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Review Article

# A Review Study on the Sources of Biosynthesis of Nanoparticles from Different Organisms and Their Applications in Nanomedicine

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## Abstract

Nowadays nanoparticles is gaining much attention across the world among the researchers. From last few decades, green nanotechnology also emerging as a significant approach in order to synthesize and fabricate the nanoparticles from different organisms. This green route stabilizing the agents from biological agent for the formation of nanoparticles. The present review article aims is to elaborate the ongoing emergence of nanoparticle formulation from different microbiota. The microbe based research often used for the generation of nanoparticles which include algae, yeast, fungi, bacteria, and plants. This study theoretically based on the different mechanisms involved in the formation of most commonly studied nanoparticles. The synthesized nanoparticles from different microbes widely used in pharmaceutical products as anti-biofilm and antimicrobial agents, targeted the delivery of anticancer drugs, biosensors, water electrolytes, treatment of wastewater, degradation of dyes, biocatalysis and protection of crops against various phytopathogens. This review will also discuss in detail study about different aspects of microbial modes of nanoparticle synthesis and the mechanism behind their synthesis by utilizing of various bioreducing agents. For a large scale production, thorough study of the molecular mechanism is the need of the hour in order to develop a technology. This study's aim is to discusses the advantages of various approaches in nanoparticle synthesis and to highlights the recent milestones achieved with future perspectives of nanoparticles. A detail study is also required in order to acknowledge the researcher that constantly focus on this green revolution.

**Keywords:** Nanoparticles, Fungi, Virus, Algae, Metals

## Introduction

A unique idea and branch of nanotechnology known as nano biotechnology has drawn attention from all over the world. Green nanotechnology is the best technique for reducing the impacts of nanoparticle production and use thereby lowering the chances of issues brought on by alternative techniques [1]. Chemical factors, such as reaction conditions, heat level, and pressure can alter the fundamental characteristics of the material, such as texture. Using nanoparticles with a very big surface area and a very small size is known as nanotechnology [2]. Chemical, optical, and thermal properties are just a few of the characteristics that nanoparticles might possess [3]. When examined on the nanoscale, synthesis of various materials show various features.Their larger aspect ratio is one known source of this phenomena. This can lead to a number of properties for various nanoparticles. In response, researchers have looked into the use of nanoparticles which have been proposed as a possible substitute for usage in several biological applications [4]. Anti-inflammatory drugs are biocompatible and so NPs are commonly used in biological, medicinal, and environmental applications because of their antibacterial action, efficient pharmacological activity, bioaccumulation, and nanomedicine, tumor focusing as well as physiological assimilation [5]. In many sectors, including computer science, nanomaterials science, and pharmacy, agricultural, sensing, atmosphere, economy, and the fields of biomedicine, optics, catalytic, computing, and nanoparticles have potential applications [6]. Copper, zinc, iron, titanium, magnesium, cerium, and zirconium oxide are only a few of the metal oxide nanoparticles in question [7]. The ultimate goal is to offer a method for green synthesis and related elements that will aid researchers working in this field and serve as an important resource for readers interested in or the topic generally [8]. In order to create nanoparticles, green synthesis techniques use viruses, bacteria, fungi, algae, and plants as examples of biological organisms. Because they shouldn't prevent the usage of synthesized nanoparticles, the bacteria, fungi, and viruses used in their manufacture are nonpathogenic in nature [7]. Several metallic nanomaterials made using synthesis and characterization and their possible use in applications is the goal of this review.The process of biosynthesis, which uses the bottom-up approach, is environmentally friendly and includes metal particles forming groups that ultimately become nanomaterials. The concept of chemical reduction is similar to that of biosynthesis, however the production of nanoparticles is done with eco-friendly materials rather than costly, harmful, toxic chemicals. To differentiate between biochemical degradation of nanomaterials made using green synthesis and a conventional wet-chemistry method, biologists used adverse reaction reporting [9]. Researchers discovered that green nanomaterials had significantly lower levels of phytotoxicity and the fact that they are safe and less harmful than wet chemical nanomaterials, and the wide range of biomedical applications they can be used for, especially studies on cancer [10]. In light of these and growing recognition of its significance, biosynthesis has been hailed as a virtuous green alternative that appears to offer the best methodology or results among the main green chemical approaches. A few organisms that are biological in nature are bacteria, Mold, yeast, and plants. The nature of living entities has a considerable impact affecting the composition and appearance of produced nanomaterials.The intriguing variety of nanoparticle shapes and sizes that evolved from the diversity of biological entities serves as a model for the development of nanoparticles. The continuous emergence of bacterial resistance has challenged the research community to develop novel antibiotic agents. Among the most promising of these novel antibiotic agents are metal NPs, which have shown strong antibacterial activity in an overwhelming number of studies. Generally, antibiotic-resistant bacteria appear in a relatively short period of time even when new antibiotics are released into the market. However, it is hypothesized that NPs with antibacterial activities have the potential to reduce or eliminate the evolution of more resistant bacteria because NPs target multiple biomolecules at once avoiding the development of resistant strains. Nowadays, there is a growing need to develop eco-friendly processes, which do not use toxic chemicals in the synthesis protocols. Green synthesis approaches include mixed-valence polyoxometalates, polysaccharides, Tollens, biological, and irradiation method which have advantages over conventional methods involving chemical agents associated with environmental toxicity. Selection of solvent medium and selection of eco-friendly nontoxic reducing and stabilizing agents are the most important issues which must be considered in green synthesis of NPs.

