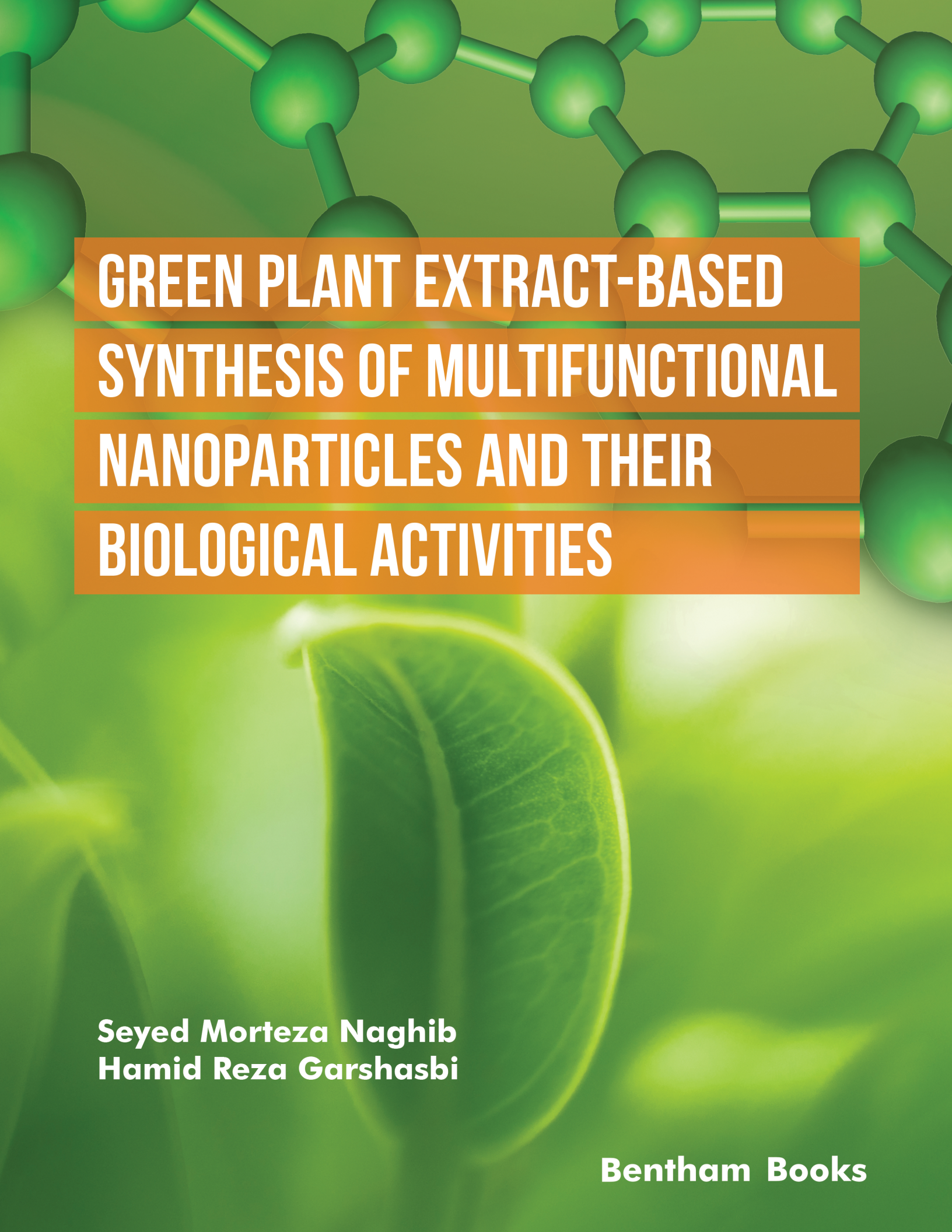

GREEN PLANT EXTRACT-BASED SYNTHESIS OF MULTIFUNCTIONAL NANOPARTICLES AND THEIR BIOLOGICAL ACTIVITIES

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Green Plant Extract-Based Synthesis of Multifunctional Nanoparticles and their Biological Activities

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PREFACE

Nanobiotechnology is gaining tremendous impetus in this era owing to its ability to modulate metals into their nano size, which efficiently changes their chemical, physical, and optical properties. Accordingly, considerable attention is being given to the development of novel strategies for the synthesis of different kinds of nanoparticles of specific composition and size using biological sources. However, most of the currently available techniques are expensive, environmentally harmful, and inefficient with respect to materials and energy use. Several factors, such as the method used for synthesis, pH, temperature, pressure, time, particle size, pore size, environment, and proximity, greatly influence the quality and quantity of the synthesized nanoparticles and their characterization and applications. In recent years, developing efficient green chemistry methods for synthesizing metal nanoparticles has become a major focus of researchers. They have investigated in order to find an eco-friendly technique for the production of well-characterized nanoparticles. One of the most considered methods is the production of metal nanoparticles using organisms. Among these organisms, plants seem to be the best candidates, and they are suitable for large-scale biosynthesis of nanoparticles. Nanoparticles produced by plants are more stable, and the synthesis rate is faster than in the case of microorganisms.

Moreover, the nanoparticles are more varied in shape and size than those produced by other organisms. The advantages of using plant and plant-derived materials for the biosynthesis of metal nanoparticles have interested researchers in investigating mechanisms of metal ions uptake and bio-reduction by plants and understanding the possible mechanism of metal nanoparticle formation in plants. In this review, most of the plants used in metal nanoparticle synthesis are shown.

