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BIO-DERIVED NANOPARTICLE-BASED DRUG DELIVERY PLATFORMS–REVIEW

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ABSTRACT

Nanotechnology has revolutionized the global healthcare sector over the past few decades. Biological approaches for nanoparticle synthesis offer a cost-effective, non-toxic, and eco-friendly alternative. This review provides an update on nanoparticle production methods and biological sources, encompassing algae, plants, bacteria, fungi, actinomycetes, and yeast. The biological synthesis of nanoparticles has distinct advantages over chemical, physical, and biological methods, including minimal toxicity and environmental sustainability, making it an attractive option for therapeutic applications as a cutting-edge drug delivery system. In addition to facilitating research, bio-mediated nanoparticles also enhance particle functionality to promote human health and safety. This review examines the medicinal applications of nanoparticles, including their antifungal, antimicrobial, antiviral, antidiabetic, anti-inflammatory, and antioxidant properties. This study highlights recent findings in the field and discusses proposed methods for describing the bio-mediated synthesis of novel nanoparticles. The production of nanoparticles via biogenic sources offers numerous benefits, including affordability, bioavailability, and environmental sustainability.

KEYWORDS: Nanotechnology, Healthcare, Biological synthesis, Nanoparticles, Drug delivery system, Biogenic sources, Algae, Plants, Bacteria, Fungi, Actinomycetes, Yeast, Bio-mediated synthesis.

INTRODUCTION

The term "nano" originates from the Greek word "nanos", meaning "minute". Nanoparticles possess at least one dimension ranging from 1 to 100 nanometers (nm).[1] However, the majority of materials utilized in drug delivery fall within the 10-200 nm range. These particles can alter their chemical and physical properties due to their distinct electronic structure, exceptional conductivity, vast surface area, and quantum size significance.

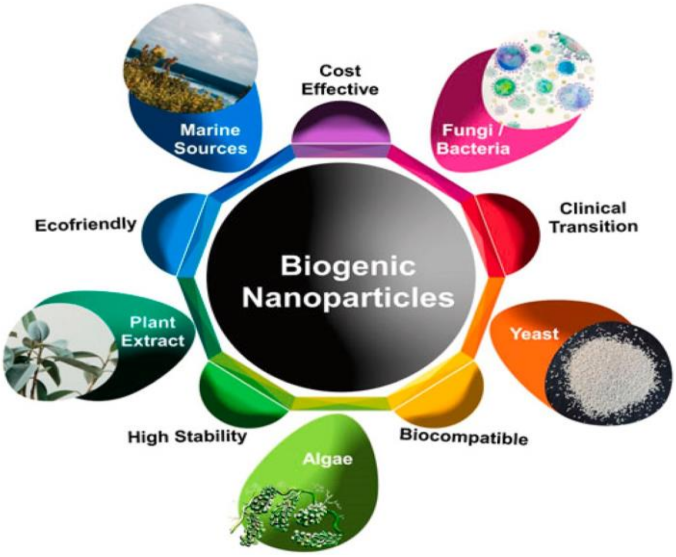
In recent years, nanoparticles have been applied in various fields, including textiles, electronics, skincare products, and antiviral treatments.[2,3] Nanotechnology is a term used to describe areas of science and engineering where phenomena occurring at nanoscale dimensions are exploited in the design, characterization, manufacturing, and applications of materials, structures, devices, and systems.

Nanotechnology has had a profound impact on various fields, and its applications continue to expand. The remarkable features of nanoparticles' minute size are crucial in various reactions. The findings of nanotechnology and nanomedicine are vast and diverse, with impressive advancements in nanomedicine elevating medication to new heights with noteworthy medical outcomes. Research on the substantial potential of nanotechnology in healthcare is essential. Numerous studies are being conducted in the medical field to investigate optimal techniques and approaches, such as cancer treatment, cardiovascular disease therapeutic gene, and nephrology. Traditional treatment has advanced significantly, and nanotechnology and nanoparticle quality have both improved, producing promising outcomes.

