Environmental and Microbial Biotechnology

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Microbial Processes for Synthesizing Nanomaterials

Springer

Environmental and Microbial Biotechnology

Series Editor

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Innovative and novel advances in microbial biotechnology are providing great understandings in to the machineries of nature, presenting fascinating prospects to apply principles of biology to different arenas of science. Sustainable elucidations are emerging to address the concerns on improving crop productivity through microbes, depleting natural resources, environmental pollution, microbial degradation of pollutants, nanomaterials, nanotoxicity & safety issues, safety of food & agricultural products etc. Simultaneously, there is an increasing demand for natural bio-products of therapeutic and industrial significance (in the areas of healthcare, environmental remediation, microbial biotechnology). Growing awareness and an increased attention on environmental issues such as climate change, energy use, and loss of non-renewable resources have carried out a superior quality for research that provides potential solutions to these problems. Emerging microbiome approaches potentially can significantly increase agriculture productivity & human healthcare and henceforth can contribute to meet several sustainable development goals.

The main objectives have provided an impetus for research on plants and microorganisms that produce novel bio-products with variable properties and understanding their mechanisms of action at cellular and molecular level. Hence, research activities of the environmental and microbial Biotechnology are comprehensively focused up on major sectors viz., bioresources, biorefining, bioremediation of organic and inorganic pollutants, environmental risk analysis of microorganisms, environmental assessment using microbiological indicators, enzymes for environment, food & industrial applications, nanomaterials & nanotoxicity, sustainable ecobiotechnology, biofertilizer, biocontrol agents for agriculture improvement and natural products for healthcare applications.

This book series is a state-of-the-art for a wide range of scientists, researchers, students, policy makers and academician involve in understanding and implementing the knowledge on environmental and microbial biotechnology to develop biologics for proper health care to continue life in smooth and sustainable strategy without any adverse effect.

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Foreword

Nanotechnology is a multidisciplinary field that evolved within the past few decades and plays a substantial role in the environment, industry, agriculture, and pharmacology. The process of creating nanoparticles is called "nanoparticle synthesis," and nanomaterials are being synthesized by different approaches—chemical vapor deposition, thermal decomposition, hydrothermal, solvothermal, pulsed laser ablation, templating, combustion, microwave, gas phase, sol-gel, etc. Coming to biomedical applications, the synthesis of nanomaterials by using chemical approaches has serious negative impacts; certain chemicals that are used for the synthesis of nanomaterials are carcinogenic and have potential genetic and cellular toxicities. Therefore, it is greatly warranted to search for emerging and eco-friendly methods that produce stable nanoparticles with an effective shape and size.

Centering around the above issue, this volume was designed to address the latest issues on microbial processes for synthesizing nanomaterials. The two sections of this edited volume are (1) Microbially synthesized nanoparticles, and (2) Biomedical and biotechnological applications. This volume was edited by four subject experts from Ecuador, Portugal, and India. There are 16 chapters contributed by 70 researchers from seven different countries (i.e., India, Nigeria, Costa Rica, France, China, Spain, and Mexico). Therefore, this volume has an immense global appeal in terms of editors and contributors. There is comprehensive revision of literature on diverse topics, such as synthesis of nanoparticles in microbial cells, biofilms, role of enzymes in the microbial synthesis of nanoparticles, and applications of microbially synthesized nanoparticles in diverse environment (i.e.,

medical, agriculture, and food science). I truly believe that this volume will have a wider readership and will serve researchers, environmental policy makers, industrialists, technicians, and students for a considerable length of time .

Universidad Técnica de Manabí Santiago Quiroz Fernández
Portoviejo, Ecuador
7 March 2023

Preface

Microbial synthesis of nanomaterials/nanoparticles is a novel approach where microbial processes have opened up new opportunities to explore novel applications, i.e., biosynthesis of metal nanomaterials in aqueous phase under gentle and environmentally benign conditions; thus this area is ahead of traditional chemical and physical methods. A microbial cell is an efficient bioreactor in the synthesis of different types of nanoparticles; therefore, by this means, it is feasible to produce biocompatible nanostructures with exotic physicochemical and optoelectronic properties. Hypothetically, microorganisms live in diverse environments, and they often interact with minerals and heavy metals in different environmental niches; and these interactions enable them to develop unique adaptations (such as cellular, physiological, biochemical, and molecular) by which microbial cells can trap, internalize, alter, and precipitate minerals and metals in the form of nanostructures. Microorganisms exhibit high metal tolerance in areas where there is metal pollution, and microorganisms can survive in such hostile environments by changing the toxic form of metals to nontoxic forms. The synthesis of bioactive nanomaterials is a characteristic feature of rhizosphere microbiome; such bioactive nanomaterials can inhibit plant pathogens. Microorganisms that live in the sludge, effluents, and mining area are capable of recovering metals from the environment and with subsequent conversion into exotic nanostructures. This is why microorganisms of different environmental niches (e.g., thermophilic, psychrophilic, acidophilic, halophilic, barophilic) are being under consideration for their nanobiotechnological applications and are even genetically modified to optimize the production of efficient nanomaterials. Fortunately, recent advancements in several science areas like material science, chemistry, metabolomics, metagenomics, and computational biology resulted in the emergence of multidisciplinary fields to trace out the specific pathways that are responsible for the synthesis of nanomaterials by microorganisms. Microbially synthesized nanoparticles have potential applications in the area of biomedicine (e.g., as antimicrobial agents, anticancer agents, diagnosis and drug delivery systems), agriculture, remediation, biotechnology, etc. Thus, "Microbial Processes for Synthesizing Nanomaterials" is an emerging research area with wide applicability and a sustainable future.

To reflect the title of the book, there are 16 chapters in two sections: (1) Microbially synthesized nanoparticles, and (2) Biomedical and biotechnological applications. With topics ranging from microscale studies to macro, it covers a huge domain of microbiology. The chapters of Section I are related types and applications of microbial nanomaterial synthesis, microbial synthesis of gold nanoparticles, synthesis of fungal-based nanoparticles, synthesis of nanoparticles in biofilms, and the role of microbial enzymes in nanoparticle synthesis. In Section II, there is an emphasis on biomedical uses of TTAHOT and Red Bromide crystals, nanodiagnostics, microbial nanoparticles in drug delivery, microbial nanoparticles as next generation antimicrobials, the role of microbially synthesized nanoparticles in biofilm inhibition, in agriculture and food industries, and biotechnological implications of extracellular vesicles.

Special attention was paid to the selection of chapter contributors for this volume. We invited around 70 subject experts (such as researchers, academicians, and industrialists) with sufficient knowledge about basic and applied microbiology from seven different countries (i.e., India, Nigeria, Costa Rica, France, China, Spain, and Mexico), so that this initiative could have a positive impact on the quality of the volume, as well, and this volume can reach a wider audience. Furthermore, all the listed editors of this volume have sound knowledge in microbiology and its applications. NRM has been working in the area of Environmental Microbiology since 2003, and his research activities were related to soil enzyme activities, microbial remediation of crude oil contaminated soils (lab and field level), bacterial biofilms, characterization of bacterial exopolysaccharides, quorum quenching for biofouling control in membrane bioreactors, etc. JMRD is an expert in Environmental Chemistry/Biotechnology, particularly in areas of bioadsorption, filtration processes, heterogeneous catalysis, nanomaterials, new bioadsorbent materials, and advanced oxidation processes (AOP). MCBSM is an expert in Analytical Chemistry/Applied Chemistry, particularly in the fields of development of sensor platforms with electrochemical transduction for food, pharmaceutical, clinical, and environmental control, emerging polymeric membranes approaches for retention, separation, applied to clinical, bioanalytical, and environmental concerns, and new degradation methods for environmental remediation. She has published over 200 articles, seven book chapters, and three patents, was a supervisor of more than 20 PhD students, and led more than 15 scientific projects. Last but not least, RP is another editor of this volume and is an internationally renowned and highly cited (~12,000 citations) researcher who has published >200 articles, and his main research areas include but are not limited to microbiology, nanotechnology, plant-microbe interaction, and nanobiotechnology. Overall, the book portrays an obvious idea about the evolving modern technologies and directs young minds on the same path. This book has been designed to serve as a kind of information hub about modern microbiology towards cleaner production for the sustainability of the

environment. It will also serve as a ready reference for practicing students and researchers in biotechnology, environmental engineering, chemical engineering, and other allied fields.