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CHAPTER 1

Green Synthesis and Antibacterial Activity of Noble Metal Nanoparticles using Plants

Abstract: The emerging properties of noble metal nanoparticles (NPs) are attracting huge interest from the translational scientific community and have led to an unprecedented expansion of research and exploration of applications in biotechnology and biomedicine. An array of physical, chemical and biological methods has been used to synthesize nanomaterials. In order to synthesize noble metal NPs of particular shapes and sizes, specific methodologies have been formulated. Although ultraviolet irradiation, aerosol technologies, lithography, laser ablation, ultrasonic fields, and photochemical reduction techniques have been used successfully to produce NPs, they remain expensive and involve hazardous chemicals. Therefore, there is a growing concern about developing environment-friendly and sustainable methods. Since the synthesis of nanoparticles of different compositions, sizes, shapes and controlled dispersity is an important aspect of nanotechnology, new cost-effective procedures are being developed. Microbial synthesis of NPs is a green chemistry approach that interconnects nanotechnology and microbial biotechnology. Biosynthesis of gold, silver, gold–silver alloy, selenium, tellurium, platinum, palladium, silica, titania, zirconia, quantum dots, magnetite, and uraninite nanoparticles by bacteria, actinomycetes, fungi, yeasts, and viruses have been reported. However, despite stability, biological NPs are not monodispersed, and the rate of synthesis is slow. To overcome these problems, several factors, such as microbial cultivation methods and extraction techniques, have to be optimized, and the combinatorial approach, such as photobiological methods, may be used. Cellular, biochemical and molecular mechanisms that mediate the synthesis of biological NPs should be studied in detail to increase the rate of synthesis and improve the properties of NPs.

Keywords: Nanoparticles, NMPS, Nanotechnology, Nanoparticles synthesis.

INTRODUCTION

Metal NPs have a lengthy preparation, characterization, and use history in several fields. Nanomaterials research is spurred by the desire to understand better the characteristics of noble metal nanoparticles (NMNPs) and to discover how they might be employed in various applications. The high surface-to-volume ratio of NPs, as well as the confinement of electrons, phonons, and electric fields, confer a broad variety of properties on them. NPs have a high surface-to-volume ratio,

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which is partially responsible for this. Because of its high surface energy and substantial curvature, the nanoparticle's surface may become unstable. NPs surfaces have a particularly high proportion of curved regions in the form of edges and corners. Edges and corners are more likely to have hanging bonds, *i.e.,* coordinately unsaturated atoms, than flat surfaces. On the surface, corners, and edges of NPs, there are many atoms with uncoordinated atoms that affect the particle's chemical reactivity and surface bonding. By changing quantum levels and altering transition probabilities, the electron confinement effect in NPs alters the spectrum features of the particle. Particle-particle and particle-environment interactions, as well as volume ratio and confinement phenomena, are influenced by the large surface area. In recent years, scientists have learned how NPs shape affects their properties. Because of their metastable properties, NPs with non-spherical geometries are effectively locked in motion. Morphology controls further alterations in internal structures, surface properties, and orientational confinement [1].

NOBLE METAL NANOPARTICLES (NMNPS)

According to their size and usual structure, NPs may have various characteristics. It is possible to employ NPs in novel ways because of their high surface-to-volume ratio.

Additionally, there is an increase in unsaturated bonds, as well as a shift in bandgap energies. In order to make nanomaterials for particular purposes, NPs must be synthesized under strict supervision. These advances allow for the development of nanostructures with specific topological and morphological attributes and specific functional properties. Metallic NPs, polymeric NPs, and magnetic NPs are plentiful. The hydrophilicity or hydrophobicity of NPs and their functionalization greatly impact their practicality. It is possible to use NPs in various applications, such as nanomedicine, drug delivery, sensors, and optoelectronics. The unique physical-chemical features of noble metal NPs (NMNPS) make them extremely versatile. AuNPs, AgNPs, and PtNPs are stable noble metal NPs materials that may be easily synthesized chemically and customized in surface functionalization. NMNPs identify bioactive compounds and pollutants using colorimetry, immunoassays, Raman spectroscopy, and sensors. This paper examines the growing use of noble metallic nanoparticles in food safety. Bioactive compounds and trace pollutants are highlighted in this chapter [2].

METHODOLOGIES OF NPS SYNTHESIS

Chemical Methods for the Synthesis of NPs

Chemical Reduction

Colloidal metal particles can be made using a simple chemical reduction process that does not require expensive equipment. Chemical-reducing agents such as sodium borohydride and citrate are the most commonly used agents. Smaller NPs are produced by powerful reducing agents than by weak reducing agents. Oligomers, clusters, and precipitates are generated from excess surface energy and thermodynamic instability in smaller particles [3].

Co-precipitation

In order to make MNPs, co-precipitation is a simple and effective process. Since 1981, when Massart reported on the creation of MNPs under acid and alkaline conditions, iron oxide MNPs have been made in this manner. To reduce a metallic ion (*e.g.,* Fe^{2+} and Fe^{3+}) combination, a basic solution (typically NaOH, NH_3OH, or $N(CH_3)_4OH$) is used in the following chemical process at temperatures below 100°C.

$$Fe^{2+}(aq) + Fe^{3+}(aq) + 8OH^{-}(aq) \rightarrow Fe_3O_4 \downarrow (s) + 4H_2O\,(0.1) \quad \textbf{(1)}$$

Since organic solvents are not required, the co-precipitation process is simple to repeat and inexpensive. However, reaction conditions significantly impact the particle size, shape, and content. Molecularly, light surfactants or functionalized polymers are required for stabilization. To make matters worse, iron oxide particles created in this method are typically unstable.

