

ADVANCES OF BIO-SYNTHESIS OF METAL NANOPARTICLES BY USING BACTERIAL STRAIN AND THEIR BIOLOGICAL PROPERTIES: A REVIEW

Abstract

In-depth research has been done on metal-based nanoparticles for a variety of biomedical applications. The World Health Organization (WHO) states that metal-based nanoparticles have been shown to be efficient against diseases in addition to their reduced size and selectivity for bacteria. Since they do not bind to a particular receptor in the bacterial cell, metal-based nanoparticles are known to have nonspecific bacterial toxicity mechanisms. This makes it more difficult for bacteria to acquire resistance to them and broadens the range of their antibacterial action. So far, the vast majority of investigations on the efficacy of metal-based nanoparticles against both Gram-positive and Gram-negative bacteria have yielded encouraging results. Metal nanoparticles produced by the plant and plant extracts are more stable as compared to those produced through different organisms. Extensive research as yielded different nanoparticles of controlled size and shape. Typically, diverse biomolecules are carried by metal nanoparticles made of gold, silver, platinum, iron, copper, zinc, etc. This review is based on the various metal nanoparticle kinds, their production process, physicochemical characterization, pharmacokinetics, and toxicological risk associated with their use as antimicrobial agents.

Keywords: antibacterial activity, bacterial resistance, nanotechnology, nanomedicine, metal-based nanoparticles, silver nanoparticles (Ag NPs), gold nanoparticles (AuNPs), zinc oxide (ZnONPs), copper nanoparticles (CuNPs).

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I. INTRODUCTION

As the first living thing discovered on the planet, bacteria have evolved into an extremely adaptive species. It all started with the development of the drug Salvarsan, also known as 606, which was one of the first treatments for the contagious disease syphilis without being hazardous to patients (Bosch and Rosich, 2008). The "golden age" of antibiotic research, which ran from 1950 to 1960, saw the inception of this research and its climax. Between 1930 and 1962, more than 20 new classes of antibiotics were created, but as more resistant bacteria have emerged, the pharmaceutical industry is now facing greater difficulty in finding new compounds having antibacterial activity. In recent years, one of the biggest issues in the clinical profession has been the incorrect and excessive use of antibiotics, which results in antimicrobial resistance. Since the first incidence was recorded, we have seen a growth in bacteria that are resistant to standard antibiotics, which has led to the emergence of so-called multi-drug-resistant (MDR) strains. According to the Centers for Disease Control and Prevention (CDC), MDR bacteria are responsible for approximately 2 million infections each year as well as 23,000 fatalities. *The pathogenic bacteria that make up the ESKAPE group include Enterococcus faecalis, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, and Enterobacter species.* Antibiotic misuse and overuse, as well as inadequate infection prevention and control, are likely to be blamed for antibiotic resistance. Several antimicrobial resistance mechanisms have been described in the literature, including (i) reducing medication absorption, (ii) altering drug targets, (iii) rendering drugs inactive, and (iv) active drug efflux. These processes, which may be innate or learned, enable the persistence of resistant strains and the spread of those strains, leading to the failure of antibacterial treatments (Reygaert, 2018).

The use of nanoparticles as novel, non-traditional antibacterial agents has been researched as one of alternative strategies. Studies conducted in vitro have shown that nanoparticles have harmful effects on a variety of bacterial strains, indicating their viability for biological applications, including drug delivery and tissue engineering. Metal and metal oxide nanoparticles (NPs) are among the most promising nanomaterials (Nikolova et al, 2020).

Metal NPs have long been known to have antibacterial properties, but the mechanisms underlying these properties are still poorly understood. Reactive oxygen species (ROS) production, ion leaching, and/or ion dissolution are a few antibacterial mechanisms that have been proposed in recent years. These mechanisms involve the loss of cell wall and cell membrane integrity and, as a result, interfere with some metabolic pathways that are crucial for bacterial viability. In this regard, nanotechnology is an effective tool for designing NPs with the necessary physicochemical characteristics to lessen their cytotoxic effect and the danger associated with their usage in biomedical applications (Abbasi et al, 2023).

This review aims to present a summary of metal nanoparticle (NP) antibacterial processes relating to various bacterial species, higher microbial organizations (biofilm), and the physicochemical characteristics of NPs themselves. To further assess the viability of various therapies used in the clinical and human safety domains, bacterial resistance methods are also examined.

II. WHAT IS NANOPARTICLE?

Nanoparticles are particles which lie in dimensions between 1-100 nm (Horikoshi and Serpone, 2013). They are made up of tiny molecules in which the active substances have been dissolved, trapped, encapsulated, adsorbed, or connected. It is a colloidal particle that is solid.

Nanospheres and nano capsules are two different forms of nanoparticles.

- **Nanospheres:** The medicine is physically and evenly spread inside nanospheres, which are matrix structures.
- **Nanocapsules:** A special polymer membrane surrounds a chamber that contains the medicine in nano capsules.

