained by electrostatic forces, adhering fluids, and microsuckers [229]. A combination of secretion-mediated capillary attractive forces with molecular contacts, as well as van der Waals interactions, have been shown experimentally to be ineffective in causing adhesion [20]. Insects produce secretory fluids in the contact area, whereas spiders and geckos do not [2-6]. This may be because the basic force in the physical form contributes to their adhesion because of this difference.

According to recent studies, gecko setae adhesion is caused by van der Waals interaction [7], which disproves the theory of capillary adhesion. Smaller setae arrays could benefit from contact mechanics, which could release more adhesive strength [2-9]. Figure 7 shows the cross-sectional arrangement of peacock feather frills, which contributes to their attractive colour patterns [6].

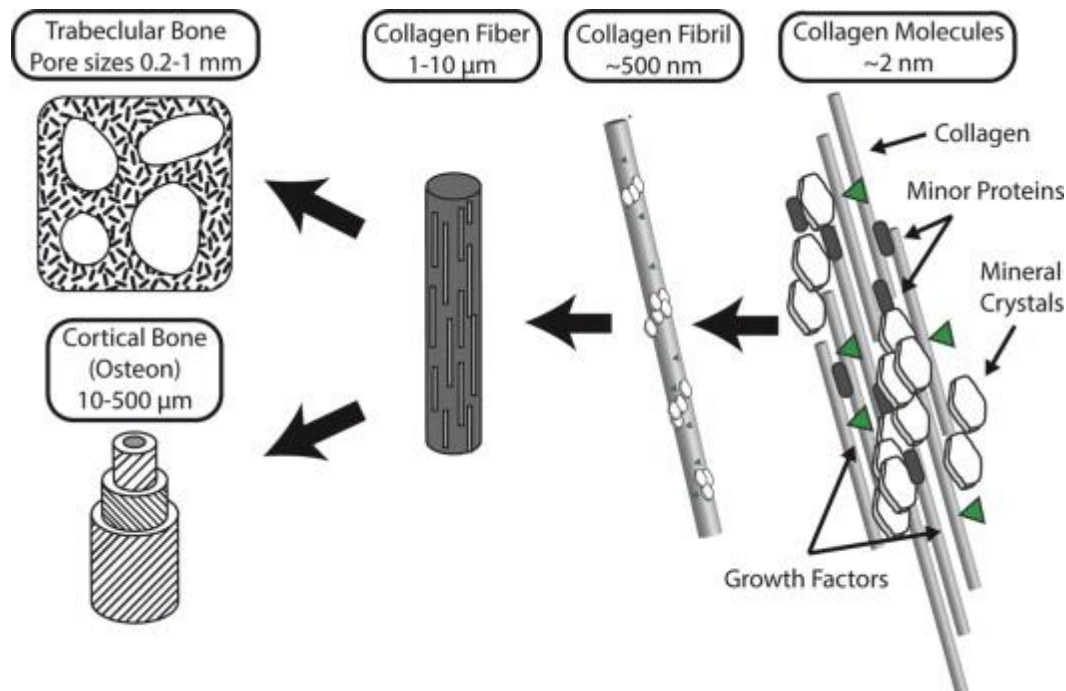
Shells of mollusks are made of "nacre," a hierarchical nanocomposite, which is found in their shells. A thin layer of bio-macromolecular "glue" separates the micrometre and submicrometer CaCO_3 aragonite platelets in nacre. Nacre's mechanical qualities, including as enhanced stiffness, impact resistance, strength, and toughness, allow for its distinctive design. Nanostructures with groovy patterns give the nacreous effect on a rough surface [20]. Additionally, gecko feet have the capacity to walk on ceilings against gravity, as well as on wet or slick surfaces, despite their appearance. They have nanometer-sized hairlike structures in their feet, which are aligned in a sequence of microscopic ridges, each with a 200 nm projection, that are associated to this feature. This results in a van der Waals interaction-mediated high surface adhesion for gecko foot [1]. Protein and CaCO_3 crystals are arranged in columns and layers of calcite to form the eggshell, which is both thin and strong. Amorphous mineral CaCO_3 NPs are first converted into crystals by the C-type lectin proteins during eggshell development. The crystal transition is triggered by the binding of proteins to ACC NPs, which then detach as the crystal grows. [2]

Biological nanoparticles and structures

It is difficult for the human body to operate normally without the presence of nanostructures. Nanostructures such as bones, enzymes, proteins, antibodies, and DNA make up the structure. Table 1 provides a list of nanostructures found in the human body. Inorganic nanohydroxyapatite and organic collagen have been categorised as a nanomaterial in various works. In addition, viruses and bacteria are nanostructures that may infect humans and cause sickness.