Sol-gel

Metal alkoxides or their precursors are often used in the condensation and hydrolysis reaction of sol-gel techniques to produce NPs. The intermediates must be heated to achieve good crystallinity in the produced NPs. Precursors for forming oxide particles that interact by van der Waals forces or H-bonding and are dispersed in a "sol" gelled by solvent evaporation or other chemical processes are metal alkoxides, which are used in this procedure. However, the alkoxide precursors are hydrolyzed in a base or acid. This results either in a colloidal gel or a polymeric gel, which can be used as a solvent in general. Condensation and hydrolysis rates greatly impact the final product's properties. Slower hydrolysis yields smaller NPs.

CHAPTER 2

Analytical Methods in the Characterization of Green Nanomaterials

Abstract: A new class of diagnostic and therapeutic tools for various diseases has been made possible by advancements in polymeric nanoparticles as innovative nanomedicines. Although there are many benchtop studies in the nanoworld, their application to already marketed goods is still in its infancy. Problems with nanomedicine characterization cause this lack of transference, among other things. Three nanoscale characterization approaches may be distinguished: physicochemical property characterization, biological interactions of nanomaterials, and analytical characterization and purification procedures. Physical qualities may be assessed using a variety of methods in many situations. Choosing the best appropriate method is made more difficult by many advantages and disadvantages of each methodology; frequently, a combinatorial characterization approach is required. Scientists from many domains must find answers to the difficulties in reliable characterization of the nanomaterials after their fabrication and various systematic stages.

Keywords: Analytical methods, Characterization techniques, Green nanomaterials.

INTRODUCTION

Since NPs have a vast surface ratio compared to their bulk counterparts, nanoscale materials have a fast-increasing molecular reactivity. These include mechanical characteristics that can vary widely amongst nanoparticles (NPs) and chemical, optical, and electrical properties. Such nanostructures can be created *via* various techniques, including mechanical, chemical, and other approaches. More nanomaterials are being created now than ten years ago, necessitating the creation of more accurate and reliable techniques for their characterization. Such characterization can, however, occasionally be lacking. This is because nanoscale materials are more difficult to analyze adequately than bulk materials. According to the complex basis of nanoscience and nanotechnology, not every research team can easily access distinct characterization techniques. Sometimes it is necessary to describe NPs in a broader sense, which necessitates a comprehensive approach that incorporates complementary approaches. The chapter provides several novel ways for characterizing NPs about the qualities being studied (Tables **1** and **2**).

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Table 1. Parameters and corresponding characterization techniques.

Entity Characterized	Characterization Techniques Suitable
Size	TEM, XRD, DLS, NTA, SAXS, SEM, EXAFS, ICP-MS, UV-Vis, MALDI, NMR
Shape	TEM
Elemental-chemical composition	XRD, XPS, ICP-MS, SEM-EDX, NMR
Crystal structure	XRD, EXAFS, STEM
Size distribution	DLS, DTA, ICP-MS, NTA, SAXS, SEM
Chemical state–oxidation state	XAS, EELS, XPS
Growth kinetics	SAXS, NMR, TEM
Surface area, specific surface area	BET
Surface charge	EPMA, Zeta potential
Concentration	ICP-MS, UV-Vis
Agglomeration state	Zeta potential, DLS, UV-Vis, SEM, TEM
3D visualization	SEM
Detection of NPs	TEM, SEM, STEM

Table 2. Summary of the experimental techniques.

Technique	Main Information Derived
XRD	Crystal structure, composition, crystalline grain size
XAS (EXAFS, XANES)	X-ray absorption coefficient – chemical state of species, interatomic distances, Debye-Waller factors
SAXS	Particle size, size distribution, growth kinetics
XPS	Electronic structure, elemental composition, oxidation states, ligand binding
FTIR	Surface composition, ligand binding
NMR	Ligand density and arrangement, electronic core structure, atomic composition, NP size
BET	Surface area
TGA	Mass and composition of stabilizers
UV-Vis	Optical properties, size, concentration, agglomeration state
PL spectroscopy	Optical properties, size, composition
DLS	Hydrodynamic size, detection of agglomerates
NTA	NP size and size distribution
ICP-MS	Elemental composition, size, size distribution, NP concentration
TEM	NP size, size mono dispersity, shape, aggregation state, study growth kinetics

(Table 2) cont.....

Technique	Main Information Derived
STEM	Combined with HAADF, EDX for morphology study, crystal structure, and Elemental composition.
EELS(EELS-STEM)	Type and quantity of atoms present, chemical state of atoms, collective interactions of atoms with neighbors, bulk plasmon resonance
SEM-HRSEM, T-SEM-EDX	Morphology, dispersion of NPs in cells and other matrices/supports, precision in lateral dimensions of NPs, quick examination–elemental composition

ANALYTICAL METHODS

Size and shape are two of the most important characteristics to consider while determining the NP's identity. Size distributions, aggregation levels, surface charges, and surface areas can all be assessed as the chemistry on the surface. Its additional properties and applications may be influenced by the NPs' size, distribution, and organic ligands on their surfaces. Currently, there are no clear guidelines in place for this. Measurements based on NP can considerably impact whether these materials are accepted for commercial use while ensuring compliance with regulatory requirements.