1. Applications of Nanoparticles: According to (Fadeel et al, 2009), nanomedicine is an emerging field of study with enormous potential for advancing human illness diagnostics and therapy. In nano biomedicine, dispersed nanoparticles are typically used as fluorescent biological markers (Otto S, 2015), medication and gene delivery agents, and in applications like the bio detection of infections, tissue engineering, tumor destruction via heating (hyperthermia), MRI contrast enhancement, and phagokinetic studies (Saman et al, 2022).

A plethora of reviews and research papers have been published studying the uses of nanoparticles in biomedicine (Emerich and Thanos, 2006) like targeted drug delivery, cancer treatment, gene therapy and DNA analysis, antibacterial agents, biosensors, accelerating reaction rates, separation science, and MRI.

2. Drug Delivery: A fundamental concern in the design and development to innovative drug delivery systems is the precise and safe delivery of the pharmaceuticals to their target areas at the appropriate time to have a controlled release and obtain the maximal therapeutic benefit. Through certain endocytotic and transcytotic transport systems that penetrate cellular barriers, they must enter target cells in order to make contact with cytoplasmic targets (Fadeel and Bennett, 2010).

Due to their small size, nanoparticle drug carriers can pass through the skin's tight epithelial junctions and the blood-brain barrier, which often prevent the delivery of medications to the intended target region. They make hydrophobic substances more soluble and appropriate for parenteral drug delivery. Additionally, they improve the stability of numerous medicinal substances, including peptides and oligonucleotides (Din et al, 2017).

3. Antibacterial Agent: Due to the frequency and proliferation of bacteria that are resistant to several antibiotics, the usage of silver-based antiseptics has increased recently. Silver nanoparticles were produced by a fungus called *Trichoderma virid* (Fayaz et al, 2010). It was found that the aqueous silver (Ag⁺) ions were decreased in solution when exposed to a *T. viride* filtrate, which produced exceptionally stable AgNPs with a size range of 5 - 40 nm.

In the presence of AgNPs, test strain resistance to the antibacterial effects of ampicillin, kanamycin, erythromycin, and chloramphenicol was enhanced. The findings offered valuable information for the creation of new antimicrobial drugs and demonstrated that antibiotics and AgNPs together have improved antibacterial properties. Using *Fusarium oxysporum*, Durán et al, 2005 demonstrated how extracellularly generated silver nanoparticles may be integrated into textile textiles to prevent or reduce infection with harmful bacteria like *Staphylococcus aureus*.

- 4. Biosensor:** Nanoparticles have fascinating electrical and optical properties that can be employed in biosensor applications. *Bacillus subtilis* has been reported to produce spherical selenium nanoparticles with sizes ranging from 50 to 400 nm (Ullah et al, 2021). Due to Se nanoparticles' excellent adhesive properties and biocompatibility, these sensors demonstrated good electro catalytic activity for the reduction of H_2O_2 . These H_2O_2 biosensors had high sensitivity and affinity for H_2O_2 with a detection limit of metal. Additionally, their findings demonstrated that the electrochemical applications of various Se nanomaterial crystals were not significantly different.

A wide range of applications involving the detection of H_2O_2 in food, pharmaceutical, clinical, industrial, and environmental investigations will thus likely show promise for the Se nanomaterials-modified electrode. According to (Zhang et al, 2013), yeast-produced Au-Ag alloy nanoparticles were used to create a sensitive electrochemical vanillin sensor. Electrochemical tests showed that the vanillin sensor based on glassy carbon electrode modified with Au-Ag alloy nanoparticles could increase the electrochemical responsiveness of vanillin by at least five times. This vanillin sensor was successfully used to measure the amount of vanillin in samples of vanilla bean and vanilla tea, indicating that it might be useful in vanillin monitoring systems. In a different study, glucose oxidase (GOx) biosensors based on AuNPs were created in response to findings indicating AuNPs can boost GOx's enzyme activity (Devasenathipathy et al, 2015). The glucose biosensor has a linear response range of 20 M to 0.80 mM glucose and a detection limit of 17 M (S/N = 3). The use of this kind of biosensor to ascertain the amount of glucose in commercial glucose injections was successful.

- 5. Reaction Rate Enhancement Agent:** Due to their huge surface areas and unique properties, nanoparticles have been widely employed as reductants and/or catalysts to improve a variety of reactions (Hildebrand and Mackenzie, 2008). Microbiological response rates have been enhanced using magnetic nanoparticles. To complete the desulfurization of dibenzothiophene (Shan et al, 2015) used *Pseudomonas delafieldii* microbial cells covered with magnetic Fe_3O_4 nanoparticles. The addition of an external magnetic field increased the potential of cell collection for reuse and assured that the cells were evenly distributed in the solution even without mixing. The outcomes demonstrated that *P. delafieldii*'s desulfurization efficiency was unaffected and that the cells could be recycled multiple times.

6. What is Green Synthesis?

Green synthesis is a method for creating nanomaterials that is clean, safe, economical, and ecologically beneficial. Microorganisms like bacteria, yeast, fungi, algae

species, and some plants are used as substrates in the green synthesis of nanomaterials (Huston et al, 2021).