## Benefits of biological synthesis

Gold (Au) nanoparticles with sizes of 8.01 nm were created from *Lonicera japonica* flower extract in a variety of geometries, comprising triangular, hexagon, face-centered square, and quasi-spherical forms [11]. Or two more reducing agents that have recently come to light are algae and seaweed. A subset of gold nanoparticles which are regarded as offering tremendous possibility in the therapy of digestive system cancer, were produced using the brown algae *Cystoseira baccata*. Protein concentrations and platinum (Pt) salt concentrations both affect the shape and size of Pt nanoparticles produced during biogenic synthesis. Another possible scale-up method for the manufacture of PtNPs is being revealed that involve fungi like *Neurospora crassa* or *Fusarium oxysporum*. Similar to this, plant extracts were used to organically synthesize metal nanoparticles including phytochemical elements that act as coating materials [12]. Research shows or Studies highlight the great range of biological species that may be found in nature and offer a number of benefits. Nanoparticle synthesis is possible by changing variables such as phytoconstituents, heating time, pH, impacts of extract aging, and temperature. The large number of biomolecules, affordability, stability, lack of harmful chemicals, and straightforward, secure operating processes make biological synthesis excellent [9].

## Nanoparticles from viruses, bacteria, fungi

It is a novel strategy to synthesize artificial nanocrystals like silicon dioxide, ferrous oxide, cadmium sulfide, and zinc sulfides by using viruses. Green chemistry is interested in semiconductor nanoparticles like zinc and cadmium sulphur. The electronics sector is actively searching ways to produce them. During the past few years, researchers have been experimenting with using whole viruses to create nanomaterials [13]. By creating a high-reactivity metal plate that can bind ions, the virus outer capsid protein contributes to the production of nanoparticles [14]. 2130 viral proteins can be found associated with tobacco mosaic virus (TMV). For

**Figure 1.** Nanoparticle synthesis from their intrinsic level.

**Table 1.** Biological synthesis of metal nanoparticles using various bacteria.

| **Sources** | **Type of nanoparticles** | **Location** | **Size (nm)** |
|---|---|---|---|
| *Pseudomonas aeruginosa* | Au | Extracellular | 15~30 |
| *Pseudomonas stutzeri* | Ag | Intracellular | 200 |
| *Bacillus subtilis* | Ag & Au | Intra & Extracellular | 5~10 |
| *Shewanella oneidensis* | U | Extracellular | 150 |
| *Lactobacillus* sp. | Ag & Au | Intracellular | 60 |
| *Escherichia coli* | CdS | Intracellular | 2~5 |