Notwithstanding these issues, nanomaterials analysis remains problematic because of their multidisciplinary nature, lack of appropriate reference materials, challenges with specimen processing for analysis, and difficulty in data interpretation. The characterization of NPs has numerous obstacles, including the inability to measure in-situ and online concentrations of NPs, particularly in large-scale production, or to analyze NPs embedded in complex matrices. Large-scale production waste and effluent need to be closely monitored as well. As the production of NPs increases in volume, more accurate measurement methods will be required. As a result, characterizing NPs made in diverse methods is essential. We study the surface ligands and the nanoparticle core to understand how they affect the particle's physical properties. In addition, we do not just focus on the most prevalent methods. The kinetics of nanoparticle creation may be monitored using modern in situ operando techniques. Recent advances in controlled defects considerably impact nanoparticle properties [1].

OPTICAL CHARACTERIZATION TECHNIQUES

Confocal Laser-Scanning Microscopy

Confocal laser scanning microscopy (CLSM) is a potent method for producing clear pictures of a sample that might otherwise seem blurry when seen under a normal microscope. By capturing several photographs at various depths within a thick object, it is feasible to reconstruct 3D structures from the images produced

CHAPTER 3

How Nanoparticles Enter the Human Body and their Effects

Abstract: The new scientific innovation of engineering nanoparticles (NPs) at the atomic scale (diameter<100nm) has led to numerous novel and useful wide applications in electronics, chemicals, environmental protection, medical imaging, disease diagnoses, drug delivery, cancer treatment, gene therapy, *etc*. The manufacturers and consumers of nanoparticle-related industrial products, however, are likely to be exposed to these engineered nanomaterials, which have various physical and chemical properties at levels far beyond ambient concentrations. These nanosized particles are likely to increase unnecessary infinite toxicological effects on animals and the environment, although their toxicological effects associated with human exposure are still unknown. These ultrafine particles can enter the body through skin pores, debilitated tissues, injection, olfactory, respiratory, and intestinal tracts. These uptake routes of NPs may be intentional or unintentional. Their entry may lead to various diversified adverse biological effects. Until a clearer picture emerges, the limited data available suggest that caution must be exercised when potential exposures to NPs are encountered. Some methods have been used to determine the portal routes of nanoscale materials on experimental animals. They include pharyngeal instillation, injection, inhalation, cell culture lines and gavage exposures.

Keywords: Intestinal tracts, NPs uptake, Respiratory system, Toxicological effects.

INTRODUCTION

"Nanotechnology" encompasses manipulating matter on a near-atomic scale to produce new structures, materials, and devices. It builds nanoparticles (NPs) whose diameter is below 100 nm by manipulating matter at the atomic level. According to Stern and McNeil, NPs can be engineered or incidental, depending on their origin. Engineered NPs such as quantum dots, dendrimers, carbon nanotubes, and fullerene, which have diameters<100 nm, can be compared to the sizes of living things. Also, NPs like diesel particles are generated incidentally, while living things like viruses are natural living cells with diameters<100 nm. Technology can be applied to biological systems, living organisms, or derivatives thereof, to make or modify products or processes for specific use at the nanoscale

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levels. It, therefore, encompasses a wider range and history of procedures with useful industrial and biological processes in modifying the needs of humanity at the nanoscale level. Some studies have also shown that microorganisms can as well be used as potential developers of NPs. With the development of these new approaches and techniques, nanotechnological industries are acquiring new horizons enabling them to improve the quality of products and life with uncertain health safety issues. NPs can enter the environment and animals' systems through different pathways. For instance, it could be through effluent, spillage, consumer products, and disposal. The intake is usually tolerated by the organism's system, but when a certain range is exceeded, it causes toxic effects and even deaths. Since NPs can cause risks to the environment and human health, therefore, research must be undertaken to understand and anticipate such risks through risk assessment and risk management. However, given the limited amount of information about the health risks of NPs, it is prudent to take measures to minimize workers' exposure to the environment.

REGULATION OF NANOMATERIALS RISK ASSESSMENT

Regulation EC No. 1907/2006 concerning the Registration, Evaluation, Authorization, and Restriction of Chemicals (REACH) governs all chemicals and their usage in goods; no special regulation exists in the European Union. Chemicals such as SiO_2 and TiO_2 are extensively used to create coatings and composites, among other things. Even though they are not explicitly addressed, NMs are part of the REACH framework. This is due to including all chemical compounds, regardless of their form or arrangement. REACH mandated the creation by the European Chemicals Agency (ECHA) of guidelines for the disclosure of information and the conduct of safety assessments. Toxicological and toxicokinetic data and appropriate safety evaluations are required for substances that come under the EC's guidelines for classifying NMs.

Also included is an evaluation of nano-specific occupational exposure, with suggestions for protective gear if other measures are ineffective. mg/cm², cm^2/m^3, and particle number/cm^3 are proposed as appropriate dosage metrics for inhalation exposure to NM. For fibers, this is especially true. Fiber less than 3 m in length and less than 20 nm in diameter is considered hazardous since it does not biodegrade in the lungs. Carbon nanotubes, silicon carbide, and fluoro-edenite have been associated with cancer development when inhaled through the parietal pleura. NMs used in biocidal goods, whether as active or inactive ingredients, must be approved by an independent risk assessment focused on nanotechnology. The intended application areas must be specified, such as antimicrobial product provision. Antimicrobials used in treating patients have developed resistance to the bactericidal nanosilver (nano-Ag), which has prompted the advice that they

must not be used in consumer products due to evidence of their accumulation in humans and the development of bacterial cross-resistance.