Nanomedicines have also been utilized in gene therapy. Various studies have focused on the use of viral vectors as drug delivery systems.[4] Scientists are becoming increasingly interested in nanoparticles, which are nanoscale platforms with a wide range of potential sizes and configurations for sophisticated applications in biotechnology. The unique thermodynamic and radiative features of nanoparticles make them useful in applications like diagnosis and pharmaceuticals. Compared to single molecules or bulk particles, these characteristics enable nanoparticles to have more focused and profound effects. This is particularly useful in fields like medicine, textiles, safeguarding, food production, agriculture, skincare products, and space exploration due to their enhanced electric transport, stimulated texture, and stability.[5]

Nanoparticles possess remarkable shape and size properties, a wide range of applications, and are utilized for extensive applications.[6] When compared to other bulk materials, nanoparticles exhibit distinct advantages. Large-scale approaches to biology and nanotechnology can be divided into two categories: first, using tools and techniques inspired by nanomaterials in biological systems; and second, using biological systems as models for the development of nanoproducts. Nanomaterials offer several benefits over conventional biotechnological techniques, including high stability, adaptability, and target selectivity. Due to its numerous applications across various fields, nanotechnology can support the global economy and a sustainable future.[7] Nanomaterials have various applications in medicine and healthcare, including drug delivery, therapeutic, and diagnostic activities.

Prior to determining a patient's condition, medical experts must diagnose diseases based on visual symptoms. However, treatment may not be as effective by the time these symptoms manifest. Conventional detection methods rely on normal organic molecules, which reduce their specificity as they break down quickly. Nanomaterials, on the other hand, can withstand a significantly higher number of cycles of excitations and light emissions. Diagnostic nanotechnology based on gold nanoparticles has been declared highly sensitive as a target-specific probe. It is also beneficial in cancer detection and viral infections.



Benefits and Sources of Biogenic nanoparticles

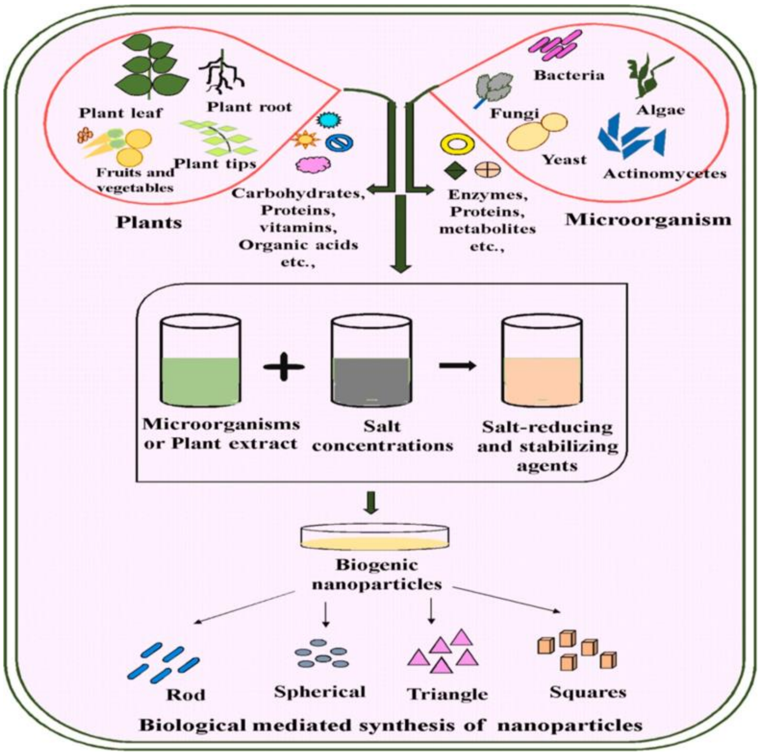
Biogenic Nanomaterials: Synthesis, Characterization, and Applications

Nanoscience explores the properties of materials within the range of 1 to 100 nm, while nanotechnology applies this knowledge to create or assess new products. The ability to manipulate structures at the atomic level enables the development of nanomaterials.[14] These materials exhibit unique optical, magnetic, and electrical properties at the nanoscale, making them applicable in various fields such as electronics and medicine.[15] Additionally, scientists classify nanoparticles into two categories: Organic and Inorganic, Organic nanoparticles consist of nanomaterials derived from carbon-based compounds, whereas inorganic nanoparticles are composed of materials that do not contain carbon.