a number of medicinal applications, any or all peptides can be employed as spike connectors to remit or create vessels that are three dimensional [15]. Amount of the synthesized nanomaterials is lower after the addition of Gold and Silver compounds to Tobacco mosaic virus in small quantities before including *Hordeum vulgare* or *Nicotiana benthamiana* plant filtrates. It increased or boosted their amounts relative to people which did not receive the virus-based compound because at higher Tobacco mosaic virus concentrations, they produced proportionally very less free nanoparticles. Tobacco mosaic virus was also used as a bio-model for the process of metal substrate of nanowires as well [16]. In contrast to the lack of a viral infection, the occurrence of an infectious agent not only decreased the Biologically synthesized Nanoparticles' size but also greatly or markedly enhanced their production. Microbial species have been used in industrial processes such as bioleaching, environmental remediation, and genetic alteration [17]. Microbes are interesting candidates for the manufacture of nanoparticles because they can reduce metal ions. Many bacterial species are used to produce metallics and other nanoparticles. Metal and metal oxide nanoparticle production frequently uses prokaryotes and actinomycetes [18]. Nanoparticles made by bacteria have been used because they are relatively simple to manage. Some of the bacteria utilized in the manufacture of nanomaterials include *Pseudomonas protease*. Enterobacter cloacae, bacteria, *Licheniformis, Klebsiella pneumoniae*, and *Morganella* bacteria like *B. Subtilis, E. Coli* DH5, *Rhodopseudomonas capsulata*, *Pseudomonas aeruginosa*, and *B. licheniformis* all produce gold nanoparticles [19]. Previously, *Clostridium thermoaceticum, Escherichia coli,* and *Rhodopseudomonas palustris,* were responsible for the production of cadmium nanoparticles [20]. Bacteria may be used as a biocatalyst in order to synthesize inorganic components, a mineralization bioscaffold, a direct contributor to the manufacture of nanomaterials. During a bacterial culture in broth medium, extracellular or subcellular nano-materials can be produced. The biosynthetic process for producing metal oxides at the nanoscale is still mostly unknown. The main cause of this is that very few people are aware of the biosynthesis-related enzymes [21]. The production of harmless metal oxides by biological synthesis has been demonstrated, however it requires meticulous cell culture, which makes it challenging to regulate crystal diameter, form, and crystalline nature [22].

Due to its use in a variety of fields, such as electronics and antimicrobials, fungus-based nanoparticle production has been the main subject of research [23]. It has been shown that the fungus *Fusarium oxysporum* can generate nanomaterials of silver with sizes ranging between 5 and 15 nanometers, and these particles are maintained by mycological proteins. Research has shown the internal creation of silver and gold nanoparticles, as well as the generation of cadmium, molybdenum, and Nanostructures made of zinc sulphide within individual cells [24]. They include a range of internal enzymes, making them exceptional biogenic components for the formation of materials and oxide nanoparticles. In comparison to bacteria, efficient fungi may produce more nanoparticles [25]. Fungi have a considerable advantage in comparison to other species due to the presence of enzymes, proteases, and reductive enzyme components on the cell surface [26]. The most likely method for producing metal nanoparticles is by enzymatic reductions (reductase) within infectious cells or in cell walls. In addition, viral infection-causing enzymes also increase the production of stable nanoparticles by synthesizing more of them and also speeding up their reductive processes [27]. It's common to believe that extracellularly produced nanoparticles are less or harmless [28]. Using a *Fusarium oxysporum* extract, extracellular Pt nanoparticles with diameters ranging between 15 and 30 nanometers are produced at cellar temperature. Note that a specific temperature was required for the fungus *Neurospora crassa* to produce Nanoparticles of silver, and the resulting particles had a diameter of 20 to 110 nm and were nearly spherical. In conclusion, the authors reported that fungi extracts might be applied to stay stable and lessen nanoparticles of platinum [29]. The fungus *Neurospora crassa* was used to make intracellularly produced Platinum nanostructures ranging in size from 4.5 to 35 nanometers. Moreover, they have the capacity to create spherical nanoagglomerates with sizes between 20 and 110 nm. All feedstock and *N. Crassa* extracts were used to create Pt nanoparticles. The nanomaterials of Platinum based extracted from *N. crassa,* single-crystal nano agglomerates have been found [23]. Additionally it was also found that Platinum nanoparticles may be made from *Fusarium oxysporum* respectively both extracellularly and intracellularly, however only in optimal amounts when created intracellularly. The endophytic fungus *Verticillium sp.* and the phytopathogenic fungus *F. oxysporum* were found to produce magnetite [common ferrous oxide] nanoparticles intracellularly.