Nanostructures in bone

Natural bone is combined with precise and meticulously developed mechanical qualities thanks to their nanoscale to macroscale architectural design.



The interaction of micro/nanoscale components with the extracellular matrix (ECM) within stem cells influences stem cell activity via passive mechanical forces. The major building components of the ECM include a diverse structural protein spectrum and polysaccharides of various length scales, with nanometer-sized collagen fibrils strands of 35–60 nm diameter and a micrometre range length dominating [9]. Figure 8 depicts bone as a multidimensional composite with several hierarchical layers. The two most essential elements of bone tissue are the cortical bone with a compact shell and the spongiosa or trabecular bone with a porous core (Figure 8a). Cortical bone is formed by repeating osteon units, whereas cancellous bone is formed by an interconnected trabeculae framework with bone marrow and open space. Similarly, calcium phosphate crystals and collagen fibres are carefully placed to produce the trabeculae and osteon units. Collagen fibrils are formed by periodic arrangement of collagen molecules with gaps of 47 and 60 nm (Figure 8b)[250,251]. To increase bone stiffness, gaps in collagen fibrils are filled by hydroxyapatite (HA) crystals (Figure 8c) [252,253]. The characteristics of bone tissues are determined by the hierarchical architecture of the ECM and cells with nanometer to centimetre magnitude [4-5].

DNA nanostructures

The genetic blueprint repository of living organisms is DNA. It aids in the synthesis of protein, which is required for the activities of living organisms [6]. A nucleotide is a mono-phosphorylated deoxyribose sugar bonded to a nitrogenated aromatic nucleobase, and it is the fundamental structural unit of DNA. DNA has a variety of sequence information storing techniques, with a density of 2.86 bits per linear nanometer [7]. A-DNA, B-DNA, and Z-DNA

are three types of DNA classifications based on the base-pairing between the strands. B-DNA is a right-handed double-helical DNA structure [5], whereas A-DNA is a comparatively short, more compact right-handed double-helical structure, and Z-DNA is a left-handed double-helical DNA created with lengthy polypurine stretches [20]. These DNAs are nanostructures in organisms, and their interactions with other NMs play an important role in nanomaterial medicinal compositions. Thus, in recent years, research on artificial DNA nanostructures has accelerated in the field of bionanotechnology. The chemical handles responsible for the production of self-assembled nanostructures by contact with inorganic NMs include a phosphate backbone with a negative charge, nucleobases with metal chelates, and the hydrophobic core with aromatic rings [2]. The creation of DNA-templated metal nanostructures is conceivable by localising transition metal cations on DNA to act as precursors and chemical handles [2]. DNA nanostructures [263] and DNA linked to NPs [4] have been manufactured for a variety of applications, including nanobarcoding and DNA sensors [6]. This research has progressed to encompass active self-reconfiguration of 1, 2 or 3-dimensional DNA-based nanoscale architectures for drug delivery, molecular electronics, and logics [6-9]. Recent advances in DNA technologies, such as Holliday junction elucidation and crossovers, aid in the virtual assembling of any DNA structure via DNA origami. [20] provides a detailed discussion of DNA origami, its uses, and possibilities. They stated that NP-templated DNA and hybridization-based DNA are revolutionary particles that will have a positive impact on future medicinal sectors.

Other nanostructures found in the human body

Antibodies, enzymes, proteins, and the majority of organelles within cells are nanostructures because they are smaller than a millimetre. Lipids, self-assembled peptides, and polysaccharides were recently added to the list of nanostructures found in the human body [1-2]. These nanostructures are artificially altered for usage in pharmaceutical industry. Nanozyme, an example of such nanostructures, is a designed nanometer-scaled artificial enzyme [273]. The enzyme's function is to imitate the general principles of real enzymes [4-5].

To mimic the structure and function of natural enzymes, a wide variety of biomolecules, such as polymers, supramoleculars, nucleic acids and antibodies, have been studied extensively. Biosensing, immunoassays, stem cell development, and environmental rehabilitation through pollution removal are just a few of the many uses for nanozymes currently under investigation [6]. Viral protein capsids have been widely studied as self-assembling NPs in the previous section. Additional biomedical applications include the use of NPs [7,8] and individual proteins/antibodies [9,10] to manipulate natural proteins and antibodies. NPs of biomolecular chemistry are expected to be extremely useful for the efficient transport of biomolecules and the treatment and diagnosis of complex diseases and genetic problems, according to researchers.