Inorganic nanoparticles offer several advantages, including being non-toxic, hydrophilic, and biocompatible with living systems. They also tend to be more stable than organic nanoparticles. Compared to organic nanoparticles, inorganic ones are smaller, exhibit better stability, have controllable surface properties, and display enhanced magnetic features. Conversely, organic nanoparticles are generally more biodegradable, biocompatible, and non-toxic than their inorganic counterparts. Inorganic nanoparticles are particularly effective for drug delivery applications. These nanoparticles possess distinct material and size properties, a high surface area-to-volume ratio, and customizable surfaces, making them ideal for targeted drug delivery and precise treatment. Their characteristics include controlled distribution, ease of absorption, reduced toxicity, improved functionality, and biocompatibility. Inorganic nanoparticles are chemically stable, meaning they do not degrade in the plasma or cytoplasm of the human body, thus maintaining their integrity throughout the delivery process.[16]

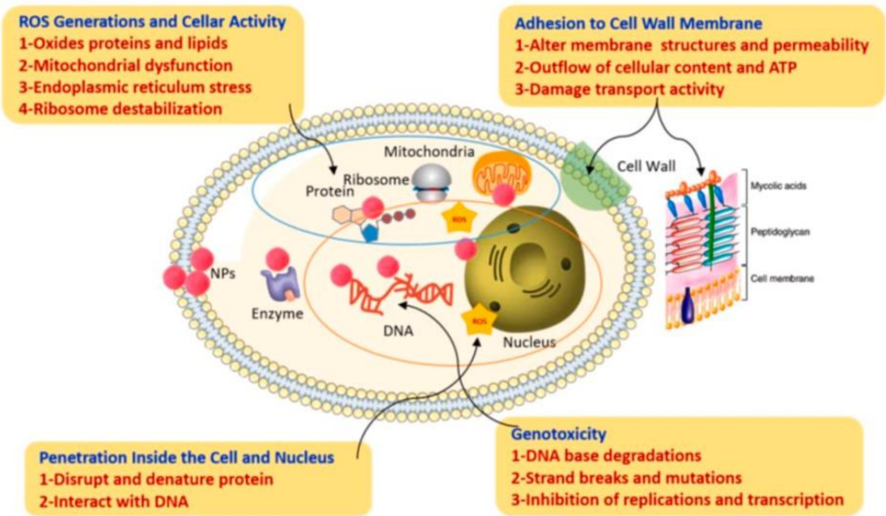
Inorganic nanoparticles (NPs) are often composed of noble metals like gold (Au) and silver (Ag). Other metals, such as nickel (Ni), cobalt (Co), iron (Fe), magnetite (Fe_3O_4), and iron-platinum (FePt), are used to create magnetic nanoparticles with superior properties in magnetic fields. Fluorescent nanoparticles include quantum dots and silicon dioxide (SiO_2).[17] The biocompatibility, hydrophilic nature, low toxicity, and stability of inorganic nanoparticles make them promising candidates for drug delivery systems and disease regulation, particularly due to their resistance to microbial attack. The tunable diameters of porous inorganic nanoparticles facilitate the delivery of small molecules to large proteins or oligonucleotide strands. The surfaces of inorganic nanoparticles can be modified to enhance targeted drug delivery and enable monitoring of drug release. When combined with drugs, inorganic nanoparticles provide a versatile platform for imaging-based therapies and diagnostics. Both inorganic and metallic nanoparticles, such as silicon, silica, and graphene, are rigid and resistant; however, they are easily altered mechanically and chemically, making them suitable for delivery into tumor cells, although their limited flexibility may hinder penetration.[18]

Due to their unique surfaces, free nanoparticles interact with biomolecules, generating both radical and non-radical reactive oxygen species (ROS). A biocompatible coating is used to encapsulate the inorganic nanoparticles to mitigate potential toxicity. By encasing a different metal, core-shell nanoparticles are produced, which enhance properties such as photoluminescence and quantum yield. Passivating the non-radiative combination sites provides air stability and reduces surface imperfections. Encapsulated nanoparticles are transported across cells via exocytosis or endocytosis.[17] Green synthesis, which refers to the environmentally friendly production of metallic nanoparticles using biological components, has garnered significant attention. This method involves the use of biomass, plant extracts, microorganisms, and various reducing agents. "Green nanotechnology" refers to the fabrication of nanoparticles from plants and microorganisms, including fungi, bacteria, and green algae.