### Algal and plants based nanomaterials synthesis

It has been demonstrated that algae can synthesize aluminum nanomaterials, as well as absorb heavy metals from their surroundings. A brown alga called *Fucus vesiculosus* is currently being studied for its capacity to bio reduce the metal gold ions [30]. Using dehydrated *Chlorella vulgaris* algal cells, lowered tetrachloroaurate ions were used to produce gold nanoparticles [31]. Algae are known as bio-nano factories, the term metabolism refers to the process of converting organic matter into usable energy. It's because they metabolize metals and reduce metal ions. Microalgae are filamentous colonies of photosynthetic microbes that fall within the Chlorophyta, Charophyta, and Bacillariophyta divisions. They contribute significantly to the biodiversity of the globe. To recover Gold from liquid waste of micro – electronic scrap and reduced hydro metallurgical mixes, bioreduction using *Fucus vesiculosus* may be a more environmentally friendly option. According to Yenumula et al. [32], proteins in the algal extract perform a variety of functions, including stabilizing, reducing, and modifying shape. The saltwater alga called *Sargassum wightii* similarly produced extrinsic nanoparticles of Au, Ag, and Au/Ag bimetallic metals. The quick external gold structure nanoparticles with ranges between 8 and 12 nanometers was discovered [33] using *S. wightii.* Some of the algae that were mentioned *Kappaphycu salvarezii*, *Fucus vesiculosus*, *Tetraselmisko chinensis, Chondrus crispus*, and *Spirogyra insignis* were all used in the synthesis of Gold and silver nanoparticles. Because of the fact that they were created using Microalgae *Euglena gracilis* that had already been established in conditions that were like autotrophic or mixotrophic (non-light-exposed and grown in carbon-rich organic culture media) [34]. Synthesized Gold nanomaterials have solubility, speed, kinetics, and outputs. Algae are simpler to work with, less harmful to the environment, and can be produced at room temperature and pressure in distilled water, and with a neutral acidity. In order to create nanoparticles a variety of algae species are used. Alkaloids, flavonoids, terpenoids, steroids, and many other bioactive substances present in plants. A variety of plants are used in the nanoparticles formation like *Acalypha indica, Passiflora foetida, Parthenium hysterophorus, Ficus benghalensis, Zingiber officinale, Plumbago zeylanica, Centella asictica,* and *Ficus benghalensis* [35]. Recently, many kinds of nanoparticles have been created using these plants. Due to their simplicity, lack of pathogenicity, and cost-effectiveness, plant extracts are more useful than microorganisms for the formation of green nanoparticles [36]. Moreover, aiding in the fine-tuning of nanoparticle size, it helps to remove harmful by-products. Iron oxide nanoparticles with spherical and non-spherical group arrangements were produced using *Camellia sinensis* extract. *Hibiscus rosa-sinensis, Acalypha indica , Calotropis gigantea, Coriandrum sinensis* as well as *Coriandrum sativum* leaf extracts are used to make zinc oxide nanoparticles. Extracts from the plants *Jatropha curcas* and *Eclipta prostrata* were used to form titanium oxide nanoparticles. *Aloe barbadensis* and *Aloe sylvestris* leaf extracts formed copper oxides nanoparticles [37]. Plant extracts contain Phytonutrients and macromolecules including phenolics, flavonoids, terpenes, phenolic acids, and ethyl alcohol that minimize and stabilize metals derived from their components. These macromolecules can be divided into two groups: [I] redoxed intermediaries for metal reductions, or [ii] capped agents for post-surface modification and non-agglomeration of nanoparticles. In addition, the generated nanoparticles are clean and useful for applications involving physiological liquids [38]. There have been many published attempts that used various plant elements to synthesize ZnO with various properties.