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Part II Biomedicinal and Biotechnological Applications

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About the Editors

Naga Raju Maddela received his M.Sc. (1996–1998) and Ph.D. (2012) in Microbiology from Sri Krishnadevaraya University, Anantapuramu, India. During his doctoral program in the area of Environmental Microbiology, he investigated the effects of industrial effluents/insecticides on soil microorganisms and their biological activities and he has been working as a Faculty in Microbiology since 1998, teaching undergraduate and postgraduate students. He received "Prometeo Investigator Fellowship" (2013–2015) from Secretaría de Educación Superior, Ciencia, Tecnología e Innovación (SENESCYT), Ecuador, and "Postdoctoral Fellowship" (2016–2018) from Sun Yat-sen University, China. He also received external funding from "China Postdoctoral Science Foundation" in 2017. He is working in the area of Environmental Biotechnology, participated in 30 national/international conferences, and presented research data in China, Cuba, Ecuador, India, and Singapore. Currently, he is working as a full-time Professor at the Facultad de Ciencias de la Salud, Universidad Técnica de Manabí, Portoviejo, Ecuador. He has published 13 books, 45 chapters, and 70 research papers.

Joan Manuel Rodríguez Díaz received his bachelor's degree in chemical sciences (2003) and M.Sc. in Process Analysis in the Chemical Industry (2007) from Universidad Central de Las Villas, Ph.D. in Chemistry in Analytical Chemistry (2013), as well as two postdoctoral degrees at the Federal University of Pernambuco (2014–2015). Currently, he is working as a Principal Professor II, Principal Investigator III, Coordinator of the master's degree in chemical engineering, and Coordinator of the Laboratory of Chemical and Biotechnological Analysis at the Universidad Técnica de Manabí (Ecuador). Since 2019, he is working as a visiting Professor of the postgraduate Program in Chemical Engineering at the Universidade Federal da Paraíba (Brazil). He is a director of several research projects and collaborator in other projects with universities in Brazil, Portugal, and Cuba. He is tutor of several Ph.D. (8) and M.Sc. students (18), in postgraduate programs at Instituto Politécnico de Leiria (Portugal), Universidad Técnica de Manabí (Ecuador), Universidade Federal de Pernambuco and Universidade Federal da Paraíba (Brazil). He published eight book chapters (Springer) and more than 45 research papers. He is a reviewer of several journals, including *Research on Chemical Intermediates*, and others. He is an expert in Environmental Chemistry, particularly in the areas of bioadsorption, filtration processes, heterogeneous catalysis, nanomaterials, new bioadsorbent materials, and advanced oxidation processes (AOP).

Maria Conceição Branco da Silva Montenegro (1957) is a full professor at the Laboratory of Applied Chemistry, Department of Chemical Sciences, Faculty of Pharmacy at the University of Porto (FFUP), Portugal, in the fields of Analytical Chemistry/Applied Chemistry. She graduated with a bachelor's degree (1980) and Ph.D. (1991) in Pharmacy and Pharmaceutical Chemistry speciality from the University of Porto. She is a senior researcher at LAQV/REQUIMTE, a Portuguese Research Centre for Sustainable Chemistry, where she leads a unit of Sensors and Biosensors. Her main research activities are related to the development of sensor platforms with potentiometric and electrochemical transduction for food, pharmaceutical, clinical,

and environmental control. More recently, she also extended her area of expertise looking for new polymeric membrane approaches for retention, and separation, applied to clinical, bioanalytical, and environmental concerns and new degradation methods for environmental remediation. She has published over 200 articles, seven book chapters, and three patents, was a supervisor of more than 20 PhD students, and led more than 15 scientific projects. She maintains several research collaborations with foreign universities, namely Charles University (Czech Republic), Technical University of Manabi (Ecuador), Federal University of Pernambuco (Brazil), Instituto de Química, Universidade de Campinas (Brazil), and University of Petra (Jordan) collaborating in research projects and in the supervision of students.

Ram Prasad Ph.D. is associated with the Department of Botany, Mahatma Gandhi Central University, Motihari, Bihar, India. His research interest includes applied and environmental microbiology, plant-microbe interactions, sustainable agriculture, and nanobiotechnology. Dr. Prasad has more than 275 publications (total citations 13735 with an h-index 59, i10-index 189) to his credit, including research papers, review articles, and book chapters, seven patents issued or pending, and edited or authored several books. Dr. Prasad has 12 years of teaching experience and has been awarded the Young Scientist Award and Prof. J. S. Datta Munshi Gold Medal by the International Society for Ecological Communications; Fellow of Biotechnology Research society of India; Fellow of Agricultural Technology Development Society, India; Fellow of the Society for Applied Biotechnology; the American Cancer Society UICC International Fellowship for Beginning Investigators, USA; Outstanding Scientist Award in the field of Microbiology; BRICPL Science Investigator Award and Research Excellence Award, etc. He has been serving as editorial board members of journals such as *Current Microbiology, Archives of Microbiology, Nanotechnology for Environmental Engineering*, and *SN Applied Sciences*, including Series editor of Nanotechnology in the Life Sciences, Springer Nature, USA. Previously, Dr. Prasad served as Assistant Professor at Amity University, Uttar Pradesh, India; Visiting

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Part I

Microbially Synthesized Nanoparticles

Microbial Nanomaterial Synthesis: Types and Applications

1

Babafemi Raphael Babaniyi, Olusola David Ogundele, Samuel O. Thompson, and Sesan Abiodun Aransiola

Abstract

The present chapter addresses synthesis of microbial nanomaterial, types, and applications. Nanomaterials can be made by combustion processes or can be purposely synthesized through scientific or engineering innovation to execute specific function. Production of nanomaterials through biogenic enzymatic processes has better quality compared to its counterpart produced via chemical processes. The biosynthesis of nanostructures involves a variety of biomolecules, including secondary metabolites, carbohydrates, and proteins released by different microbes. Extracellular polysaccharides aid the reduction of various metal ions and the stability of metal nanoparticles because proteins in bacterial membranes are crucial for titrating metal ions. Terpenoids and flavonoids, which are organic molecules, are efficient at stabilizing and sealing nanomaterials, which affect their overall composition, size, and form. Additionally, algae species and morphological diversity influence the secretion of nanostructures. Nanomaterials occupy a large surface area per volume ratio due to the arrangement of nanoscale size that contributed to their structures, together with indistinguishable proportions to biomolecules which enhance distinctive properties for numerous usages. Microbiologically produced nanomaterials offer a wide range of potential uses in a variety of industries, including agriculture, coatings, cosmetics, packaging, food, beverages, drug deliveries,

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bioremediation, biomedicine, diagnostics, and electronics production. Actually, scientists have started paying attention to this technology since the resulting nanoparticles displayed unique characteristics such as biocompatibility, a larger range of uses, cost-effective production techniques, and environmental sustainability. Additionally, a variety of natural biological resources, including plants, algae, fungi, actinomycetes, bacteria, viruses, and even secondary microbial metabolites, are utilized to manufacture nanoparticles.