The green synthesis method offers straightforward, affordable, and reproducible methods for producing ecologically friendly metallic nanoparticles.

7. Why Green synthesized?

In medical research, the use of antibiotics is used to control infections, but due to the advent of Multiple Drug Resistance (MDR) bacteria, it is extremely challenging to treat individuals who have MDR harmful bacterial infections (Duin and Paterson, 2016). An interesting alternative maybe found in the green synthesis of nanoparticles (Bahrulolum et al, 2021). For the synthesis of nanoparticle, researcher have tried different methods like physical and chemical methods. These methods were time consuming, expensive, electrical equipment. Synthesis of nanoparticle is important because the nanoparticles made by green technology are far superior to those manufactured with physical and chemical methods based on various aspects produced using physical and chemical processes. Green methods, for instance, produce ecologically friendly products and by products while using less energy and costlier chemicals.

III. VARIOUS TECHNIQUES HAVE BEEN UTILIZED TO CREATE METAL-BASED NANOPARTICLES

- 1. Thermolysis Methods:** In order to prevent surface oxidation of the nanoparticles, this method relies on the dissociation of organometallic precursors in organic solvents at temperatures typically higher than 100 °C under inert atmosphere. As a drawback of this approach, reactions are challenging to apply to large-scale synthesis because of their exothermic and extremely diluted circumstances. The production of silver nanoparticles (AgNPs) without the use of organic solvents can also be accomplished utilizing various techniques, such as controlled thermolysis of silver alkyl carboxylates. The ability to use regulated thermolysis in commercial large-scale synthesis at a very cheap cost is a benefit of this approach (Iravani et al, 2014).
- 2. Chemical Reduction Methods:** In these procedures, a metal precursor that has been dissolved in a solvent is combined with an appropriate reducing agent and a surfactant in a batch reactor that is constantly stirring while being enclosed in an inert gas. This method of producing metastable metal nanoparticles appears promising. The options for the reducing agents are numerous, but it may depend on the particular redox thermodynamics (Crisan et al, 2022). Additionally, the majority of the time, the pH of the solution has a significant impact on the activity of reducing agents. For instance, the precursor copper acetate is dissolved in swirling deionized water to create copper nanoparticles (CuNPs). After adding the reducing agent hydrazine to the solution, the nanoparticles start to form.
- 3. Biochemical Methods:** Plants, algae, yeasts, fungus, bacteria, and even viruses have lately been employed in conjunction with chemical reagents in these approaches. The

growth process uses enzymatic or nonenzymatic reduction activities and can take place inside or outside of cells. According to the particular host cells and process conditions, bacteria or fungus could produce gold and silver nanoparticles in a variety of shapes (cubes, triangles, spheres, plates, or wires). Although these techniques are mentioned in multiple patents, optimizing the biosynthesis process is still a challenge (Lopez et al, 2020).

- 4. Electrochemical Method:** In the synthesis of size-or shape-selective, very pure metal nanoparticles, electrochemical approaches have shown certain significant advantages over chemical methods. Anodically dissolving a metal sheet creates an intermediate metal salt, which is then reduced at the cathode to create metallic particles stabilized by ammonium salts. Bimetallic Cd-Ag nano alloys have been reported to be created by sequentially electrode positing two distinct cations on a carbon electrode, according to certain publications. Other authors described the direct electro reduction of bulk gold ions to produce AuNPs, using polyvinylpyrrolidone (PVP) to promote the creation of gold nano particles and prevent metal deposition on the cathode (Nam and Luong, 2019).
- 5. Wave-Assisted Chemical Methods:** Sono chemical processes use an ultrasonic source to create cavitation in a solution comprising a metal precursor, a reducing agent, and a stabilizer (surfactant). During radiolytic procedures, a metal precursor combined with the proper reducing agent is exposed to electromagnetic or particle irradiation, including an accelerated electron beam, gamma rays, X-rays, and UV rays. AgNPs can be created by reducing AgNO_3 with a strong reducing agent, like sodium borohydride, in the presence of ultrasonic waves (Suslick, 1990). Microwave aided synthesis has gained popularity as a quick and efficient process in recent years. This is true because less harmful substances, like chitosan and polymers, can be used in place of the stabilizer and complexing agent. Additionally, this technique may perform chemical transformations in a matter of minutes. AgNPs, for instance, can also be made by complexing PVP with Ag^+ ion and reducing it with N, N-dimethylformamide.
- 6. Cementation Methods:** When a very electropositive metal A (sacrificial element) is left in contact with a solution containing ions of a less electropositive metal B, the following spontaneous reaction is thermodynamically permitted, and metal B separates in elemental form as $\text{A} + n/m \text{Bm}^+ = \text{An}^{++n} / m \text{B}$.