### Factors affecting synthesis of nanoparticles

When employing nanoparticles for biomedical applications, toxicity must be taken into account to ensure their safety and efficacy [39]. Nano – particles have been found to be harmful for humans in some research. The size and surface load of metal nanoparticles determine how dangerous they are. It is necessary to be aware of any potential health risks caused by nanoparticles. Investigating minute DNA alterations in cell damage and human tissues subjected to oxidative stress is important to remove potential genotoxicity. When using

**Table 2.** Biological synthesis of metal nanoparticles using various Fungi.

| Sources | Type of nanoparticles | Location | Size (nm) |
|---|---|---|---|
| *Phoma* sp. | Ag | Extracellular | 71~74 |
| *Fusarium oxysporum* | Ag | Extracellular | 5~15 |
| *Verticillium* | Ag | Intracellular | 25 |
| *Aspergillus fumigates* | Ag | Extracellular | 5~25 |
| *Trichoderma asperellum* | Ag | Extracellular | 13~18 |
| *Phaenerochaete chrysosporium* | Ag | Extracellular | 50~200 |

nanoparticles for implants, chemical inertness is a major element as well. Commonly used oxides of iron, zinc, and titanium can be formed and changed into carbon derivatives, allowing them to bind to antibodies, medicines, and ligands [40]. According to researchers [41], noncovalent interactions between hydroxyl groups and surface metal ions or ligands may help nanoparticles function. The stability of nanoparticles is closely related to the amount of heat used to produce them [42]. The morphological properties of nanoparticles can be controlled by a number of variables, like pH, reactant amounts, reaction duration, and temperature [43]. These traits are essential for understanding how environmental factors affect NP biosynthesis because they can be used to maximize the production of metallic NP that is used in biological processes. However, earlier studies have shown that the more extract used, the faster the synthesis rate, as more chemical components were there in the solution to interact with the substrate and promote rapid bio-reduction and nanoparticle stability. To achieve the perfect condition for green nanoparticle manufacturing, the volume of green extract and concentration of precursor nanoparticles required in balance ratio.

## Applications

The advantages of nanotechnology are increasingly spreading around numerous industries. Inks, sun filters, blemish clothes, agriculture and medicines, completed fabrics, wound treatments, and sun protection and moisturizers are just a few examples that use nanoparticles formation [44]. The properties of nanoparticles have generated a lot of interest in biology and medicine. Nanoparticles have many biological uses, including drug transport, therapies, cancer treatment, antibacterials, implants, and wound healing [1].

### Anti-microbiological action

The antibacterial properties of nanoparticles are complicated and involve numerous mechanisms. As a result of this, the process behind antibacterial action is still unknown. Nanoparticles have been shown to have an antibacterial effect at low doses. According to several articles, nanopowders of Zinc oxide have lower inhibitory and microbiological values than Acetate of zinc. ZnO nanopowders work against Gram-positive and Gram-negative bacteria. Copper, zinc, and iron oxide nanoparticles were tested [45] for their antibacterial activity against Gram positive and Gram negative microbes. In this study, various possible pathways have been identified, namely I oxidative stress brought on by the production of ROS [46], [ii] NM disbanding that produces zinc ions, and [iii] uptake of all of these nanometerials in nuclei cause cell death. The main mechanism is the formation of reactive high oxygen generation of reactive oxygen species, that is connected to particle size, pore volume, and nature's crystalline structure [47]. As nanomaterials interact in the presence of bacteria, negative effects commonly occur, which are typically suppressed for antimicrobial uses in industries like food and farming. Since, by using bactericidal nanoparticles in place of some antibacterial drugs, the issues related with the spread of antibiotic resistance strains that are brought on by bacterial transfer of antibiotic resistance genes may be overcome [48].

### Drug distribution

Silver and Gold nanoparticles, two noble metal nanomaterials with distinctive properties, adapt optical properties and are made possible in the formation of targeted drug delivery systems. In addition to the typical form of nanocapsules for delivery of critical biomolecules, liposomes could be used as medication delivery vehicles. The green nanomedicine which tries drug delivery in clinics safer utilizing nano routes, was made as a result of applying the concept of green synthesis to drug dealing [49]. The often used targeted compounds are nanoparticles due to their relative ease in producing, firmness, and control of coupling chemistry. The specificity or affinity of particular molecules might be lacking. Because of its excellent reactivity Biotin [vitamin H] has been used to replace streptavidin, commonly nanoparticles [50]. Folic acid has been recommended to use in cancer (Malignant neoplasm) with high amounts of folate receptor proteins because of its great affinity for endogenous folate receptors [51]. There have been other more challenging polysaccharides, antibodies, and small molecules made and utilized in the same way. There remain a number of problems that need to be resolved or improved technologies developed in order to transport medications to the various destinations, even though many drug delivery systems have been done smoothly in recent times. In order to develop more efficient medication delivery systems, nano-based drug delivery systems are currently under study [52]. Extra–cellular particles, another name for cell-released biological nanoparticles, are one of the advanced drug delivery systems that are still being developed. Drug medication using extracellular vesicles takes full advantage of the body's natural molecular transport systems. Extracellular vesicle biology and synthesis along with medical knowledge from synthetic nanoparticles, are likely to work together to greatly increase delivery of medicines [53].