Keywords

Nanomaterial · Synthesis · Biogenic · Bacteria · Polysaccharides

1.1 Introduction to Microbial Nanomaterial Synthesis

Recently, nanomaterial (NM) gained attention in biological, medical, agricultural, and engineering fields because of their flexibility and diverse usage. Nanomaterials occupy a larger surface area per volume ratio due to the arrangement of nanoscale size that contributed to their structures and indistinguishable proportions to biomolecules which enhance distinctive properties for numerous usages (Ghosh et al. 2021). Production of nanomaterial through biogenic enzymatic processes has better quality compared to its counterpart produced via chemical processes. Though, chemical processes produce larger quantities of nanomaterial with a definite shape and size within brief period. Although, the procedure is cumbersome, not cost effective also emit noxious wastes that impact human and the environment (Li et al. 2011b). Biogenic enzymatic method eliminated the utilization of expensive chemicals, exploring the green route is safer and does not require intensive energy. The microbial enzymatic technique is favored with a large number of the microbe's ability to cope in ambient environment of different pressure, temperature, and pH. Nanoparticles produced through this method possess concentrated catalytic responsiveness, higher definite surface area together with well-developed contact within enzyme and metal salt as a result of the microorganisms carrying NM (Li et al. 2011b). Biogenic synthesis of NM has advantages over physical and chemical methods, synthesis via microorganisms enhances reliability, sustainability, and environmentally friendly and safe procedures (Prasad et al. 2016, 2018; Eftekhari et al. 2023). Microorganisms include bacterial, fungal, algal, and yeast cells trap metals within their surroundings thereafter, process them into nanoparticles constituent that could be secreted or stored (Esmail et al. 2022; Ghosh et al. 2021; Prasad 2019a, b; Koch et al. 2023). Also, nanomaterials have been isolated in some viruses. Notably, prevention of aggregation coupled with stabilization enhancement of NM and capping agents are usually emitted in the course of biosynthesis processes (Ghosh et al. 2021). The enzymatic procedures could be in two ways, intracellular and extracellular production with regards to the site where NM is developed. The intracellular processes involve the movement of ions into the microbial cell to form nanomaterials with the action of enzymes while the extracellular production of NM

consists of accumulation of metal ions on the surface of the cells and reducing ions through the action of enzymes.

Application of nanotechnology that employs materials usage within the scope of 1–100 nm (nm) has provided new approaches toward the delivery of drugs along with biosensing. For instance, nanomaterials application during the production of biosensors enhances their sensitivity and achievement through the introduction of many signal transduction strategies (Noah and Ndangili 2022). Molecules of nanomaterial and properties are basically alike proportion of biological units which could effortlessly pass-through barriers of blood tissue (Pastorino et al. 2019; Ahmad et al. 2021). Also, nanocarriers react through biomolecules within surface of cells without interfering with the behavior and biochemical components of the molecule (Gao et al. 2020; Stillman et al. 2020). This provision in interior of the living cell establishes irrefutable clinical benefits and adequate research knowledge. However, the development of unmatched optical components like fluorescence and surface plasmon resonance (SPR) in recent times, is an indication that nanomaterials are gaining more attraction in biomedical utilization (Aminabad et al. 2019; Elahi et al. 2019) to be precise the production of optical-based analytical instrument employed in bioimaging (Chisanga et al. 2019; Kumar et al. 2019; Tanwar et al. 2021) and biosensing (Celiksoy et al. 2020; Noori et al. 2020). With respect to such biomedical procedures, biocompatibility of a metal surface is needed, and consideration should be given to metal nanomaterials produced through biological means, because of their efficient production of metals ions with greater affinity of biocompatibility (Ghosh et al. 2021). The production of nanomaterials majorly depends on green chemistry proceedings in other words, green strategies that embrace 12 principles of green chemistry that promote reduction of environmental pollution (Begum et al. 2022).

In spite of many wonderful research studies in the field of nanotechnology adopting physicochemical methods, so also, the production of plant-based nanoparticles has been researched extensively following the green processes. More so, a good number of researchers have tried to evaluate the bio-secretion and efficient exploitation of underutilize agricultural materials to synthesize nanoparticles (Begum et al. 2022; Prasad 2014). Biological advancement through experimental approaches for the production of nanomaterials is considered a vital landmark in the field of nanotechnology. Owning to the vast affinity of microbes to accumulate and secrete nanomaterial, this current chapter reviewed types of microbial nanomaterial, enumerate their formation processes, applications of synthesized microbial nanomaterial, and factors affecting microbial nanomaterials with special consideration to future studies.

1.2 Microbial Nanomaterials, Types, and Formation

Although specialists did not agree on a clear description, scholars do believe that nanomaterial can be characterized by their extremely small size, measured in nanometers. A nanometer is in a million of millimeter, i.e., 100,000 size smaller

than the diameter of a human hair (Shukla 2020). Materials with just one exterior dimension between 1 and 100 nm are referred to as nanomaterial. According to the criteria provided by the European Commission, at least half of the materials in the number size distribution should have a particle size of 100 nm or less (Willner and Vikesland 2018).

Nanomaterials should have at least one dimension which is less than 100 nm, however, nano-sized materials can exist naturally or artificially made from a number of materials, including minerals such as silver and carbon (Lu et al. 2016). Nanomaterials can be made by combustion processes, occur naturally, or can be purposely synthesized through scientific or engineering innovation to execute specific function. These particles may differ from their mass counterparts in terms of their physicochemical characteristics. The majority of nanoscale materials cannot be seen with bare eyes or with normal laboratory microscope but with the use of special laboratory equipment (Lu et al. 2016).

Engineered nanomaterials are materials generated on a small scale that can exhibit electrical, magnetic, optical, and other properties. Medicine, engineering, science, and other fields stand to benefit greatly from these emerging innovations (Willner and Vikesland 2018). They are of great importance in (1) pharmaceuticals that specifically target biological cells or organs, such as cancerous cells, can be created using nanomaterials, increasing the efficacy of its treatment; (2) ceramics, fabric, cement, and other textile products can also be strengthened while remaining lightweight by the addition of nanomaterials; and (3) removal of pollutants or environmental clean-up to mitigate or neutralize contaminants and many others (Shukla 2020).

Green technologies are becoming more in demand for industrial applications lately. The production of nanoparticles via microbial nanomaterials may be exploited to degrade contaminants in industrial effluent (Lu et al. 2016). Owing to the development of green nanomaterials from microbes and extracts from microorganisms, there are numerous research opportunities toward bioremediation and environmentally friendly cleanup of pollution (Borah et al. 2022; Maddela et al. 2023). Another significant use of microbial nanomaterial is environmental sensing to mitigate pollution (Rizwan et al. 2014).

The time-consuming, expensive, and labor-intensive processes required by conventional systems of pollution sensing are the major disadvantages (Shukla 2020). The specific nature and composition of the pollutant can be hard to determine using conventional sensors. Classical sensors can identify the active compounds of pollutants in biological materials including soil, air, and water at low concentrations up to ppm and ppb (Thota and Ganesh 2016). However, advances in nanotechnology made it possible for easy detection of organic and inorganic compounds, pathogens, and heavy metals could all be detected by nanoparticle sensors even at low concentrations (Zhou et al. 2018; Willner and Vikesland 2018). For the cleanup of pollutants from wastewater, carbon nanomaterial, carbon nanotubes, metals, and metal-oxide nanomaterials have been used. Due to chemical usage and self-agglomeration in the environment, chemical-based nanomaterials may have adverse effects on the environment. Application of microorganisms to create nanomaterials

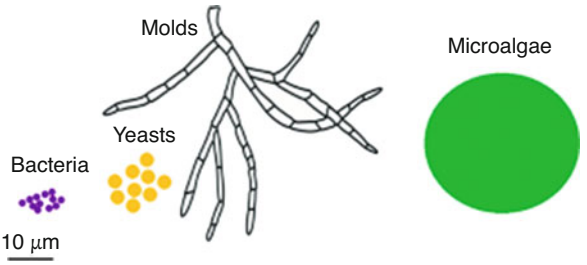

Fig. 1.1 The average size of molds, bacteria, yeasts, and microalgae

makes nanotechnology more environmentally friendly and sustainable (Lu et al. 2016). Hence, a novel and promising approach that could produce metallic nanoparticles by acting as lowering agents for the metal complex salt is the green synthesis of nanomaterials from fungi, bacteria, and plants (Shukla 2020).