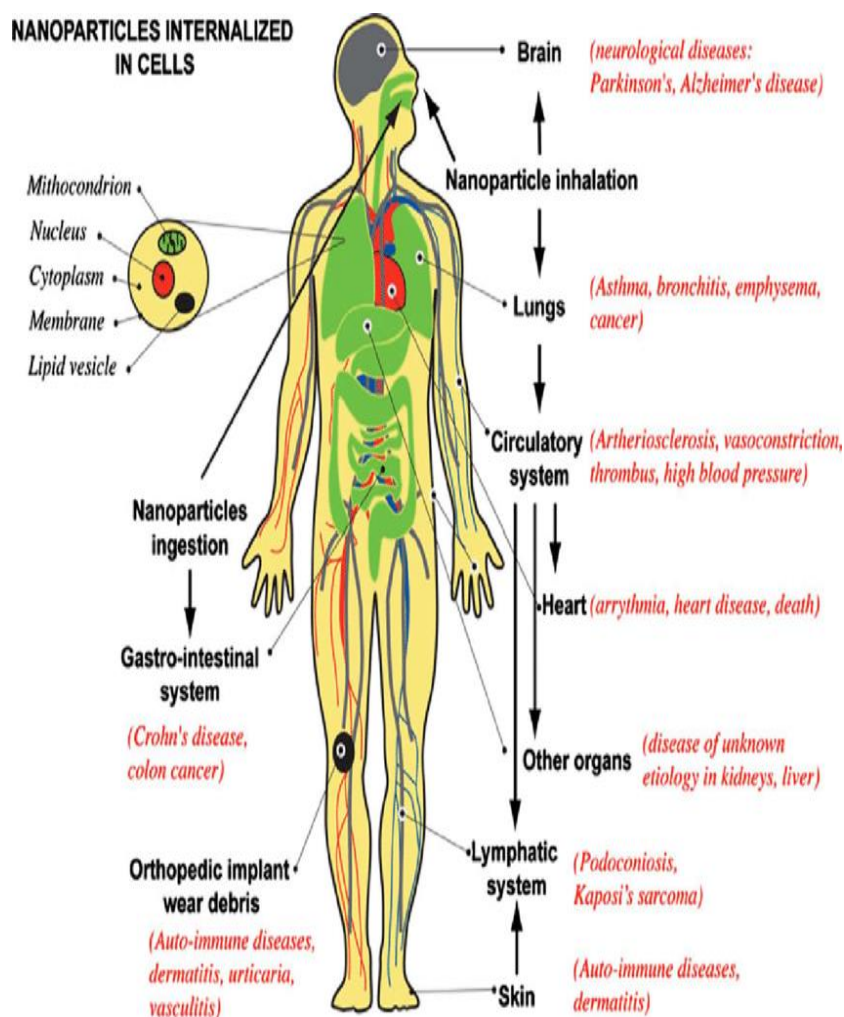
Nanomaterials' challenges and risk evaluation

Recent studies and the frameworks covered in prior studies highlight the general characteristics of NMs in terms of risk assessment.. Aside from their synthesis methods, these qualities are

determined by the fundamental characteristics of NPs [1]. It summarises the features of NPs and how they can be used to reduce obstacles and toxicity risks.

Toxicological effects of nanomaterials

Due to natural processes, humans are exposed to NPs. The primary causes of nanoparticulate emissions into the environment, whether in their original or modified forms, are the production, use, disposal, and waste treatment of items that contain nanoproducts. Organs that are vulnerable to foreign contaminants include the lungs and digestive system. The size of NPs is comparable to that of viruses. In the case of the HIV particle, for example, its diameter is in the range of 100 nanometers [4]. When breathed, nanoparticles can easily enter the bloodstream and other parts of the human body, such as those in the liver, heart, or blood cells, without a problem. It is important to note that the toxicity of NPs is influenced by their source. According to [8], many of them appear to be safe, while others have beneficial health effects.



Active chemical species can be transported via the skin, lung, body tissues, and organs because of the small size of NPs. There are numerous ways in which the composition of nanoparticles (NPs) can lead to oxidative stress, organelle damage, asthma, and even cancer. Exposure to NPs and nanostructured materials has a wide range of acute harmful consequences, including the formation of reactive oxygen species, protein denaturation, mitochondrial dysfunction, and alterations in phagocytic activities.