This reaction, which is frequently used in industry to purify solutions in hydrometallurgy, can be utilized to decrease cations to obtain metal nanoparticles or aggregates with a fairly straight forward and inexpensive technique (Singh and Satija, 2022). The two main drawbacks of this approach are its inability to control nanoparticle aggregation and the cemented metal phase B's tendency to attach to surface element A. These issues can be avoided by mechanical damping combined with a customized hydrodynamic control. For instance, copper can be reduced from a copper nitrate salt in the presence of iron, which can lead to the development of copper nanoparticles (CuNPs).

- 7. Biological Methods:** Metal-based nanoparticles are created using biological techniques that take advantage of the defense systems found in particular species (against high concentrations of metal ions). These techniques can be extracellular (like bio absorption,

biomineralization, complexation, or precipitation) or intracellular (like bioaccumulation. Since fungi are more resistant to the flow pressure and agitation of the bioreactors than bacteria are, using them to produce metal-based nanoparticles has advantages for industrial scale manufacturing. However, in recent years, the majority of studies have emphasized using plant extracts since, in addition to the benefits listed above, doing so makes it easier to treat samples, scale up production, and collect the desired output (Shah et al, 2015).

- 8. Bio-Synthesis by Bacterial Strains:** Fe (III)-reducing bacteria like *Geobacter* sp., *Magnetospirillum magnetotacticum*, and others can be used to bio-remediate toxic metals like Fe (III) through reduction, in which iron is actively taken up by the cell and re-oxidized to hydrous oxide (low density) to Fe (III) oxide (ferrihydrite). In the final phase, the Fe (III) ions are reduced, and the magnetosome vesicles undergo dehydration to create magnetite. The generated nanoparticles exhibit the qualities listed below, among others (Pacioni et al, 2015): high purity, few crystalline flaws, small size, mono-dispersive, etc. Antibacterial medicines that work against gram positive or negative bacteria have been created by MDR (multi-drug resistant) microorganisms. In contrast to gram-positive bacteria, which have a thick coating of cell wall and exhibit greater resistance to antibacterial treatments, gram-negative bacteria have a very thin layer of peptide glycan that makes them vulnerable to the action of nanoparticles. Accordingly, there is a chance that the gold nanoparticles will also be able to function against gram-positive bacteria (Gogineni et al, 2011).
- 9. Biological Synthesis of Nanoparticles:** Since the beginning of life on Earth, biological organisms and inorganic materials have been in constant communication with one another. This constant contact allowed life to exist on this planet with a well-organized mineral deposit. Numerous bacteria can create inorganic nanoparticles via extracellular or intracellular pathways, according to studies. The creation of different nanoparticles using biological processes is covered in this section, along with the categories of oxide nanoparticles made up of magnetic and nonmagnetic oxide nanoparticles, sulphide nanoparticles, and other ad hoc nanoparticles, such as gold, silver, alloy and other metal nanoparticles are also covered.

Table1: Biological Activity of Metal Nanoparticles Synthesized From Bacterial Strains

Bacteria	Product	Size (nm)	Shape	Biological activity	References
<i>Sargassum wightii</i>	Au	8–12	planar	Anti-oxidant	Singaravelu et al., 2007
<i>Rhodococcus sp.</i>	Au	5–15	spherical	Anti-microbial	Ahmad et al., 2004
<i>Shewanella oneidensis</i>	Au	12±5	spherical	Anti-bacterial	Suresh et al., 2011
<i>Plectonema boryanum</i>	Au	25–100	cubic	Anti-microbial	Lengke et al., 2006
<i>Plectonema boryanum</i>	Au	10–6	octahedral	Anti-microbial	Lengke et al., 2006
<i>Escherichia coli</i>	Au	20–30	Triangles, hexagons	Anti-cancer	Mazdeh et al., 2014
<i>Yarrowia lipolytica</i>	Au	15	Triangles	Anti-fungal	Agnihotri et al., 2009
<i>Rhodopseudomonas capsulate</i>	Au	10–20	Spherical	Anti-microbial	He et al., 2007
<i>Brevibacterium casei</i>	Au Ag	10–50	Spherical	Anti-microbial	Kalishwaralal et al., 2010
<i>Trichoderma viride</i>	Ag	5–40	Spherical	Anti-oxidant	Fayez et al., 2010
<i>Phaenerochaete chrysosporium</i>	Ag	50–200	Pyramidal	Anti-fungal	Vigneshwaran et al., 2006
<i>Corynebacterium glutamicum</i>	Ag	5–50	Irregular	Anti-microbial	Krishnamurthy et al., 2010