The international market for nanomaterials is anticipated to expand at an average annual growth rate of at least 25% from 2017 to 2023. The sustainable development of nanomanufacturing processes is one of the main barriers to the development of the nanomaterials sector on a worldwide scale (Ribeiro et al. 2015). Compared to production methods for bulk materials, typical top-down or bottom-up chemical and physical nanomanufacturing technologies are more energy intensive. Additionally, they frequently have low process yields (containing chemicals and organic solvents) and produce greenhouse gases. Additionally, they frequently need specialized equipment, operative circumstances (such as medium to high vacuum), and highly pure levels of feedstocks (Yuan and Zhang 2013).

The innovation of more environmentally friendly process industries, including those for nanomanufacturing, can be greatly aided by the principles of green chemistry (the innovation, design, and bioprocesses to mitigate or reduce the generation and use of harmful chemicals) (Osherov et al. 2023) and biotechnology, which uses living tissue such as plant, yeasts, bacteria, and mold, with enzymatic secretion of industrial scale products (Yuan and Zhang 2013). A prospective biotechnologically based nanomanufacturing method that offers a "sustainable" substitute to chemical and physical methods of nano secretion is the microbial-mediated synthesis of nanomaterial. Different strains of microbes including yeast, microalgae, molds, and bacteria were considered to facilitate biosynthesis of metallic, nonmetallic, and metal oxide nanomaterials (Ribeiro et al. 2015; Srivastava et al. 2021; Kisimba et al. 2023). Furthermore, several microbes have demonstrated the potential to biosynthesize novel nanomaterials, including organic nanomaterials like bacterial nanocellulose extracellular enzymes nanoparticles and bacterial nascent iron oxide nanoparticles (Fig. 1.1).

A recent study used a fungi species (*Aspergillus tubingensis*) isolated in sediments of rhizospheric samples of *Avicennia officinalis* to successfully remove Zn(II), Pb(II), Ni(II), and Cu(II) from effluent using biologically fabricated monodispersed, ferromagnetic, spherical, and crystalline nanomaterials. In endothermic procedures, the metals were chemically adsorbed onto the nanomaterial surface.

The researchers discovered that the produced nanomaterials have a regenerative potential of up to six adsorption/desorption cycle which can remove up to 85% of the heavy metals from aqueous matrix (Mahanty et al. 2020). *Exopolysaccharides* from *Chlorella vulgaris* were isolated in iron-magnetic nanoparticles in recent research, and they were used as a nontoxic nano mechanism for treatment of wastewater. According to the findings, the nanocomposite successfully eliminated 84% of NH_4^+ and 90% of PO_4^{3-} under ideal condition. The biologically active nanoparticles may serve as photocatalysts for the remediation of textile wastewater and azo dye disintegration (Govarthanan et al. 2020).

Industrial effluents contain significant amounts of heavy metals and azo dyes, which, if directly applied to farmlands without first undergoing remediation, could degrade the agricultural land by adversely affecting its physico-chemical/biological and nutrient characteristics (Cheng et al. 2019). There is a lot of interest in using biologically active metallic nanoparticles for the photoelectrocatalytic destruction of effluent contaminants because of their distinctive biological and physico-chemical properties, high efficiency, and environmental protection (Noman et al. 2020).

1.3 Mechanism of Microbial Nanomaterials Synthesis

Considering the synthesis, characterization, and mechanism of action of nanoparticles by either physical or chemical means, there has been a significant advancement in the field of nanotechnology. Although the latter technologies were more efficient and took less time, the metal nanoparticles and oxides they created had ecotoxicological effects when released into the environment. Microorganisms must "biosynthesize" or "green synthesize" nanoparticles in order to get around these problems (Ghaffar et al. 2016). In recent years, scientists began to pay attention to this technology since the resulting nanoparticles displayed unique characteristics, biocompatibility, a larger range of uses, cost-effective production techniques, and environmental sustainability. Additionally, the creation of nanoparticles through green synthesis is thought to be environmentally benign. Additionally, a variety of natural biological resources, including plants, algae, fungi, actinomycetes, bacteria, viruses, and even microbial secondary metabolites, are utilized in the manufacture of these nanoparticles (Singh et al. 2017).

Green nanoparticles are better than their chemical counterparts due to their organic origin and harmless characteristics. An investigation revealed that polysaccharide of *Arthrospira* sp. was applied to produce nanoparticles of silver in an ecofriendly pattern with higher antibacterial properties against infections caused by *Pseudomonas aeruginosa*. Chelation-based capping with exopolysaccharides was responsible for the proven safety (El-Deeb et al. 2020). This method of shielding against the toxicity of silver nanoparticles was quite successful. Additionally, it is recognized that microbial nanoparticle has diverse usage in the study of clinical microbiology. They can be employed as biosensors, fluid detoxifiers, gene and medication delivery vehicles, and pathogen diagnostics in addition to their significant antibacterial function (Li et al. 2011a).

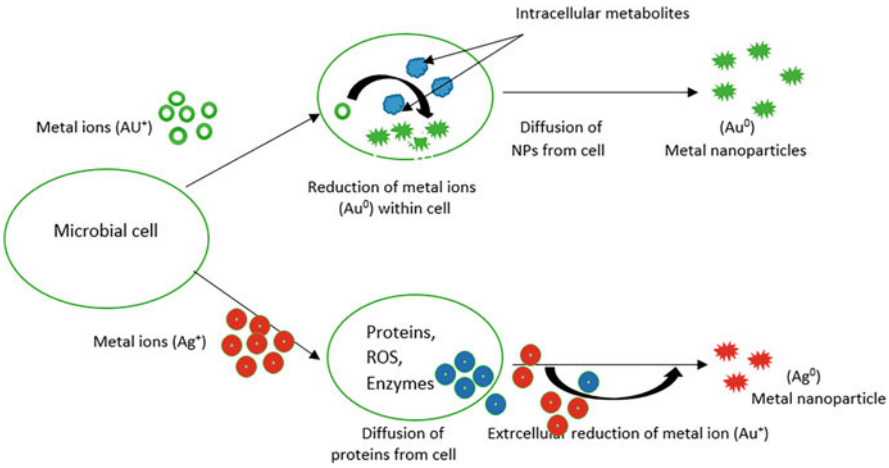

Fig. 1.2 Microbial synthesis of nanomaterials (Purohit et al. 2019)

Numerous microorganisms can produce nanoparticles via various processes. Furthermore, metal ions initially store on the surface or within the microbial cells, which is how nanomaterials are often generated. The trapped metal ions are converted to nanoparticles through enzymatic processes. Microorganisms, in general, have two different effects on the production of minerals. They can alter the solution's makeup to make it more or less supersaturated with regard to a certain phase than it was before. The creation of organic polymers by microbes is a second way they can affect mineral formation. These polymers can affect nucleation by hindering the stability of the earliest mineral seeds (Benzerara et al. 2011).

The precise mechanisms by which *Verticillium* sp. or microalgae secret intracellular gold and silver nanoparticles are yet to be established. However, the fact that nanoparticles developed on the surface of the mycelia and not in the solution supports the theory that the silver or gold ions were initially attracted to the negatively charged wall of bacterial by the enzyme carboxylate groups, triggers contact of electrostatic. Enzymatic oxidation of metal ions in the production of silver or gold nuclei enhances nuclei accumulation and reduction (Fig. 1.2) (Sneha et al. 2010).

Nitrate reductase enzyme promotes synthesis of silver nanomaterial in *B. licheniformis*, according to Kalishwaralal et al. (2008). The enzyme converts silver ions to metallic silver through the activation of nitrate ions. The electron shuttle enzymatic metal reduction process is a potential mechanism that could include the reduction of silver ions. Metal nanoparticle manufacturing depends on nitrate reductase enzymes that are dependent on NADH. Notably, the cofactor NADH and NADH-dependent enzymes, particularly nitrate reductase, are secreted by *B. licheniformis*. This suggests that these enzymes may be involved in the bioreduction of Ag^+ to Ag and subsequent production of silver nanoparticles (Husseiny et al. 2007).