For example, NPs have been shown to have long-term harmful effects on the nervous system, nucleus, and even the DNA of cells in the nucleus, which can lead to organ dysfunction and possibly organ hypertrophy. NPs are classified by their dimensions, composition, morphology, aggregation, and homogeneity.

Similarly, nanostructured thin films or fixed nanoscale circuits within computer microprocessors and free NPs have important characteristics that make application classification easier. There are no restrictions on free NP movement, making it easier for them to proliferate across the ecosystem and represent a potential health danger through human exposure.

In contrast, proper handling of fixed NPs, in which the nanostructured pieces are linked to a big item, poses no health risk. Asbestos is an excellent example of a material whose main states are safe. Later, asbestos mining produces nanoscale fibrous particles, which are turned into an airborne aerosol, which is carcinogenic and poses a major health risk after being absorbed in the lungs [4].

It is also worth noting that, aside from size and ageing, the chemical composition and shape of the particle are the key factors contributing to nanoparticle toxicity. Many NPs are harmless in this context, whereas others have low toxicity or may have long-term health impacts [4].

With their cellular penetration and translocation capabilities, foreign NPs cause irreversible cell harm via oxidative stress or/and organelle destruction [4]. As demonstrated, electrostatic charges, van der Waals forces, interfacial tension effects, and steric interaction of NPs connect with cellular components and trigger cell death [4]. A wide range of NPs can produce reactive oxygen species and cause cellular damage by lipid peroxidation, protein modification, DNA disruption, signalling function interference, and gene transcription regulation [4]. The fate of oxidative products is determined by the NPs' chemistry, shape, size, and position. Nanoparticles can move or distribute to several cellular regions, including the cytoplasm, cytoplasm components, and the nucleus. Because of their cellular localization impact, NPs can disrupt cell organelles or DNA and trigger cell death.

The toxicity of NMs is determined by a number of factors, according to toxicological data:

- The effect of dose and exposure time. The quantity of NMs that penetrate the cells is directly proportional to the molar concentration of NPs in the surrounding media multiplied by the exposure time [4].

- The effect of aggregation and concentration. Numerous contradicting data exist regarding the toxicity of NPs at various concentrations. Aggregation is facilitated by increasing the NP concentration. Because the majority of NP aggregates are micrometer in size, a large number of aggregated NPs may be unable to penetrate cells, thus losing their toxicity.
- The effect of particle size. The toxicity of NPs is size dependent. Ag NPs with a diameter of 10 nm are more capable of penetrating and disrupting the cellular systems of numerous organisms than Ag⁺ ions and Ag NPs with a diameter of 20–100 nm [9].
- The effect of the particle's form. Shape-dependent toxicity exists for NPs, i.e., distinct toxicity levels exist for NPs with varying aspect ratios.

For example, 10 m long asbestos fibres can induce lung cancer, 5–10 m long asbestos fibres can cause mesothelioma, and 2 m long asbestos fibres can produce asbestosis [10].

- The influence of surface area. The toxicological effect of NPs typically increases as particle size and surface area decrease. It's also worth noting that human cells react differently to nano and microparticles of the same mass dosage.
- The effect of crystal structure. NPs may have variable cellular absorption, oxidative processes, and subcellular localisation depending on their crystal structure [288]. For example, the toxicity of the two crystalline polymorphs of TiO₂ (rutile and anatase) differs. Rutile NPs (200 nm) cause DNA damage in the dark via oxidation, whereas anatase NPs (200 nm) do not cause DNA damage in the dark [11].
- The effect of surface functionalization. Surface characteristics of NPs have been found to have significant effects on translocation and subsequent oxidation processes [12,13].
- The effect of pre-exposure. Shorter exposure times or pre-exposure to lower NP concentrations can boost cellular phagocytic activity [64]. The human body adapts to NPs to some extent as a result of this pre-exposure [14].

Regulations on nanomaterials

Nanomaterials have strong chemical bioactivity and reactivity, as well as the ability to penetrate cells, tissues, and organs, and have a higher bioavailability. NMs excel in biomedical applications due to their unique features. These qualities, on the other hand, can lead to toxicity. Several government bodies have enacted regulations in the form of legislation, laws, and guidelines to reduce or eliminate the dangers connected with NMs [13]. However, there is no clear international legislation, protocols, or legal standards for NP manufacturing, processing, or labelling, toxicity testing, or assessing their environmental impact.