8. Gold Nanoparticles: Gold nanoparticles (AuNPs) have attracted interest in biotechnology due to their distinctive optical and electrical properties, high chemical and thermolability, good biocompatibility, and potential applications in a variety of life sciences-related applications, such as biosensing, bioimaging, and drug delivery for cancer diagnosis and therapy (Kumar et al., 2013). The required functionalization of nanoparticles is very possible and exact thanks to their predictable and dependable surface modification chemistry, typically by gold-thiol binding. This method has been used to attach a range of medicinal chemicals, such as anti-cancer medications, bacterial agents, and different oligonucleotides for gene therapy (Zumaya et al., 2022). Microorganisms including bacteria, fungus, and algae have the ability to create AuNPs. For instance, Koul et al., 2021 used the mesophilic bacteria *Shewanella* algae with H₂ as the electron donor to produce microbial production of gold nanoparticles. He et al. (2007) incubated *R. capsulata* biomass along with an aqueous chloroauric acid (HAuCl₄) solution. The pH of the solution played a significant role in both of these studies in regulating the location and morphology of biogenic gold deposition. These observations concur with those made by Klaus et al, 1999), who found that changes in incubation conditions affect particle size. The utilization of gold nano particles in numerous applications, such as the direct electrochemistry of proteins, is noteworthy (Du et al, 2007). Kalabegishvili et al. (2012) examined the creation of gold nanoparticles using two distinct strains of *Arthrobacter* sp. 61 Band *Arthrobacter globiformis* 151B, which were obtained from basal trocks in Georgia. *Pseudomonas putida* DSM291, *Bacillus subtilis* DSM10, and *Pseudomonas stutzeri* NCIMB134 20 were reported to produce intracellular gold by Gericke and Pinches, 2006. *Rhodospseudomonas capsulata* was shown by He et al. (2007) to be able to produce gold particles extracellularly. The generated gold nanoparticles are soluble and stable. The extracellular manufacture of gold nanoparticles in the study by Malarkodi et al. (2013) is accomplished by a simple biological process using *Klebsiella pneumoniae* as the reducing agent.

Table 2: Biological Activity of Gold Nanoparticles Synthesized From Bacterial Strain

Microorganism	Size(nm)	Shape	Biological activity	Reference
<i>Brevibacterium casei</i>	10–50	Spherical	Antimicrobial	Kalishwaralal et al, 2010
<i>Escherichia coli</i>	20–30	Triangle hexagon	Anticancer	Gericke and Pinches, 2006
<i>Klebsiella pneumoniae</i>	5–32	Spherical	Antibacterial	Malarkodi et al, 2013
<i>Rhodococcus sp.</i>	5–15	Spherical	Antimicrobial	Ahmad et al, 2003
<i>Rhodospseudomonas capsulate</i>	10–20	Spherical	Antimicrobial	He et al, 2007
<i>Shewanella oneidensis</i>	12–17	Spherical	Antibacterial	Suresh et al, 2011

9. Silver Nanoparticles: Microorganisms produce silver nanoparticles as a result of their defense mechanism. The bacterium uses its cellular machinery as a defense mechanism to change the reactive silver ions into stable silver atoms. It is now understood that alkaline circumstances promote the synthesis of more nanoparticles than do acidic settings (Saklani et al, 2012). First, different Ag⁺ complexes are broken down to metallic silver atoms (Ag⁰). Ag⁰ then gathers into oligomeric clusters as a result (Sharma et al, 2009). Colloidal AgNPs are eventually formed from these clusters (El-Nour et al, 2010). It has been shown that the low molecular weight peptide glutathione (GSH), proteins like metallothioneins and phytochelatins, and enzymes like oxidoreductases, NADH-dependent reductases, nitro reductases, NADH-dependent nitrate reductases (NRs), and cysteine desulfhydrases all play a role in the formation of nanocrystals in yeast, bacteria, and fungi. The majority of the silver nanoparticles produced by these bacteria are discovered to be spherical particles, with the exception of some that are found to be asymmetrical (Mukherjee et al, 2001b; Ahmad et al, 2004; Fayaz et al, 2010). In one of the initial investigations into this technique, Slawson et al, 1992 discovered that *Pseudomonas stutzeri* AG259, a silver-resistant bacterial strain obtained from silver mines, collected AgNPs in the periplasm. Importantly, the particle size was found to be between 35 and 46 nm (Iravani et al, 2014). Klaus et al. (1999) group described the difference in particle size to variations in cell growth and metal incubation conditions. According to Parikh et al, 2008, *Morganella* sp. RP-42 developed extracellular crystalline AgNPs measuring 205 nm when treated to silver nitrate (AgNO₃). In *Morganella* sp, a silver-resistant species, three gene homologues (silE, silP, and silS) were found. The silE homologue from *Morganella* sp. shared 99% of its nucleotide sequence with the gene previously identified as silE, which codes for a protein that binds silver in the periplasm (Parikh et al, 2008). This is the only study to explain the molecular basis of bacteria's resistance to silver, which may be related to a synthesis mechanism. In a different study, Nair and Pradeep, 2002 exposed common *Lactobacillus* bacteria found in buttermilk to high metal ion concentrations, which led to the formation of tiny crystals of gold, silver, and gold-silver alloy with clearly defined shape. Amazingly, the cells maintained their viability even after crystal formation when the bacteria created them intracellularly (Nair and Pradeep, 2002). Notably, AgNP production has been seen in cyanobacteria as well. For instance, *Plectonemaboryanum* UTEX485, a filamentous cyanobacterium, has been used to successfully produce AgNPs (Lengke et al, 2007). The authors suggested that nitrate metabolism at 25 °C and/or organics released from dead cyanobacteria at 25 ° to 100 °C could be the methods through which AgNPs are produced by cyanobacteria. AgNPs were produced by fungi *Verticillium*, *Fusarium oxysporum*, or *Aspergillus flavus* in the form of a film, in solution, or accumulating on their cell surfaces (Mukherjee et al, 2001b; Senapati et al, 2004; Bhainsa and D'Souza, 2006; Bakshi et al, 2017; Jain et al, 2011). Using the fungus *Verticillium*, Mukherjee et al, 2001b investigated the creation of intracellular AgNPs. The scientists found that when the fungal biomass is exposed to aqueous Ag⁺ ions, the metal ions are reduced intracellularly and 25 nm AgNPs are produced. Bhainsa and D'Souza, 2006 reported that the filamentous fungus *Aspergillus fumigatus* was used in the extracellular production of AgNPs, and that the process was quick.