The metallophilic microorganism's evolved proteomic with genetic response to hazardous conditions can be blamed for the creation of great metallic nanomaterials. Ag^{+}, Cd^{2+}, Zn^{2+}, Co^{2+}, Cu^{2+}, $CrO_4{}^{2+}$, Pb^{2+}, Ni^{2+}, and Hg^{2+} are some of heavy metal ions with harmful effects on microbial viability. Microbes created proteomic and genetic answer to rigorously manage metal homeostasis in order to combat these effects (Kim et al. 2018). Various metal transgenes clusters found in microorganisms enable detoxification of cells in a variety of processes, including reductive precipitation, efflux, and complexation. Hence, metallophilic organisms survive in conditions with high levels of free heavy metal ions, including efflux streams from metal manufacturing industries, mine dust rock piles, and natural mineralized regions (Mergeay et al. 2003).

BacMP biomineralization is considered to have a multistep molecular mechanism. The cytoplasmic membrane is encroached in the initial phase, and the vesicle that results functions as the precursor of the BacMP layer. But it is still unknown how the membrane is formed. It is most likely that a particular GTPase mediates the stimulation of the engulfment together with processes of vesicle production for magnetostatic bacteria that are comparable to those of most eukaryotes (Arakaki et al. 2008). The generated vesicles and cytoskeletal filaments were then put together into a ring. The transmembrane iron transporters accumulate ferrous ions into the vesicles during the second phase of BacMP biomineralization. By means of siderophores and transport proteins, external iron is internally absorbed. An oxidation–reduction mechanism rigorously regulates the inner iron. Finally, closely bound BacMP proteins start the formation of magnetite crystals and/or control their shape. Numerous proteins connected to the BacMP membrane may have functional functions in the production of magnetite (Kim et al. 2018).

This would include building up supersaturating iron concentrations, maintaining oxidizing iron and reductive conditions to cause mineralization, or stylishly reducing ferrihydrite and dehydrating it to form magnetite (Arakaki et al. 2008). Perez-Gonzalez et al. (2010) have proposed another potential mechanism for the biosynthesis of magnetites via *Shewanella oneidensis*, which comprises of both active and passive mechanisms. First, active Fe^{2+} synthesis happens when bacteria use ferrihydrite as an electron acceptor, and the pH around the cells increases most likely as a result of bacterial biosynthesis pathway. The localized concentration of Fe^{3+} and Fe^{2+} at the negatively charged cell structures, or cell wall then triggers a localized spike in the system's saturation in reference to magnetite, leading to the precipitation of magnetite stage via a passive mechanism.

According to Sanghi and Verma (2009), the creation of CdS Nanomaterials occurs via disulfide (cystine) bridges and may be explained by the cleavage of the S-H bond and the production of a new bond, the -S-Cd bond of the Cd-thiolate (Cd-S- CH_2COOH) complex (Tang et al. 2005). The -COOH groups from the cadmium-thiolate complexes react with hydrogen bonds rather than the protein's $-NH_2$ groups, which they do not react with. As a result, hydrogen bonds between the capped CdS nanoparticles and $-NH_2$ groups are formed. The thiol group competed with the carboxylic group that will store on the surfaces of the CdS nanoparticles

Table 1.1 Synthesis of gold nanoparticles by microorganisms (Li et al. 2011a)

Microorganisms	Location	Size (nm)	Culturing temperature (°C)	References
Shewanella algae	Intracellular	10–20	25	Konishi et al. (2007)
Sargassum wightii	Extracellular	8–12	36	Suresh et al. (2011)
Rhodopseudomonas capsulate	Extracellular	10–20	30	He et al. (2007)
Candida utilis	Intracellular	<10–25	37	Gericke and Pinches (2006)
Rhodococcus sp.	Intracellular	5–15	37	Ahmad et al. (2003)
Yarrowia lipolytica	Extracellular	15	30	Agnihotri et al. (2009)
Plectonema boryanum	Intracellular	<10–25	25–100	Lengke et al. (2006a, b)
Pseudomonas aeruginosa	Extracellular	15–30	37	Husseiny et al. (2007)
Shewanella oneidensis	Extracellular	12 ± 5	30	Suresh et al. (2011)
Escherichia coli	Extracellular	20–30	37	Du et al. (2007)
V. luteoalbum	Intracellular	15–30	37	Gericke and Pinches (2006)
Plectonema boryanum UTEX 485	Extracellular	10 nm to 6 μm	25	Lengke et al. (2006a, b)

since one of the oxygen atoms in the carboxylic group (-COOH) created the link between the Cd^{2+} ion and oxygen atom (Table 1.1) (Løver et al. 1997).

1.4 Biotemplates of Microbial Nanomaterial Synthesis

It is already well-recognized that diverse NPs can be biosynthesized utilizing microbial templates. Due to their unique characteristics, this microbial method has evolved as an effective mechanism for the synthesis of nanomaterials. Basically, microbiological processes exhibit enormous skeletal diversity ranging from nano to microscale, which can be used to create appropriate biotemplates. In addition to different microbial morphologies, their nanoscale-sized cell walls are also preferred. Understanding the relevance and process of the biochemical components of the entire cell, as well as its components and cell extracts, such as exo-polysaccharides, proteins, and enzymes, is essential for nanomaterial synthesis.

1.4.1 Fungi Biotemplate

Fungi are another promising alternative for the creation of metal nanomaterial, much like bacterial cells. Proteins and enzymes produced by fungi are always employed to develop metal NPs because they aid metal salts reduction to nanomaterial. Metal nanomaterial of various sizes and shapes are typically created either extracellularly or intracellularly (Abdel-Aziz et al. 2018). In comparison to intracellular synthesis, which requires the upsurge of metallic ions inside the cell of fungal preceded by bio-reduction to metal ions, this synthesis involves the biosorption of metal charges within wall of fungal cell filament including decrease through bacterial secretion of extracellular enzymes, and metabolites (Dhillon et al. 2014; Koch et al. 2023).

Generally, fungus instead of bacteria are chosen for the large-scale synthesis of nanomaterial. Their variety of forms (from microfilaments to unicellular structures), greater adaptation in different ecologies, with environmental stress tolerance makes them ideal for the job (Sastry et al. 2003). Additionally, mycelia of fungal produce more cellulose and have a wide outer part to interact with metal salts, which speeds up the production of nanomaterials. As a result, it is advantageous to explore and use fungus for the production of nanomaterials (Pantidos and Horsfall 2014).

1.4.2 Bacteria Biotemplate

For the creation of nanoparticles, a variety of bacterial cells with various morphological characteristics and structures of the surface can be a biotemplate (Selvakumar et al. 2014). The primary determinant is the makeup of the cell surface structure, which includes the wall of cells with exo-polysaccharides or proteins in the outer layer. In essence, several functional groups comprising of carboxyl, phosphate, and amide groups present in the microbial cell wall enhance binding of metal along nucleation mechanism of assemblage to secret nanomaterials (Iravani 2014).

Exo-polysaccharide in bacterial is an efficient constituent in synthesis of metal NPs and is one such component. The exo-polysaccharide layer's polyanionic functional groups, such as the hydroxyl, carboxyl, and amino groups, interact with metal-positive ions to haste process of reduction (Sanyasi et al. 2016). Also, exo-polysaccharide is employed as effective capping agents for chelating metal nanoparticles to stabilize their fundamental structures, which controls the particle size and shape (Gomaa 2017). Exo-polysaccharides' mucoadhesion feature causes NPs to have a neutral, low surface energy, which prevents them from clumping to ensure uniform particle dispersion after prolonged storage.