### Theranostic application

The relatively new field of medicine called theranostics combines appropriate treatment with diagnostic testing. It is a technique for getting x-rays and giving a patient a therapeutic dosage of radiation while making use of diagnostic markers in human tissue. It is now possible to merge medication distribution tools with 154 new agent compositions that have combined target therapy or diagnostic tools, thanks to recent advances in nanomedicine technology [54]. SPION is another typical theranostic drug. SPION as an MRI contrast material has been certified by the Food and Drug Agency. Synthetic magnets can lead SPION magnetically to the proper regions. Several methods are used in cancer treatments. Studies show that cancer cells in the breast that are sensitive to DOX, such as the MCF-7 resistant to DOX 1 M cell line, are not taken up by SPIONs that have been loaded with DOX. Advantages of this process include reduced medicine dosages and fewer harmful effects [55].

### Oncology treatment

Millions of people die due to cancer every year, in spite of the availability of medications. In addition, a group of patients is susceptible to unfavorable outcomes of the use of current antitumor medications. Due to the fact that recent NP-based treatments are more efficient, have less adverse effects, and specifically highlight cancerous tissues. For these reasons recent NP-based treatments have attracted a lot of attention. These effects could be the result of NPs' large surface area, which supports the mixing of high pharmacological dosages [56]. Zinc oxide nanoparticles are excellent antitumor medications due to the specific bioactivity, specificity, easy manufacturing process, and capacity to solubilize at low pH. ZnO-Gd-DOX nanoparticles were produced [57] and used to treat and diagnose mice cancer. Liposomes, dendrimers, and metallic nanoparticles are all examples of polymeric nanoparticles, and are a few types of nanoparticle drug carriers that have been studied in cancer treatment which can minimize the negative side effects of typical treatments to stop or prevent cancer drugs and increase the anticancer drug effectiveness of specific procedures [58].

### Wounds healing

Attachment of bacteria and growth in biomedical implants traumatized patients. The removal of infected implants is necessary because they can induce bone resorption. Studies have focused on developing antimicrobial coatings on grafts that either function by themselves or in conjunction with the supplied antibiotic to stop the spread of bacteria. While determining whether or not to use antibacterial substances. There are so many properties evaluated on the basis of bioactivity, antiinfective efficiency, reliability, and physical stress. Biomedical implants typically use the material titanium. Implants with a titanium coating offer a biocompatible surface for cell attachment and growth [59]. It has also been shown that alumina ($Al_2O_3$), ZnO, and CuO nanoparticles are effective anti-infection coating substances for medical implants [60]. To increase the general properties of wound treatment substances based on composite skin tissue engineering, nanoparticles'(NPs) of Metal oxide are used in polymeric nanofibers and hard tissue healing. The formation of extracellular matrix, fibroblast proliferation, and an increase in growth factor synthesis all helps in wound healing and re-epithelialization. According to research [61], ZnO nanoparticles do not pass through the skin and gradually dissolve as ions in the solution. ROS produced by the nanoparticle made of metal oxide, however, plays a regulatory and indicating function within the cells regeneration. It has been found that ROS play a function in tissue blood transmission and also have antimicrobial properties in the process of wound healing [62].

### Vaccines

Conventional vaccines based on live-attenuated pathogens possess risk of reversion to pathogenic virulence while inactivated pathogen vaccines frequently lead to a weak immune response. Nanoparticle-based vaccinations are a unique strategy or technique that have the potential to greatly improve upon the drawbacks of traditional vaccines. Recent developments in both biological and chemical technology have enabled the production of nanomaterials of exact length, structure, efficiency, and exterior control characteristics, resulting in improved appearance of antigens and potent antigenicity [63].