In case of cosmetics, this is a specifically controlled product. A cosmetic product must notify the European Commission (EC) about the toxicological profile of the NM and necessary safety data before it may be sold in Europe. According to the European Commission's suggestion, NM is defined in a way that excludes the idea of a nanoscale proportion, which is important. A rigorous safety evaluation is required for all NM-based UV filters, colorants, and preservatives before using them. To evaluate and assess the safety of cosmetic compounds, the Scientific Committee on Consumer Safety's Notes of Guidance should be used. The special characteristics of NMs must also be considered. As a UV filter in sunscreens, nano-TiO_2 in concentrations up to 25% was found to have no dermal absorption and consequently no adverse effects on people, whether applied to healthy or sunburned skin. Inhalable powders and sprays are exempted from this rule. We still need to improve the risk evaluation for non-medical devices. Respirable particles' toxicokinetic characteristics must be taken into account. As long as specific requirements are met and a proper risk assessment is carried out, the European Commission has permission to use nano-TiO_2 in cosmetic UV filters. Cosmetic sprays that emit aerosols that can be inhaled constitute a risk. European Union member states and the European Commission approve NMs in agriculture, food, and feed. For food and feed chain risk assessments, EFSA's guideline document for nanotechnology and nanoscience is used. Animal feed, food additives, and packaging materials are just a few of the many uses for which these substances are evaluated in this manner. There are five stages in which an engineered nanomaterial (ENM) needs to be evaluated: (1) as a generated material (pristine state); (2) in food/feed products; (3) in food or feed matrixes; (4) in media used for toxicity testing; and (5) in bodily fluids of humans and animals. Based on the persistence and ingestion of particles, six scenarios were developed to measure exposure in Table **1**.

There is now a revision of the EFSA guidance. When it comes to food and feed safety assessments, there are many technological hurdles that EFSA must overcome. Nano-encapsulates and Ag were the most often used nanomaterials in agriculture, feed, and food. The importance of food additives and touch materials was emphasized.

When conducting risk assessments, it is necessary to provide a comprehensive report of physicochemical parameters and their analytical methodologies, depending on the NM and its measuring environment. Applied procedures must be proven appropriate for the task at hand and capable of producing repeatable results. Even so, this area of analytical chemistry is still relatively new. As a

CHAPTER 4

Protein–Nanoparticles Interactions

Abstract: Large surface area, small size, strong optical properties, controllable structural features, variety of bioconjugation chemistries, and biocompatibility make many different types of nanoparticles (NPs), such as gold NPs, useful for many biological applications, such as biosensing, cellular imaging, disease diagnostics, drug delivery, and therapeutics. Recently, interactions between proteins and NPs have been extensively studied to understand, control, and utilize the interactions involved in biomedical applications of NPs and several biological processes, such as protein aggregation, for many diseases, including Alzheimer's. These studies also offer fundamental knowledge on changes in protein structure, protein aggregation mechanisms, and ways to unravel the roles and fates of NPs within the human body.

Keywords: Nanoparticles interactions, Protein interactions, Protein structure.

INTRODUCTION

In biology, it is a (near) universal law that material is always covered with proteins when it comes into contct with a physiological environment. Much of the bionanoscience world will be better understood if these phenomena can be explained. The particle's “corona” of serum and other physiological fluid proteins, rather than the particle itself, is the effective unit of attention in cell nanomaterial interactions, according to a recent hypothesis. Understanding that live cells read more than just the protein layer's content and organization is crucial. They also take note of how quickly the proteins on the NPs swap. There is a wide range of protein binding affinity on a particle; hence the nanoparticle surface reveals a variety of protein residence times. There is not a solid layer present; instead, a protein-linked 'corona' is seen. As a result of the wide variety of binding strategies (one for each protein), we may anticipate a wide range of equilibrium constants (some of which are quite competitive).

Surface protein concentration and interaction rate will be high on nanoparticle surfaces. In order to gain an understanding of how a specific nanoparticle's protein corona varies over time, we may evaluate the kinetic on/off rates of each protein in the plasma. This corona may not be able to reach equilibrium promptly when exposed to biological fluid. There is a need to replace proteins with low concen-

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tration, slower exchange, and higher affinity with those that dissolve fast in the presence of other proteins. There may be a need for exchange systems when particles move between different compartments or organs, such as the circulation into cells or the movement of the cytosol to the nucleus. Because of this, the cell perceives and interacts with the protein corona as its biological self. Adsorption of bovine serum albumin (BSA), myoglobin (Mb), and cytochrome C (Cyt C) onto Au NPs is characterized by an irreversibly adsorbed portion and a proportion of protein adsorption that may be reversed. NPs and proteins are reported to have a hard corona, which has a long residence time and has strong adsorption to NPs.

Shorter residence times or lower affinities are common among the proteins that make up an easier-to-fold corona. According to a literature review on nanoparticle-protein binding, most nanoparticle types investigated too far bind apo lipoproteins. At first look, this seems to be a completely unexpected outcome. Although apolipoproteins are found in lipoprotein complexes at the nanoscale, this proves that they are a component of lipoprotein complexes in general.

Several NPs and the apolipoprotein E molecule have a role in nanoparticle transport in animals and humans. Due to their role in cholesterol metabolism, lipoprotein complexes are crucial to NPs interaction with cells. This means that NPs may enter cells through receptors on the cell surface that recognize apolipoprotein complexes that have been surface-adsorbed. As apolipoprotein E is important in the trafficking of cells to the brain, this might have substantial repercussions for neurotoxicity and neurotherapeutics development. The nanoparticle-protein corona may impact both the ultimate subcellular position of a nanoparticle after it interacts with a cell and the range of disease processes it may access (in addition to size and shape).