Fungi-based nanoparticles synthesis

The most prevalent type of microorganisms, fungi are employed in many scientific fields for purposes such as enzyme synthesis, bioremediation, and nanotechnology production.[17] Fungi able to produced nanoparticles that produced by bacterial cells due to their greater capacity to endure metal concentrations and their greater ability to bind with cell walls for metal ions. Mostly filamentous mushrooms, imperfect fungi, and other fungi, ascomycetes produce around 6000 physiologically active chemicals. In addition to being more valuable than bacteria at creating nanoparticles, fungi also have a greater tendency to accumulate metals. During intracellular synthesis, metals were first introduced into the culture and rotated inside the biomass. In order to remove the biomass and release the nanoparticles after biosynthesis, the produced nanoparticles must be extracted using centrifugation, filtration, and chemical processing. Significant advantages include the ease of downstream processing and scaling up, the economic viability, and the presence of mycelia, which offers a greater surface area. Fungal-based NP is produced by a bio-mineralization mechanism that includes multiple metal ion reduction by both extracellular and internal enzymes and biomolecules. Silver was a preferred metal for both research and manufacture of nanoparticles production based on fungi. Then, Ti, Au, Cu, Se and Zn have been utilized by fungus in nanoparticles production.[18] Different fungal species was employed in the biosynthesis of bio nanoparticles such as *Rhizopus*, *Verticillium*, *Fusarium*, *Aspergillus*, *Penicillium*, and *Trichoderma sp.*[19] Fungi-derived nanoparticles have been widely applied as an anticancer drug, antivirals, antimicrobials, antifungals, antibiotics, in addition to its commonly application in medicine, disease diagnosis, bio-imaging, agriculture, and industry. Fungal cells generate a significant amount of NPs in comparison to those of bacteria due to the ability of fungi to secrete more proteins leading to greater nanoparticles output.[20]



Mechanism of action of Fungicidal activity of biogenic nanoparticles

Application of bio-nanomaterials

Biomedical applications of nanoparticles as a promising drug delivery system

The purpose of nanoparticles in disease-causing organisms is to disrupt the cell membrane’s polymer subgroup. The challenging role of nanoparticles efficiently is damaging bacterial cell membrane and disrupting protein synthesis. Silver nanoparticles in a high concentration can rupture bacterial cell membrane and successfully destroy the bacterial cell wall. The bacterial cells exposed to silver nitrate grew more quickly than exposed to R. apiculate-mediated silver nanoparticles. This difference in growth rate could be attributed to the size of the particles and enhanced external interaction that caused induced cell membrane rupture and cell interruption.[21]

Combination of both platinum nanoparticles and microorganisms to target different disease. Numerous antibiotics are effectively resistant to microbes. Various microbes exhibit resistance to different antibiotics. Meanwhile, nanoparticles have highly antimicrobial activity. Numerous investigations on metallic nanoparticles, including gold, silver, lead, platinum, zinc oxide, and titanium dioxide, have demonstrated a significant contribution to their antibacterial characteristics against pathogenic microorganisms.[22] Platinum nanoparticles with significant antibacterial activity against *S. aureus* were produced biogenic using apigenin, an extract from chamomile. Furthermore, it was investigated that the growth of *E. coli* is inhibited by platinum nanoparticles.[23] Another study discovered that *Streptococcus mutans* is suppressed by a mixture of partial ammonium and platinum nanoparticles, which possessed antibacterial properties.[24] Combinations of polyamides, such as sulfones, exhibit more potent antibacterial effects against *S. aureus* and *E. coli.*[25] Silver- platinum nanoparticles loaded with particles that ranged from 2 to 3 nm demonstrated substantial antibacterial activity versus *S. choleraesuis, P. aeruginosa, K. pneumonia*, and *E. coli*. Recent research suggests that growth of bacteria was inhibited by mitochondrial membrane integrity and ATP production.[26] Furthermore, Polyvinylpyrrolidone (PVP) when coupled with platinum nanoparticles has good antibacterial activities against *Lactococcus lactis, K. pneumonia,* and *E. coli.*[27]