Table 3: Biological activity of silver nanoparticles synthesized from bacterial Strain

Microorganism	Size (nm)	Shape	Biological activity	Reference
<i>Bacillus cereus</i>	4–5	Spherical	Anti-bacterial	Babu and Gunasekaran, 2009
<i>Brevibacterium casei</i>	10–50	Spherical	Anti - microbial	Kalishwaralal et al., 2010
<i>Corynebacterium glutamicum</i>	5–50	Irregular	Anti-microbial	Gurunathan, 2009
<i>Ureibacillus thermosphaericus</i>	50–70	Spherical	Anti-microbial	Juibari et al., 2011
<i>Pseudomonas stutzeri</i>	200	Spherical	Anti-microbial	Klaus et al., 1999

10. Cadmium Nanoparticles: Over the past 50 years, researchers have studied the health dangers that cadmium poisoning poses. Cadmium causes oxidative stress at the cellular level by depleting natural antioxidants like glutathione. It is also linked to mitochondrial damage, the activation of apoptosis, and disruption of intracellular calcium signaling. Macro-Raman spectrum of silver nanoparticles drop-cast on Si (100) single crystals notwithstanding the considerable studies on cadmium toxicity. Regarding its method of action, intracellular harm, and environmental exposure, there is still a lot of ground to cover in Nanoparticles Synthesized by Microorganisms. CdSe was created by Cui et al., (2009) using the yeast strain *Saccharomyces cerevisiae*. The anaerobic bacterium *Veillonellaa typica* created selenide (Se [II]) from selenite (Se [IV]), and Pearce et al. (2008) added CdCl₂O₈ to create CdSe nanoparticles. Due to its toxicity to bacteria, cadmium was introduced for CdSe production after microbial selenide creation in the last two investigations (Pearce et al, 2008; Cui et al, 2009). As a result, they created CdSe by two-vessel methods that involved reducing selenite to selenide and then creating CdSe from selenide and cadmium ion. In contrast, a one-vessel process in which the fungus generates CdSe when selenite and cadmium ions are present was only reported by Kumar et al, 2007. This method may be more economically efficient due to the fact that it requires fewer reaction vessels to operate. Ayano et al, 2014 discovered CdSe synthesis in *Pseudomonas* sp. RB. When grown in the same medium as the enrichment culture, this strain accumulated nanoparticles (10–20 nm) made up of selenium and cadmium inside and on the cells, as shown by transmission electron microscopy and Energy Dispersive Spectroscopy (EDS). The isolation of a selenite-reducing and cadmium-resistant bacteria is described in this article for the first time (Ayano et al, 2014). Cadmium telluride (CdTe), a substantial group II-VI semiconductor material with a large exciton Bohr radius (7.3 nm) and a tiny bulk band gap of 1.5 eV, has demonstrated tremendous potential for LED (energy), FRET (electronics), and biological applications due to its size-dependent characteristics. These nanoparticles are investigated in live cell bio-imaging because they outperform organic dyes in terms of photostability, narrow emission, and quantum yield (Svechkarev and Mohs, 2019). *Fusarium oxysporum* is a fungus that Syed and Ahmad,

2013 use to create extremely fluorescent extracellular CdTe (quantum dot) nanoparticles. The procedure enables bottom-up, one- step nanoparticle production by using highly diluted Cd and Te precursors. Different methods, including Selected Area Electron Diffraction (SAED) and X Ray – Diffraction (XRD), were used to characterize them, confirming the crystalline nature of the bio synthesized nanoparticles. Against both Gram-positive and Gram-negative bacteria, the se nanoparticles demonstrated antibacterial action. This study shows that using a fungus-based strategy to synthesize nanomaterials offers a fresh, logical, and environmentally benign synthesis protocol. According to Syed and Ahmad, 2013 this is the first instance of a fungal-mediated method for the manufacture of Cd Te quantum dots.