The biomolecule corona, which facilitates nanoparticles' interface with cellular machinery, should be used in the future to classify NPs. Toxicology at the nanoscale might be revolutionized, as could nanomedicine delivery systems. It has been shown for the first time that protein adsorption to NPs has a direct biological impact. Single-walled carbon nanotubes (SWNTs) and albumin-coated amorphous silica reduced lipopolysaccharide-induced activation of Cyclooxygenase-2 (Cox-2) in macrophages. Nonionic surfactants are used to prevent albumin adsorption, which has anti-inflammatory characteristics, on the NPs.

The presence of adsorbed proteins is suggested to modulate the detrimental effects of SWNTs and nanoscale amorphous silica. Despite this, it is unclear whether albumin would attach to NPs in other binding contexts, such as a plasma or the inside of a cell [1].

FORMATION OF THE PROTEIN CORONA

More and more people are seeing how nanotechnology's ability to make ever-smaller NPs while simultaneously improving control over their physical and chemical properties has propelled the ability to do so. These NPs are more reactive due to an increase in the number of atoms on their surfaces. Targeted medication delivery and imaging may be accomplished *via* intravenous injection of NPs developed for biological uses like this. To create the "protein corona," NPs quickly get coated with certain blood plasma proteins to reach the biological environment (plasma, for example). To reach plasma proteins through other routes of exposure, NPs must first cross the body's physiological barriers (the skin, gastrointestinal system, and the lungs, for example), collecting up biomolecules along the way.

As a result of the protein-coated particles' ability to expose new epitopes, alter the adsorbed protein conformation (either temporarily or permanently), alter protein function, and possibly even cause avidity effects due to the close spatial repetition of the same protein, a wide range of biological effects are possible. One layer is made up of proteins with long half-lives and rapid exchange rates with free proteins, while the other layer is made up of proteins with shorter half-lives and a slower exchange rate with free proteins, as revealed by researchers (the soft corona). Hard coronas have a longer life span. The hard corona, rather than the smooth NP surface, is now thought to interact with cell receptors and impact NP fate. To ensure the safety of nanomedicines and consumer products, it is essential to establish the proteins that adsorb on the NP surface and their respective lifetimes and conformations.

Biomedical applications may benefit from developing "safe by design" NPs if the interactions between NPs and proteins can be better understood and predicted. Many different qualities of the NP and the adsorbing proteins may affect the corona's appearance, including its physical and chemical properties.

The hard corona of protein-coated NPs has a substantial biological impact because of their high affinity (*i.e.,* the capacity to arrange themselves in a certain manner to trigger a specific receptor response). Proteins with high abundance may initially bind but are rapidly replaced by proteins with lower quantities and greater affinity. Since the timescales of cellular processes are so short, it is crucial to evaluate protein lifetimes on the surface of NPs to determine NP biological response. NP interactions with living matter are believed to be mediated by proteins with a more tightly attached corona (hard corona). The structure and affinity of proteins adsorbed on NP surfaces must be well elucidated. To do this characterization, proteins must be separated from the NPs' surfaces. It is difficult

CHAPTER 5

Toxicity of Nanomaterials-Physicochemical Effects

Abstract: Nanoparticles (NPs) have the potential to produce deleterious effects on organ, tissue, cellular, subcellular, and protein levels due to their peculiar physicochemical features. Metal NPs are gaining prominence and are being used in a variety of medicinal, consumer, industrial, and military applications. Furthermore, as particle size falls, some metal-based NPs become increasingly poisonous, despite the fact that the same substance is rather innocuous in its bulk form. NPs can also interact with proteins and enzymes within human cells, causing reactive oxygen species to be produced, an inflammatory response to be initiated, and mitochondrial disruption and destruction, ending in apoptosis or necrosis. As a result, deciding whether the advantages of NPs outweigh the hazards presents various challenges.

Keywords: Cellular toxicity, Cytotoxicity, Nanotoxicity, Nanoparticles toxicity.

INTRODUCTION

Muller's (1927) work on “artificial transmutation of the gene” in the fruit fly, Drosophila melanogaster, prompted interest in exploring harmful effects on inherited genetic information in cells. The earliest scientific study on chemically induced mutation used Muller's fruit fly model to describe the mutations caused by exposure to sulfur mustard. In 1966, geneticists at a meeting sponsored by the National Institutes of Health in the United States proposed that food additives, medications, and substances with extensive human exposure be systematically examined for mutagenicity. NPs are frequently employed in electronics, agriculture, textile manufacture, medicine, and other sectors and sciences. The key obstacle restricting their application in disease therapy and detection is NP toxicity in live organisms. At the moment, researchers commonly encounter the challenge of reconciling the favorable therapeutic impact of NPs with the toxicity-related adverse effects. Choosing an appropriate experimental paradigm for assessing toxicity *in vitro* and *in vivo* is crucial in this respect. Whereas *in vivo* tests enable you to estimate the NP toxicity for particular organs or the body as a whole, *in vitro* models make it simpler to assess the NP's harmful effects on individual cell components and tissues. The concentration, length of their contact with living things, stability in biological fluids, and capacity to build up in tissues and organs are other factors that affect NPs' potential toxicity. Understanding the

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connections between all the variables and the processes driving NP toxicity is essential for the creation of safe, biocompatible NPs for the detection and treatment of human illnesses.