Biogenic synthesis of silver nanoparticles, which derived from bacteria, fungi, algae different parts of plant or extract possess an efficient antibacterial activity as well as overcoming multidrug-resistant against numerous infectious diseases caused by different bacteria species as *S. aureus* and *S. epidermidis*. Aspergillus fungi produce powerful silver nanoparticles with antibacterial activity versus methicillin-resistant. *S. epidermidis* and *S. aureus*. Silver nanoparticles synthesized with the help of *Aspergillus oryzae* filamentous mold have exhibited antibacterial effects against S. aureus KCCM 12256. Furthermore, *Bipolaris nodulosa* fungi is a potential stabilizing agent for silver nitrate, leading to the generation of silver nanoparticles in *B. subtilis* and *P. vulgaris* pathogens.[28] Moreover, biosynthesized silver nanoparticles were achieved using gilled mushrooms of the *Pleurotus sajorcaju* species, demonstrating effectiveness against *S. aureus.*[29] A previous research focused on investigating the ability of *Phoma glomerata* fungal plant pathogens to synthesize silver nanoparticles and enhance their anti- bacterial efficacy against *S. aureus.*[30] *Trichoderma viride,* a mold species, utilizes bio-mediation to bind with nanoparticles, showing efficacy against vancomycin-resistant *E. coli*. In comparison to alternative techniques of producing colloidal silver nanoparticles, biogenic silver nanoparticles shown superior bacterial characteristics towards *S. oneidensis*, as demonstrated by bacterial toxicity testing. The following figure represented the mechanism of action of antibacterial activity of biogenic nanoparticles [Fig. 17]. In general, smaller nanoparticle size have more antibacterial action than larger ones. This is due to their higher surface-area-to-volume ratios, which allow for more interaction with bacteria and in hence influence its antibacterial activity.

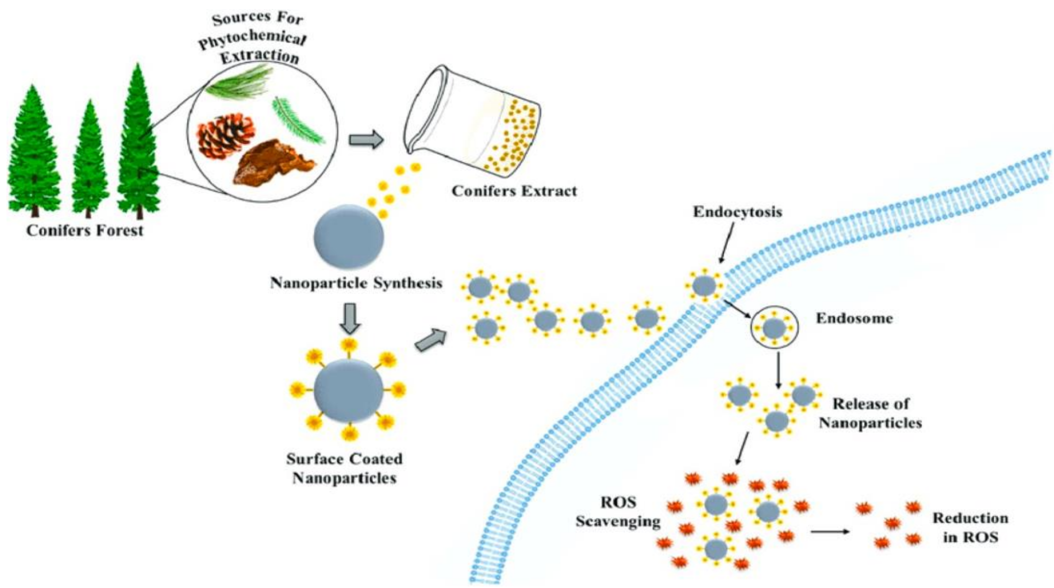
Fungicidal activity

Alternative treatments are therefore required for fungal illnesses because general antifungal medications can have a number of side effects, including diarrhea, increased renal failure, nausea, and elevated body temperature. According to a recent study, platinum nanoparticles showed antifungal effectiveness against a number of dangerous fungi, including *P. drechsleri*, *D. bryoniae, C. fulvum, C. acutatum,* and *P. capsici*. The antifungal activity of biopolymer-based platinum nanocomposites were evaluated against a range of fungal strains. Previous studies have reported that the antifungal characteristics of platinum nanoparticles in a nano-mixture-induced membrane breakdown, increased the ROS ratio, altered the mycelia's structure, and caused cellular breakage and DNA damage.[37] Biosynthesized metallic nanoparticles have a more effective fungicidal action mechanism than widely used antibiotics like fluconazole and amphotericin. The use of silver nanoparticles derived from plant extracts has successfully exposed *Candida sp*. membrane disruption, which disrupts fungal intracellular components and causes cellular damage.[36] Certain antifungal drugs that are currently accessible have limited their application, reduced their activity, and failed to cure microbial infections. Silver nanoparticles' broad-spectrum characteristics have an intriguing effect on spore spreading of fungus and seriously hinder fungal growth. As described in the following figure, the structure of the fungal cell wall was significantly changed by expo- sure to nanoparticles.[36]