11. Oxide Nanoparticles: Over the past ten years, there has been a sharp increase in the industrial use of metallic oxide nanoparticles in a wide range of applications. These applications use silicon, titanium, iron, and other metallic oxide nanoparticles, increasing the exposure of humans and other species to these nanoparticles in the workplace and other environments (Lai et al, 2008). However, due to the lack of regulatory oversight of their environmental impact, the health impacts of metallic oxide nanoparticle exposure on humans and other species have not been thoroughly studied (Lai et al, 2008). Li et al, 2011 reviewed the biogenesis of oxide nanoparticles in this section. The majority of instances of biological systems that produce magnetic oxide nanoparticles and nonmagnetic oxide nanoparticles using magneto tactic bacteria.

12. Zinc Oxide: Zinc oxide (ZnO) NPs are a wide band gap semiconductor with special optical and electrical properties that have made them increasingly useful in biosensors, nanoelectronics, and solar cells. Because of their transparency and capacity to reflect, scatter, and absorb UV radiation, these NPs are also utilized as food additives and in the cosmetic and sunscreen industries. The use of zinc oxide NPs in future biological applications, such as antibacterial agents, drug delivery systems, and bioimaging probes, is also being studied (Jayaseelan et al, 2012). It has been reported on a low-cost and straight forward method for producing zinc oxide nanoparticles utilizing the repeatable bacterium *Aeromonas hydrophila*. The crystalline nature of nanoparticles was established by X-ray diffraction (XRD). Atomic force microscopy (AFM) revealed that the nanoparticles were created by Microorganisms and their morphology was spherical and oval with an average size of 57.72 nm. With comparable good diffusion and minimal inhibitory concentration, the antibacterial and antifungal activities came to a stop. According to Jayaseelan et al. (2012), ZnO NPs (25 g/mL) showed the greatest zone of inhibition against *Pseudomonas aeruginosa* (*22 1.8 mm) and *Aspergillus flavus* (*19 1.0mm).

Table 4: Biological Activity of Zinc Nanoparticle Synthesized from Bacterial Strain

Microorganism	Size	Shape	Biological Activity	Reference
<i>Serratia nematodiphila</i>	1.05µm	Rod shaped	Antimicrobial	Bajpai et al, 2012
<i>Fucus vesiculosus</i>	2.5cm	Disc shaped	Antibacterial	Hamouda et al, 2023
<i>Pseudomonas aeruginosa</i>	0.51.0µm	Rod shaped	Antibacterial	Salomoni et al., 2017
<i>Lactobacillus plantarum</i>	0.91.2µm	Rod shaped	Antifungal	Yusof et al., 2020

13. Copper Nanoparticle: Copper precursor is easily available in the marker, as well as it is cheap as compare to silver or gold precursors. Copper nanoparticles are having good thermal properties, which can be utilized in lubricants for heat dissipation. Copper nanoparticles or having remarkable trin biological properties, low hardness leads to reduction in friction, and low elastic modulus reduces the wear.

Table 5: Biological Activity of Copper Nanoparticle Synthesized from Bacterial Strain

Microorganism	Size (nm)	Shape	Biological Activity	Reference
<i>Pseudomonas fluorescens</i>	2.0-2.5µm	Rod shaped	Anti-fungal	Castaldi et al., 2021
<i>Bacillus cereus</i>	9×2 microns	Rod shaped	Anti-fungal	Ingle and Rai, 2017
<i>Streptomyces sp.</i>	0.5-2.0µm	Spherical shaped	Anti-bacterial	Liu et al., 2019
<i>Stenotrophomonas sp.</i>	0.4-0.7µm	Rod shaped	Anti-microbial	Talebian et al., 2023

14. Cerium Oxide: Nanoparticles researchers in the fields of physics, chemistry, biology, and materials science have been particularly interested in cerium since it is the first element in the lanthanide group to have four free electrons. Cerium dioxide, out of all the Cerium minerals, has drawn the most interest in the worldwide nanotechnology industry because of its practical uses in catalysts, fuel cells, and fuel additives. For usage in manufacturing and pharmaceuticals, a number of minerals containing the Ce-carbonate, -phosphate, -silicate, and-(hydr)oxide ions have historically been mined and processed. Cerium nanoparticles' potent antioxidant properties have a wide range of biomedical applications for them. According to Dhall and Self, 2018, industrial uses for this substance include polishing agents, ultraviolet-absorbing compounds for sunscreen, solid electrolytes for solid oxide fuel cells, fuel additives to accelerate combustion, and automotive exhaust catalysts. CeONPs have also been utilized to treat cancer,