Bacteria walls also comprise surface proteins, which generate self-assembling nanostructures on their surface to preserve the cellular morphology, similar to exo-polysaccharides. This S layer interacts weakly with metal ions and has a high surface area with consistent pore size. This causes ionic and covalent bonds between molecules to bind specifically to S-layer lattices, which can be exploited to synthesize cadmium (Cd), gold (Au), and other metal nanomaterials (Selvakumar et al. 2014). Following separation, layer of S proteins is crystallized onto solid support

substances such as glass, silica, carbon, mica, electron microscopy grids, polymers, or liposomes in order to achieve certain symmetry.

1.4.3 Viral Biotemplate

A virus is a nucleoprotein particle that is encased in a proteinaceous capsid and contains genomic nucleic acid. They are regarded as natural nanoarchitectures because of their particular shapes and sizes at the nanoscale (Flenniken et al. 2009). Protein subunits, which are composed of amino acids with carboxylate, amino, and thiol group side chains that represent a highly reactive layer and have a high affinity for interacting with metal ions, are densely packed over the three-dimensional structural system of viral proteins. This aids in their nucleation and metallization at the outer surface (Shah et al. 2015).

Additionally, within the viral capsid, virus particles feature a shallow interior cavity where certain particles can penetrate and react with protruding amino acid ligands. In order to create metal nanomaterial of the desired structure, the interior cavity of virus particles can be used as a nanoreactor. Hence, the coated protein exterior area with inside compartments could be used to build different objects, such as nanotubes and nanowires (Selvakumar et al. 2014).

1.4.4 Microalgae Biotemplate

Another innovative strategy is the synthesis of nanomaterials using microalgal biotemplate. Microalgal species' utilization in the production of metal nanostructures is entirely dependent on their physical and structural characteristics and released biomolecules (Davis et al. 2003). The biosynthesis of nanostructures involves a variety of biomolecules, including secondary metabolites, carbohydrates, and proteins released by different microalgae. Extracellular polysaccharides aid reduction of various metal ions and the stability of metal nanoparticles because composition of proteins in algal membrane is crucial for titrating metal ions. Terpenoids and flavonoids, which are organic molecules, are efficient at stabilizing and sealing nanostructure, which affects their overall composition, size, and form. Additionally, algae species and morphological diversity encourage the creation of nanostructures. Depending on the algae species, NPs with various sizes and morphologies (spherical, elongated, or irregular) are produced (Patel et al. 2015). Microalgae are thought to be beneficial for the production of nanoparticles because they facilitate the economical and mass secretion of very balance, secure, and non-harmful nanomaterials with superior biological capabilities (Fig. 1.3) (Siddiqi and Husen 2016; Aziz et al. 2015).

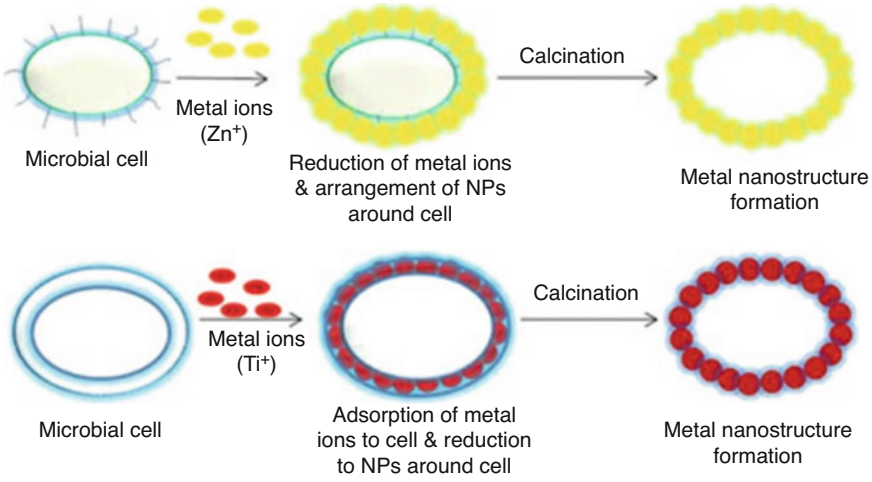

Fig. 1.3 Synthesis by bacteria

1.5 Application of Nanomaterials

Microbiologically produced nanomaterials offer vast potential of uses in many industries, including agriculture, coatings, cosmetics, packaging, food, beverages, drug deliveries, bioremediation, biomedicine, diagnostics, and electronics production. This section discusses a few of these applications.

1.5.1 Antimicrobial Agent

Due to the enormous number of bacteria that are responsible for antibiotic resistance, the importance of nanoparticle synthesis utilizing microbial templates has increased recently. These bio-secreted nanoparticles can be used as antibacterial, antifungal, antiviral, and anti-inflammatory agents, among other antimicrobial uses (Fayaz et al. 2010). AgNPs, for example, have a very high aspect ratio due to several inherent characteristics of nanoparticles that make it simple for them to interact with other particles, greatly increasing their antibacterial effectiveness (Thakkar et al. 2010; Aziz et al. 2014, 2015, 2016, 2019). By attaching and piercing the bacterial cell wall, fungi-enhanced AgNPs demonstrated substantial bactericidal capability in contrast to Gram-positive and Gram-negative bacteria. They also altered pathways of cellular signaling through dephosphorylating putative critical peptide substrates on tyrosine residues. *Fusarium oxysporum* and *Trichoderma* sp. can be utilized in the production of extracellularly synthesized silver nanomaterials, or AuNPs, which can then be integrated into a variety of materials, including textile textiles. These safe, antibacterial fabrics with silver nanoparticles incorporated in them could be

medically adopted to prevent the spreading of dangerous pathogens like *Staphylococcus aureus* (Durán et al. 2007). Silver nanoparticles made intra- or extracellularly utilizing microorganisms may be extremely valuable due to their significant biomedical features.

1.5.2 Food Microbiology

By altering the size of the particles, potential cluster formation, and surface charge of food nanomaterials, nanotechnology enhances the texture, digestibility, consistency, and taste of food (Nile et al. 2020). In addition to extending the shelf life of several food-related components, nanotechnology also lowers the amount of food wasted as a result of microbial deterioration (Singh et al. 2017; Pradhan et al. 2015).

Usually, food additives are applied to nanocarriers without changing the fundamental morphology of food products (Singh et al. 2017). The ideal delivery system should be able to efficiently maintain active components at the proper levels for long durations, as in the case of food storage processes, ensure the availability at an exact time and proper rate, and deliver the active ingredient to the precise target site (Lamprecht et al. 2004). Nanomaterials can produce efficient distribution mechanisms with characteristics such as creating emulsions, biopolymer matrices, encapsulation, association colloids, and simple solutions. Because of the small size of nanoparticles used in delivery systems, extensive penetration into various tissues is made possible, allowing for superior distribution of active ingredients to their intended major organs (Ubbink and Krüger 2006).

Comparing nanoencapsulations to traditional encapsulation techniques, the former has superior characteristics and a higher release effectiveness. For instance, nanocapsules can mask odors or tastes, regulate the release of bioactive compounds, ensure their availability at a precise time and rate, and preserve them from moisture, heat, chemical, and biological decomposition during processing and storage. They can also make sure that other ingredients in the food matrix are compatible with one another (Weiss et al. 2006).

Because nanomaterials are subcellular in size, they can increase the bioavailability of nutraceutical substances and raise medication bioavailability. Rutin is a commonly consumed flavonoid with strong medicinal effects, but due to its weak solubility, it has limited use in the food sector. According to a recent research, ferritin cage at the nanoscale increased not only its water solubility but also its thermal and UV radiation stability (Zhang et al. 2014). Researchers created nanoemulsions supplemented with vitamin E utilizing natural biopolymers including gum arabic and protein isolate. They discovered that protein powder produces smaller particles than gum arabic at low concentrations. Gum arabic-based nanoemulsions have more resistance to salt, acidity, and heat. Compared to free vitamin E, nanoemulsions made from both emulsifiers were relatively more stable (Yang et al. 2015; Ozturk et al. 2015).