The production, use, disposal, and waste treatment of products containing NPs are the primary causes of their release into the environment. Typically, the epidermis protects against external chemicals, whereas the lungs and digestive system are vulnerable organs. NPs are around the size of viruses. For instance, the diameter of the human immunodeficiency virus (HIV) particles is 100 nm [1].

The circulation and other organs, including the heart, liver, and blood cells, are simple entry points for inhaled NPs. It is crucial to understand that NPs' toxicity is influenced by their source. Some seem to provide health advantages, while others seem to be nontoxic [2]. The transfer of active chemical species through organismal barriers such as the skin, lungs, body tissues, and organs is made easier by the small size of NPs. Therefore, NPs can result in asthma, cancer, irreversible oxidative stress, organelle damage, and other conditions depending on their makeup. The formation of reactive oxygen species, protein denaturation, disruption of mitochondrial function, and alteration of phagocytic activities are only a few of the typical acute toxic consequences brought on by exposure to NPs and nanostructured materials. Common chronic harmful consequences of NPs include uptake by the reticuloendothelial system, nucleus, neuronal tissue, and the formation of neoantigens that could lead to organ growth and malfunction. The general characteristics of NPs that are used to categorize them include dimensionality, composition, morphology, aggregation, and homogeneity.

Like free NPs, nanostructured thin films and fixed nanoscale circuits found in computer microprocessors all have key distinctions that make it simpler to categorize them for specific applications. Free NP movement is unrestricted, which makes it simpler for them to spread across the environment and pose possible health problems when exposed to people.

On the other hand, handling fixed NPs properly poses no health dangers because the nanostructured components are affixed to a substantial object. An excellent example of a material whose initial states are safe is asbestos. The subsequent mining of asbestos results in the creation of nanoscale fibrous particles, which are then turned into an airborne aerosol, which is carcinogenic and poses serious health risks when ingested [1].

It is also important to remember that, in addition to size and age, the chemical makeup and form of the particle are the key determinants of nanoparticle toxicity. Many NPs in this situation are harmless, while others have diminished toxicity or could even have long-term negative health impacts [1].

Due to their propensity to penetrate cells and move within them, foreign NPs cause organelle injury or oxidative stress that permanently damages cells. Other than penetration, NPs bind to cellular components and kill cells by electrostatic charges, van der Waals forces, interfacial tension effects, and steric contact. Reactive oxygen species are produced by various NPs, which can then damage cells by altering lipids, proteins, DNA, signaling processes, and gene transcription [1]. The chemistry, shape, size, and placement of the NPs all affect how the oxidative products are disposed of. The cytoplasm, cytoplasmic components, and nucleus are only a few examples of diverse biological places where NPs might move or spread. Due to their cellular localization impact, NPs can damage cell organelles or DNA and result in cell death. According to toxicological data, the toxicity of NMs depends on various factors:

- Effect of exposure duration and dose. The molar concentration of NPs in the nearby media multiplied by the exposure period directly determines the number of NMs that enter the cells [1].
- Effect of accumulation and concentration. The toxicity of NPs at various concentrations has been the subject of numerous conflicting reports. Aggregation is encouraged by an increase in NP concentration. As most NP aggregates are only a few micrometers, their toxicity may be reduced because a sizable portion of them may not enter cells.
- The impact of particle size. The toxicity of NPs is size dependent. Ag NPs with a diameter of less than 10 nm have a stronger capacity to infiltrate and disturb the cellular systems of multiple species than Ag+ ions and Ag NPs with bigger diameters.
- Effect of particle shape. NPs have shape-dependent toxicity, meaning toxicity levels vary depending on the aspect ratio. For instance, asbestos fibers as short as 5 to 10 microns can produce mesothelioma, asbestos fibers as long as 10 microns can cause lung cancer, and asbestos fibers as long as 2 microns can cause asbestosis [3].
- Effect of surface area. The toxicological impact of NPs typically grows as surface area and particle size decrease. Also, it should be emphasized that human cells respond differently to nano and microparticles at the same mass dose.
- The impact of crystal structure. Depending on the crystal structure, NPs can exhibit a variety of cellular uptake, oxidative reactions, and subcellular localization. The toxicity of two crystalline polymorphs of TiO_2 varies, for example. In the dark, rutile NPs (200 nm) induce DNA damage by oxidation, but anatase NPs (200 nm) do not cause DNA damage [4].
- Effect of surface functionalization. The surface characteristics of NPs have dramatically impacted translocation and ensuing oxidation processes [5, 6].

CHAPTER 6

Nanoparticles in Environmental Pollution Remediation of Xenobiotics

Abstract: Environmental deterioration is currently a major problem for both emerging and wealthy nations. Extensive industrialization and intensive agricultural activity are the main causes of land, water, and air contamination. There are numerous conventional treatments for various environmental contaminants, but each has drawbacks. As a result, a different approach is necessary, one that is efficient, less harmful, and produces better results. In terms of cleaning up the environment, nanomaterials have garnered much interest. Nanomaterials outperform more traditional methods for environmental remediation due to their enormous surface area and strong reactivity. For particular applications, they can be altered to include new functionalities. Nanoscale materials can be very reactive due to the high surface-area-to-volume ratio and a greater number of reactive sites. These traits enable greater contaminant interaction, which prompts a rapid decrease in pollutant concentration. In order to remove toxins from diverse environmental media (*e.g.,* soil, water, and air), environmental remediation primarily uses various methods.