Antioxidant activity

Enzymes and non-enzymatic agents in addition to antioxidant activity control free radical generation. In addition to brain damage, malignancy, and heart disease, radicals can damage the cells. Free radicals are produced by ROS, including SOD and hydrogen peroxide. Bio- constituents that efficiently control the production of free radicals include proteins, lipids, glycoproteins, phenolic, and flavonoids. Additionally, the ability of antioxidants to scavenge pathogens is crucial for managing a number of illnesses, including metabolic and neurological conditions. When it comes to antioxidants, silver nanoparticles outperform conventional medications like ascorbic acid. Both the tea extract and the nanoparticles demonstrated higher levels of flavonoids and phenolic components as well as improved antioxidant activity. Free radicals and reactive oxygen species have shown biological system activity, according to Yazdi et al.[37] These agents are byproducts of normal metabolism that harm cell development, causing cell rupture, cellular constituent inaccuracy, and destruction to shared characteristics across multiple cells. Oxidative stress contributes to the spread of dis- eases such as cancer, Alzheimer's, and blindness. Plants contain many antioxidants, which protect human health because they strongly pre- serve biological systems against these substances, select toxic free radicals, and lower cell destruction. The nanomaterial is familiar as a vehicle system for selected drug transmission in current years.[31]

Ceric oxide nanoparticles utilized as cancer therapy vehicles may normalize ROS because to their antioxidant properties. According to the above-mentioned studies, these nanoparticles exhibit anti-cancer prop- erties while also acting as antioxidants and protecting healthy cells.[35]



Antioxidant activity of biogenic nanoparticles

Bio-sensing applications

The employment of nanoparticles in biological material sensing is highly beneficial.[34] These kinds of bio-sensing applications involve the utilization of many nanoparticles.[35] In one work, cancer was examined via the green synthesis of gold-silver nanoparticles mediated by chloroplasts.[36] Platinum nanoparticles produced by *S. myriocystum* were employed to identify asthma and allergies.[37] The synthesis of gold nanoparticles mediated by *Hypnea valencia* was utilized to identify pregnancy in females.[15] Moreover, the ability of *Noctiluca scintillan*s-mediated silver nanoparticles production to identify problems with mouth gums and oral discharge was assessed.[15] The following figure illustrated the role of biogenic nanoparticles in medicine suggesting that it could be a promising technology in bio-health and as a novel drug delivery system.

Conclusions and future scope

The discipline of nanotechnology generates novel biomedical nanoparticles for use in pharmaceutical and therapeutic applications, and it is primarily tied to the fields of physics, chemistry, biology, and material science. The substantial applications of nanoscience in the chemical, pharmaceutical, medical diagnosis, electronics, space, agriculture, and illness healing industries have attracted the attention of researchers in recent years. Nowadays, it's believed that nanoparticles are incredibly beneficial materials. Actinomycetes, bacteria, fungus, plants, and yeast are some of the organisms that provide the biologically mediated nanoparticles. With less harmful side effects, bio-mediated nanoparticles have been extensively employed to treat a wide range of pathogenic disorders. Furthermore, metallic nanoparticles mediated by biological processes are less costly, less hazardous to the environment, and non-toxic. Moreover, employing genetic engineering techniques, the produced nanoparticles may increase activity. Certain characteristics of bio-mediated nanoparticles include increased biocompatibility, increased surface area, increased reactivity, and lack of toxicity. A clear perspective on the several sources of synthetic nanoparticles and their medical uses, including antibacterial, antifungal, antiviral, anti-inflammatory, antidiabetic, and antioxidant properties.

A thorough analysis of the risks associated with nanomaterials and their use in biological systems is still lacking. This necessitates the development of a uniform technique for measuring toxicity or other harmful impacts on people and the environment. The public's acceptance of nanobiotechnology, safety concerns, risk assessment, and regulation are a few of the major obstacles it may encounter. To achieve a successful application, understanding the structure-function relation- ship of nanomaterials is crucial. Finding the ideal nanomaterial for a given use will be difficult, but so will producing nanomaterials in an economical, scalable, and sustainable manner. Biodegradable nano- particles could be used to deliver treatments that are either water sol- uble or insoluble and have better biocompatibility and retention duration. The industrial sector has the potential to extend the scope of nanobiotechnology by producing substances such as the nanoadditives and nanozymes. Medical equipment and technologies can be designed to create highly selective molecular or subcellular interactions.

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