### The challenges in nanoparticles

One of the challenges in resolving toxicity in ENMs is the difficulties to standardize and implement the method that reflects the real toxicity of organs and the exposure root in which the ENMs entered the body [64]. The exposure roots include lung, skin, and mucous membranes, endothelium and blood cell components in addition to different organ toxicity, such as spleen, liver, nervous system, heart, and kidney [65]. Once ENMs have entered the body as drug delivery or diagnostic tools, they induce physicochemical interactions with the immunology mechanisms in blood, muscle tissue, liver, spleen, and kidney [66]. For inhaled ENMs, where immune cells can uptake and translocate them across epithelial and endothelial cells to the blood circulation system spreading to key organs, including the cardiovascular system, bone marrow, lymph nodes, and spleen [67]. The translocation of inhaled ENMs causes them to retain around the respiratory tract regions through diffusional mechanisms, resulting in further medical complications. Besides, ENMs have also been detected on the CNS. Adsorption of ENMs through the skin seems to be distributed through the lymphatic system [66]. Orally administrated ENMs are mainly digested in the gastrointestinal system which is an acidic environment. The remaining surviving ENMs from gastric juice may pass to the intestine and reach the bloodstream if not absorbed in hepatic portal circulation and eliminated by the liver. Despite the rapid development trend in nanotechnology research, the field of nanotoxicology research is growing relatively slow [68]. However, the uprising awareness about the toxicity of engineered nanomaterials (ENMs) in nanotechnology and nanomedicine communities provokes much attention toward nanotoxicology research. Several strategies and frameworks have been proposed in identifying the toxicology of ENMs in nanomedicine, including strategies in nanotoxicology identification and sharing of knowledge among the research and regulatory personnel. Fundamentally, the toxicity of ENMs is caused by several factors.

### Use of nanoparticles

The effect of $Zn^{2+}$ doping on photocatalytic and biomedical properties of CuO synthesized by the simple hydrothermal method was analyzed in this study. The phase structure, morphology, and surface chemistry of synthesized CuO and $CuO:Zn^{2+}$ samples were analyzed. XRD analysis revealed the monoclinic phase of synthesized CuO. Due to the concentration of precursors and optimization of processing conditions, the morphology of CuO appears to be like pine needles. It is transformed from pine needles to blocks by incorporating Zn into the CuO matrix [69]. Silica nanoparticles (SiNPs) have many physical and chemical characteristics that them make it useful tools for different medical and biological applications. However, toxicities and biodistribution of SiNPs after *in vivo* administration need further investigation, when these materials are used as drug delivery systems (DDS) [70]. A new Schiff base ($H_2L$) generated from sulfamethazine (SMT), as well as its novel micro- and nanocomplexes with Ni(II) and Cd(II) metal ions, have been synthesized. The proposed structures of all isolated solid compounds were identified with physicochemical, spectral, and thermal techniques. Molar conductance studies confirmed that the metal complexes are not electrolytic [71,72].

## Conclusion and Prospectus

Nanomedicine is a burgeoning field of research with tremendous prospects for the improvement of the diagnosis and treatment of human diseases. The biosynthesis of nanoparticles by microbes is thought to be clean, nontoxic, and environmentally acceptable green chemistry procedures. The use of microorganisms and plants including bacteria, yeast, fungi, and actinomycetes can be classified into intracellular and extracellular synthesis according to the location where nanoparticles are formed. The rate of intracellular particle formation and therefore the size of the nanoparticles could, to an extent, be manipulated by controlling parameters such as pH, temperature, substrate concentration, and exposure time to substrate. Research is currently carried out manipulating microorganisms at the genomic and proteomic levels. With the recent progress and the ongoing efforts in improving particle synthesis efficiency and exploring their biomedical applications, it is hopeful that the implementation of these approaches on a large scale and their commercial applications in medicine and health care will take place in the coming years.

## Conflict of Interest

The authors have no conflict of interest to declare.

## Author Contribution Statement

**Hafiza Farhat** wrote the manuscript and finalized the article. **Kainat Iqra** and **Shahid Ullah** did the material collection.

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