Keywords: Environmental remediation, Pollution, Xenobiotics.

INTRODUCTION

The world is on the verge of a severe environmental catastrophe that will bankrupt us. The environment as it exists now is constantly decaying. Global environmental problems are escalating, and we must act as though there is an emergency in our world. We must adopt a fresh outlook and confront disasters with new ideas and tactics and our full knowledge and seriousness in advance. Nature takes millions of years to clean up pollution in the air, water, and soil. The two main sources of most environmental pollution are industry and automotive exhaust emissions. Humanity is at risk from air pollutants such as NO(x), SO_2, highly reactive and dangerous organic chemicals, POPs including dioxins, and PAH (polycyclic aromatic hydrocarbons). Carbon monoxide (CO), when inhaled in large amounts, can cause rapid poisoning. According to the various levels of exposure, many heavy metals, including Pb, can cause immediate or chronic poisoning when ingested by living things. The above substances contribute to pulmonary conditions like COPD, asthma, bronchiolitis, malignancies, heart conditions,

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brain dysfunctions, and skin disorders. Condensation, flocculation, froth flotation, sand filtration, and AC adsorption are long-used techniques. These restrictions, however, include the ineffective scraping of metal ions, excessive energy input, and creation of non-recyclable compounds. Nanotechnology looks to be an emerging solution to these issues. Nanotechnology has the potential to contribute significantly to the creation of cleaner, greener technologies that have considerable positive effects on both the environment and human health. For their potential to offer solutions for pollution management and mitigation as well as to enhance the effectiveness of conventional environmental cleanup approaches, nanotechnology techniques are being researched.

By using less energy throughout the production and manufacturing processes, enabling products to be recycled after use, and creating and utilizing environmentally benign materials, nanotechnology can benefit the environment. Currently, nanotechnology shows much promise for solving sustainability problems, but we also need to consider any potential harm to the environment and human health.

NANO REMEDIATION

Using nanoparticles (NPs) to clean up contaminated water, soil, or air is known as nano-remediation. By adsorbing contaminants, accelerating the reaction, and lowering the hazardous valence to a stable metallic state, this innovative remediation technology has shown to be particularly successful at degrading toxins. The reaction is further sped up by the nanoscale, which creates a surface area with a greater optimal for adsorption. The carbon-based NPs CDs, GOs, and Carbon Nano Tubes (CNTs), as well as non-carbon-based NPs nZVI and zeolites, are some of the several nanoparticle agents employed in nano-remediation. However, it has been observed that the NPs employed in nano-remediation, such as GOs, rGOs, and CNTs, are harmful to human cells, particularly the lungs and breasts. The reactive surface with the exchangeable ions and the piercing size of the NPs are what cause toxicity. By adding functional surfactants to the reactive surfaces, these toxicities are typically reduced. The surface-functionalized NPs are, therefore, suitable for environmental applications, including cleanup [1].

SOURCES OF XENOBIOTICS AND POPS

All manufactured substances discharged into the environment have the potential to pose an environmental hazard. However, some may have a higher or lower dose than others. Excessive pollution is emitted from each source of xenobiotic contamination.

Xenobiotics can be released as a harmful component or a mixture of organic contaminants. Xenobiotics can use a single pollutant or a combination of pollutant substances, making environmental protection a major effort to be engaged in. The properties of xenobiotics have classed natural or manufactured releases as planned or accidental, direct or indirect. Pollutants emitted into the atmosphere by factories, which move to soil surfaces and waterways, are the primary source of most xenobiotics. It is necessary to classify xenobiotics' origins to limit the spread of potentially dangerous pollutants. According to the Stockholm Convention 2009, the transport potential should be computed as the sum of all discharges from a specific place. In huge quantities, people are exposed to POPs, halogenated xenobiotic chemicals, through various commodities and other non-point sources. The microbiome's food supply chain can be disrupted by these airborne contaminants, which are poisonous and highly bio accumulative. According to EPA regulations, the prevalence of illnesses generated by these poisons is high in marine and coastal ecosystems. Those who have adapted to contemporary conveniences by consuming synthetic chemicals are intentionally released into the environment. The four levels of POPs are (i) the most dangerous chemicals, (ii) the medium-level chemicals, (iii) the inadvertent release of chemicals during the production process, and (iv) the use of compounds that are currently being investigated.

The screening results from diverse communities at the international level will be used to take the necessary procedures for pollution management at the sites. The parameters were monitored regularly. Campaigns slowed down POP creation, use, and release. As non-degradable contaminants, they remain in the environment for a long time. Because organisms absorb these pollutants, their toxicity might fluctuate, or their metabolism can be disrupted.

ECOLOGICAL RISKS ASSOCIATED WITH XENOBIOTICS AND POPS

It has become a global issue since xenobiotics emitted by numerous businesses and agricultural activities have such a large impact on the ecosystem. This pollutant release has resulted in many diseases in food-producing animals, directly impacting human health. Organo-chlorinated insecticides, used in agricultural fields for decades, are the primary cause. It is impossible to eliminate these substances from the soil entirely. POPs are absorbed into the soil when wastewater is recycled. Therefore, it harms plant-microbe co-existence, damaging plants by changing their soil microbial populations. It also harms agricultural yields due to the imbalance in soil fertility. In other words, the roles of microbial biosynthetic pathways have been shifted, resulting in inadequate pollution cleanup. Ecological risk data predicted the adsorption of POPs in low-temperature zones. There is a chance that POPs will be transferred to marine habitats due to

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