The introduction of NMs into the biomedical field has resulted in changes to medical standards in the areas of ethics, environmental safety, and medical governance [5,6]. NMs' potential dangers are currently controlled by strong regulatory organisations and guideline legislation in the United States and the European Union (EU). NMs are specifically mentioned in numerous

pieces of EU legislation and technical guidelines published by the European Commission. This legislation has been utilised within EU countries to ensure regulatory consistency and to ensure that an NM used in one sector is regarded the same way when it is used in another. According to the European Commission, a nanomaterial is "a natural, incidental, or manufactured material containing particles, in an unbound state or as an aggregate or as an agglomerate, and where one or more external dimensions are in the size range of 1 nm to 100 nm for 50% or more of the particles in the number size distribution." The rules of these laws apply because the specifications of the materials and products meet the substance definitions of the European Chemical Agency (REACH) and the European Classification and Labeling of Chemicals (CLP) [7]. Furthermore, the European Union has established the Scientific Committee on Emerging and Newly Identified Health Dangers (SCENIHR) to assess the risks linked with NMs [8]. "An insoluble or bio-persistent and purposely formed material with one or more external dimensions, or an internal structure in the range of 1 to 100 nm, which includes man-made fullerene, single-walled carbon nanotubes, and grapheme flakes," according to the rule. The USFDA's Federal Food, Drug, and Cosmetic Act (FFDCA), the Personal Care Products Council (PCPC), the Voluntary Cosmetic Registration Program (VCRP), the EU Cosmetics Product Notification Portal (CPNP), REACH, the Scientific Committee on Consumer Safety (SCCS), and the International Cooperation on Cosmetic Regulation all have regulations and restrictions on cosmetics (ICCR). Nanotoxicity via cosmetics is a big worry for both scientific politicians and industries making consumer products, as seen by these laws from the US and EU, as well as other nations such as Japan and Canada [20].

Regulatory bodies in the United States, such as the Food and Drug Administration (FDA), the United States Environmental Protection Agency (USEPA), and the Institute for Food and Agricultural Standards (IFAS), have begun developing guidelines to address the potential dangers of NMs and nanoproducts. The FDA has been working on identifying NMs' sources, evaluating their environmental effect and dangers to people, animals, and plants, and determining how these risks might be avoided or minimised since 2006 [1].

Hazardous NMs are regulated by the European Medicines Agency (EMA) and the United States Food and Drug Administration (USFDA). Apart from that, a coalition of US domestic and international advocacy groups issued "Principles for the Oversight of Nanotechnologies and Nanomaterials," which was endorsed by 70 organisations from six continents. This paper calls for a robust and comprehensive oversight of NM-derived products. This includes a precautionary foundation for specific nanomaterial rules, as well as public and worker health and safety, transparency, public involvement, environmental protection, and the consideration of broader implications and manufacturer liability [2]. In the same way, the Nanomaterials Policy Recommendations study discusses measures to avoid or reduce the risk of NMs in the food industry. Companies should also develop a clear public policy for NMs usage, publish NMs safety evaluations, issue supplier standards, label NPs below 500 nm, and use a hazard control strategy to avoid NP exposure, according to this paper [3]. The use of engineered NPs in food

has already been restricted by organic providers such as the UK Soil Association [4], the Biological Farmers of Australia [5], and the Canada General Standards Board [6]. To avoid these types of NM prohibitions, researchers and producers should be trained on regulatory regulations and legislation prior to nanomaterial development. It is widely accepted that NMs are not inherently dangerous, and that many of them appear to be harmless, while others offer health benefits. However, future risk assessments will decide whether NMs and their products are dangerous and whether any additional actions are required.

Conclusion

The toxicity profile of NMs has become a hot topic in recent years. There have been natural NMs present in the environment for a long time, and they have various mechanisms in place to lessen the harm they bring to living creatures. Acute harmful effects of nanoparticles on living systems have been discovered through recent study developments. These findings show that NMs from human activities and those manufactured for use in consumer products can have harmful effects on animals. It is also necessary to conduct thorough cytotoxicity experiments on new NPs, such as viruses and nanozymes, in order to determine the safest methods of use and dose levels. As a result of the dangers of manufactured NMs in consumer products, numerous countries have adopted rules and laws. To identify and avoid harmful nanoparticles, extensive study in the field of nanotoxicology and tight regulations by government authorities are required.

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