Pathogen screening and quantitative study of food ingredients are also applications of nanotechnology in food science (Reddy et al. 2022). Nanomaterials

serve as indicators that detect minor changes in environmental factors including pathogen attack, food spoilage, temperature changes, or humidity in storage units (Helmke and Minerick 2006; Karlo et al. 2023).

With exceptional optical, physical, and chemical, carbon nanotubes serve as substrates for the immobilization of biomolecules at their surface and are one of the best materials for the transmission of signals related to the identification of metabolites. Toxins, infections, and other degrading compounds have all been successfully detected in foods and beverages using carbon biosensors. It is an easy, quick, and sensitive method for detecting aquatic toxins because toxin antibodies coupled to single-walled carbon nanotubes caused a noticeable change in conductivity (Wang et al. 2009).

1.5.3 Cosmeceutical Industry

Because of tissue engineering affinity toward self-cleansing, compatibility to skin, antimicrobial properties, and dermatological character, novel nanocarriers such as liposomes, nanocapsules, nanostructured carrier of lipid, nanoemulsions, etc. are used as cosmeceuticals to condition the skin, hair, and nail as well as for lip care, aging, and hyperpigmentation (Singh et al. 2016). Nanomaterials often have a wavelength that is lower than critical wavelength of light, making them visible. They are suitable for use in the cosmetic industry because of this characteristic (Raj et al. 2012). Due to the highly reflective nature, and absorption with reflection of UV rays of nanoparticles, they have been found useful for skin conditioning, metal nanoparticles, specifically titanium (Ti) and zinc (Zn) oxide nanomaterials, have been employed in sunscreens (Morganti 2010). Because of these characteristics, nanoscale materials are used widely in the personal care sector (Jassal et al. 2022; Kavitha et al. 2023).

1.5.4 Clinical Microbiology

The domains of clinical microbiology and nanotechnology have contributed to the advancement of science and technology. However, the advent of various secondary health issues increased the need for interdisciplinary research to combine clinical microbiology and nanotechnology. Combining the two disciplines may result in creative approaches to tackling health-related issues in a logical way (Ball et al. 2019).

It's interesting that nanomaterials are of great importance in clinical microbiology, the appropriate use of microbes in the manufacture of crucial nanoparticles for medicine. Additionally, they play a significant role in the prevention, treatment, and diagnosis of numerous infectious diseases as well as in the creation of nanovaccines (Gurunathan et al. 2009; El-Sayed and Kamel 2020; Maddela et al. 2021). The distribution of prospective diagnostic components has been developed using a variety of nanoscopic vectors. Liposomes, bio-based nanoparticles, micelles,

polymeric nanoparticles, and dendrimers are some of these nanoscale delivery systems. Additionally, a variety of therapeutic substances, including proteins, medicines, siRNA, and genes, can be created employing the aforementioned nanovectors to be delivered to their targets in the sick tissues in a more intelligent manner (Ball et al. 2019).

Due to its capacity to perform diagnosis at the level of both single cells and molecules, nanotechnology is crucial to the design of biochips. As a result, covalently linked nanoparticles to biomolecules like nucleic acid and antibodies have been applied as nanoprobes. As a result, the functionalized nanoparticles have been used to give a very sensitive, quick, and direct method for viral detection. Another approach created for the detection of infections brought on by the *Salmonella typhimurium*, *Staphylococcus aureus*, and *Mycobacterium tuberculosis* complex is fluorescent silica nanoparticles (El-Sayed and Kamel 2020). The early diagnosis of harmful diseases and airborne virus particles is successfully accomplished with the aid of nanocantilever detectors. These silicon biosensors look like miniature diving boards. When pathogens adhere to them, they have the capacity to vibrate at a range of frequencies (Gopinath et al. 2015). The emergence of cutting-edge hybrid technologies is another approach highlighting the promising future of nanotechnology. For instance, the fusion of biology and nanotechnology to control genetic material for identifying the immune response perturbations, for instance, screening methods based on nanotechnology that make use of silicon nanowire paired with siRNA with transcriptional profiling over time may be interesting (Pedrosa and Baptista 2015).

Potential nanotools, such as silver and gold nanoparticles, are commonly utilized to deliver biomolecules, particularly thiol-containing polymers like antibodies and nucleic acids. Drug and gene delivery have both used conjugation using these probes. Additionally, resonance scattering confocal microscopy was used it. Liposomes are membrane nanoparticles made of an aqueous interior and a phospholipid bilayer (Ghaffar et al. 2016). They serve as a delivery system for either hydrophilic or hydrophobic treatment of infectious diseases. Through targeting ligands attached to their surfaces, they are accumulated within tissues. Rapid liposome-based techniques have been used to find cholera or botulinum food-borne toxins, for instance. For prophylaxis against group A *streptococci*, cationic liposomes enclosing lipopeptide-based vaccination (nanovaccine) were created (Ghaffar et al. 2016).

1.5.5 Drug Delivery

The fundamental goal in designing and creating novel drug delivery systems is to precisely position the drug in the proper molecule to address a particular issue at the appropriate moment. As a result, it is possible to deliver drugs precisely and safely while minimizing side effects to get the greatest therapeutic effect (Dhillon et al. 2012). Nanomaterials have been widely studied as a drug delivery method during the past 10 years (Gref et al. 1994). Due to their small size and ability to quickly pass

across barrier of blood in the brain and the constricting epithelial junctions, silver (Ag) nanoparticles have become important as medication delivery network. Because of greater outer area-to-volume ratio, it also improves the pharmacokinetics and biodistribution of therapeutic components, which decreases toxicity through their preferential collection at the desired site (Kalishwaralal et al. 2009; Boroumand Moghaddam et al. 2015). Similar to this, magnetic nanomaterials Fe_3O_4 and Fe_2O_3 have undergone dynamic investigation because they are known to be biocompatible for a variety of uses, including gene therapy, target cancer treatment, DNA analysis, trained drug delivery, stem cell sorting, and MRI (Xiang et al. 2007).

1.5.6 Agricultural Application

Globally, it is evident that a variety of pests and pathogens are persistently impeding agricultural productivity and negatively influencing plant growth, which causes significant financial losses and jeopardizes the security of the world's food supply (Ingale and Chaudhari 2013). Farmers use a variety of agrochemicals indiscriminately to manage these plant pests and diseases, which degrades the quality of the sand and water. Repeated as well as excessive application of pesticides has ecotoxicological impact and can sometimes lead to the resistance of agrochemicals (Prasad 2017; Bhattacharyya et al. 2016; Osherov et al. 2023). These toxins can occasionally find their way into the food chain and build up in people's bodies. More work should be put into creating safe management techniques that can take the place of synthetic pesticides with greater efficacy and less risk to human and animal health (Prasad 2017). So, in addition to providing a fresh, simple, ecologically safe, and cost-effective solution, green secretion of metal nanomaterials utilizing microbial template also assures a sustainable pest management strategy (Prasad et al. 2017a, b). Reduction of application rate between 10 and 15 lower than the standard measurement, the nanopesticides perform a vital role in developing the process of non-harmful and better advancement of pesticide delivery to improve global food supply in sustainable agriculture (Ingale and Chaudhari 2013; Prasad et al. 2014, 2017c).

1.5.7 Environmental Application

Since the inception of the twentieth century, NPs' distinctive physicochemical characteristics have been an excellent option to disinfect environment components (Dhillon et al. 2014). Environmental remediation of different pollutants can be achieved with advancing NPs (Liu 2006). It's significant that this capability of microbes to use their natural metabolic process to change inorganic metal ions to metal nanomaterials in conjunction to their surrounding give rise to a very recent and mostly untapped research area. Benzyl butyl phthalate (BBP), rate of transformation in environmental pollutant caused by *Pseudomonas putida* and *photocatalytic* ZnO nanomaterials, was examined by Songara et al. (2018), who came to the conclusion

that the photocatalytic activity of ZnO nanomaterials dosage relied on time in the transformation of BBP. Studies also revealed green metal nanomaterials (Ag, Fe, Pt, Pt-Co, Pt-Ni, and Fe-Co) produced intracellularly and extracellularly are involved in the redox process that leads to the detoxification of pollutants (Shah et al. 2015). Additionally, zero-valent iron (iron in the form of granules) is utilized to remediate chlorinated compounds due to its reducing and absorption properties (Oh et al. 2016). Recently, material scientists have showed interest in microorganisms that could potentially function as environmentally benign input in a variety of environmental remediation technologies (Li et al. 2011a; Shash et al. 2019).