inflammation, and to shield cells from radiation (Kaliberov and Buchsbaum, 2012). The physicochemical characteristics of CeO₂ nanoparticles in low temperature geochemical environments have a significant impact on their environmental fate. While it is obvious that aquatic and terrestrial creatures have been exposed to CeO₂NPs, there is room for improvement in the analytical method for detecting/ quantifying these nanoparticles in various environmental media. This could have severe influence on human and ecosystem health. It's interesting to note that conflicting data exist about the toxicological effects of CeO₂ nanoparticles, which can either operate as an antioxidant or a factor in the generation of reactive oxygen species (Nita and Grzybowski, 2016). This presents a problem for future environmental risk assessments and legislation governing the use of CeO₂ nanoparticles. *Gloriosa superba* L. leaf extract is used by Arumugam et al., (2015) to successfully synthesize CeO₂ nanoparticles. The cubic structure of the synthesized nanoparticles was preserved, and X-ray diffraction analyses supported this claim. XPS investigations verified the elements' oxidation states (C [1s], O [1s], and Ce [3d]). According to antibacterial investigations conducted on a variety of bacterial strains, Gram-positive bacteria were more vulnerable to NPs than Gram-negative bacteria. Due to the synthetic NPs' uneven ridges and oxygen flaws, CeO₂ NPs' toxicological behavior was discovered. The fungus *Curvularia lunata* has been successfully used to create CeO₂nanoparticles (Munusamy et al, 2014). Studies on the SAED patterns, Micro Raman spectra, and XRD patterns point to the creation of a cubic CeO₂ NPs fluorite structure. The spherical form was visible in the TEM pictures, with an average size of 5nm. The antibacterial activity of synthesized CeO₂ NPs was studied. The analysis revealed that 100 g of CeO₂ NPs had the most notable antibacterial impact because the bacterial cell membrane was bound by high electrostatic forces, which prevented bacterial growth.

15. Silica Dioxide: In the natural world, quartz and beaches are both made of silica. Silica is a poor conductor of heat and electrons, unlike metals like gold and iron. Despite these drawbacks, silicon oxide nanoparticles serve as the structural foundation of silica aerogels. Silica aerogels are made of silica nanoparticles that are dotted with air-filled nanopores. Nano aerogels are among the greatest thermal insulators in existence because of these characteristics. By attaching molecules to a nanoparticle that can also connect to another surface, such a cotton fiber, silica nanoparticles can also be functionalized. Nanoscale pores adorn another variety of silica nanoparticles. In order to slowly release therapeutic molecules in a diseased area of the body, such as close to a cancer tumor, researchers are developing drug delivery techniques (Argyo et al, 2014). Due to the rising demand for innovative materials with superior thermal, mechanical, physical, and chemical properties, the use of silica nanoparticles as fillers in the creation of nanocomposite of polymers has received significant attention. *Acinetobacter* sp. was shown by Singh et al, 2008 to produce silicon/ silica nanoparticle composites. It is demonstrated that when the bacteria is exposed to K₂SiF₆ precursor at ambient circumstances in silicon/ silica nanocomposite forms. This bacterium is thought to release reductases and oxidizing enzymes that result in the creation of Si/SiO₂ nanocomposite materials. The ability of bacteria to produce silica nanoparticles illustrates the organism's adaptability, and the production of elemental silicon using this ecologically acceptable method broadens the potential applications of microorganism-based nanomaterial synthesis.

Table 6: Biological activities of silica nanoparticles synthesized from bacterial strain

Microorganism	Type Of Nanoparticle Synthesized	Size (nm)	Shape	Biological Activities	Reference
<i>Curvularia lunata</i>	CeO ₂	5	Spherical	Antimicrobial	Singh et al., 2008
<i>Fusarium oxysporum</i>	TiO ₂	6–13	Spherical	Anti-fungal	Gaber et al., 2023
<i>Fusarium oxysporum</i>	BaTiO ₃	4–5	Spherical	Anti-fungal	Rai et al., 2020
<i>Fusarium oxysporum</i>	ZrO ₂	3–11	Spherical	Anti-fungal	Bansal et al., 2004
<i>Lactobacillus sp.</i>	BaTiO ₃	20–80	Tetragonal	Anti-bacterial	Jha and Prasad, 2010
<i>Lactobacillus sp.</i>	TiO ₂	8–35	Spherical	Antibacterial	Jha et al., 2009
<i>Saccharomyces cerevisiae</i>	Sb ₂ O ₃	2–10	Spherical	Anti-oxidant	Jha et al, 2009

IV. CONCLUSION

Engineering and biomedical sciences both make substantial use of metal-based nanoparticles. The present study, updated the key characteristics of AgNPs, CuONPs, AuNPs, and ZnONPs, which are frequently used in pharmaceutical and medical applications, such as antibacterial, antifungal, antiviral, anti-amoebic, anticancer, and anti-angiogenic medicines. Due to their well-documented anti-bacterial effect against Gram-positive and Gram-negative bacteria, these particles have been proposed as an alternative to traditional antibiotics to tackle bacterial resistance. With the benefit of being effective against bacteria that have already evolved antibiotic resistance, nanoparticles use different methods of action than conventional therapies. They also target several biomolecules, which hinders the emergence of resistant strains. The physicochemical characteristics, dosage, and mode of administration of metal nanoparticles, which control their pharmacokinetics and pharmacodynamics, are responsible for any potential risk of toxicological effects in humans. In the early stages of pharmaceutical development, a thorough physicochemical characterization is advised because these particles can have a limited therapeutic window. Additionally, for the success of pharmaceutical development, understanding their in vivo behavior throughout preclinical and clinical trials is a crucial source of information, preventing failures in the last stages of research and development.

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