1.6 Factors Affecting Microbial Nanomaterials

The synthesis and application of nanomaterials are all influenced by a number of variables. Numerous studies have documented how the type of adsorbate and the activity of the catalysts used in the synthesis process affect the nanomaterials.

1.6.1 Method

Nanomaterials can be produced using a variety of approaches, which could be physical ones involving mechanical processes to chemical or biological ones involving various organic or inorganic compounds and living things. Each method has unique advantages and disadvantages. However, as opposed to conventional procedures, biological approaches for the synthesis of nanoparticles use nontoxic and environmentally safe components along with green technology, making them more palatable and eco-friendlier (Vadlapudi and Kaladhar 2014; Srivastava et al. 2021; Sarma et al. 2021).

1.6.2 Pore Size

The porosity of the produced nanoparticles has a significant impact on their quality and use. It has become possible to immobilize biomolecules onto nanomaterials to expand their utility in the biomedical and medication delivery fields (Ruckenstein and Kong 1999).

1.6.3 Environment

The nature of the produced nanomaterials is significantly influenced by their environment. In many situations, a single nanomaterial quickly transforms into a core–shell nanomaterials by absorbing substances or interacting with other substances through the processes of oxidation or corrosion. The manufactured nanoparticles develop a covering in a biological system that increases their thickness and size. In

addition, the chemical and physical makeup of the produced nanoparticles is influenced by their environment. There are not many instances that demonstrate how the environment affects the nature of produced nanomaterials (Kuchibhatla et al. 2012).

1.6.4 Temperature

Another crucial factor that influences the three different processes of synthesizing nanoparticles is temperature. The temperature needed for the physical approach is the highest (>350 °C), but the temperature needed for the chemical method is lower. Green technology typically demands temperatures below 100 °C, or ambient temperature, for the creation of nanoparticles. The type of produced nanoparticle depends on the reaction medium's temperature (Patra and Baek 2014).

1.6.5 pH

When using green technology to synthesize nanomaterials, pH is a significant component. Researchers have shown that the size and texture of the produced nanoparticle are affected by the pH of the solution media. Therefore, by adjusting the pH of the solution media, nanomaterial size can be adjusted. Soni and Prakash showed how pH affected the size and structure of the produced silver nanoparticle (Soni and Prakash 2011).

1.6.6 Pressure

For nanomaterials production, pressure is crucial. The size and shape of the produced nanomaterials are influenced by the pressure that is applied to the reaction media. At ambient pressure circumstances, it has been discovered that biological agents significantly speed up the rate of reduction of metal ions (Patra and Baek 2014).

1.6.7 Proximity

Sometimes, surface contact of isolated nanomaterial with another nanomaterial could alter their properties. The observed alteration might be a base for fresh nanomaterial development. Effects due to proximity are not limited to charging of the particles and interaction of the substrate but also extend to magnetic component of the nanomaterials (Patra and Baek 2014).

1.6.8 Particle Shape and Size

The size of nanomaterial is a prominent determinant factor that cannot be overlooked. The decrease in melting point of nanomaterials is associated with the size of nanomaterial attaining nanometer scale. More so, nanomaterial with different configurations exhibits comparable energy which promotes easier transformation of their shape. The form of energy expended when evaluating nanomaterials enhances transformation in their shape. Dynamism in nature and shape of the produced nanomaterial largely influence their chemical components (Patra and Baek 2014).

1.7 Conclusion

This study takes cognizant of recent trends in the synthesis of nanoparticles in relation to types and applications. Particular attention is focused on microbial secretion of nanomaterial. Production of nanomaterials through biogenic enzymatic processes has better quality compared to its counterpart produced via chemical processes. Though, chemical processes produce larger quantities of nanomaterials with a definite shape and size within a short period. Although, the procedure is cumbersome, not cost effective also emit noxious wastes that impact human and the environment. Although specialists did not agree on a clear description, scholars do believe that nanomaterials can be characterized by their extremely small size, measured in nanometers. A nanometer is one-millionth of a millimeter, i.e., 100,000 size smaller than the diameter of a human hair. Materials with at least one exterior dimension between 1 and 100 nm are referred to as nanomaterials. According to the criteria provided by the European Commission, at least half of the materials in the number size distribution should have a particle size of 100 nm or less. Owing to the development of green nanomaterials from microbes and extracts from microorganisms, there are numerous research opportunities toward bioremediation and environmentally friendly cleanup of pollution. The international market for nanomaterials is anticipated to expand at an average annual growth rate of at least 25% from 2017 to 2023. The sustainable development of nanomanufacturing processes is one of the main barriers to the development of the nanomaterials sector on a worldwide scale.

The green synthesis of microbial nanoparticles offers biocompatible, environmentally friendly, and economically advantageous production techniques as benefits. Other than that, no additional stabilizing agents are needed because the components of microbial cells themselves serve the purpose of capping and stabilizing materials. Hence, microbial nanomaterials in touch with complicated biological fluids, their surfaces progressively and selectively absorb biomolecules, creating a corona that reacts with biological processes and offers greater efficacy than naked biological nanomaterials. By lowering the number of stages needed for physiochemical secretion couple with attachment of functional groups to the surface of nanomaterial to make them physiologically reactive, it becomes a less time-consuming, more productive, and beneficial one-step procedure. Other benefits

include the ease with which different parameters, such as pH and temperature, may be used to readily alter the size of produced nanomaterials. Because angular shapes have a smaller radius of curvature in the same volume as spherical shapes, they are preferred over spherical nanoparticles because they have stronger catalytic activity. When a lipid layer is applied to nanoparticles, it can give them physiological solubility and stability, which is necessary for biomedical applications and the limitation of other synthetic techniques. Therefore, more studies should be channeled toward microbial nanomaterials based on their ecofriendly nature and cost-effective production.

References

Abdel-Aziz SM, Prasad R, Hamed AA, Abdelraof M (2018) Fungal nanoparticles: a novel tool for a green biotechnology? In: Fungal nanobionics: principles and applications. Springer, Singapore, pp 61–87

Agnihotri M, Joshi S, Kumar AR, Zinjarde S, Kulkarni S (2009) Biosynthesis of gold nanoparticles by the tropical marine yeast Yarrowia lipolytica NCIM 3589. Mater Lett 63(15):1231–1234

Ahmad A, Senapati S, Khan MI, Kumar R, Ramani R, Srinivas V, Sastry M (2003) Intracellular synthesis of gold nanoparticles by a novel alkalotolerant actinomycete, Rhodococcus species. Nanotechnology 14(7):824

Ahmad R, Srivastava S, Ghosh S, Khare SK (2021) Phytochemical delivery through nanocarriers: a review. Colloids Surf B: Biointerfaces 197:111389. https://doi.org/10.1016/j.colsurfb.2020.111389

Aminabad NS, Farshbaf M, Akbarzadeh A (2019) Recent advances of gold nanoparticles in biomedical applications: state of the art. Cell Biochem Biophys 77:123–137. https://doi.org/10.1007/s12013-018-0863-4

Arakaki A, Nakazawa H, Nemoto M, Mori T, Matsunaga T (2008) Formation of magnetite by bacteria and its application. J R Soc Interface 5(26):977–999

Aziz N, Fatma T, Varma A, Prasad R (2014) Biogenic synthesis of silver nanoparticles using scenedesmus abundans and evaluation of their antibacterial activity. J Nanoparticles, Article ID 689419, 2014. https://doi.org/10.1155/2014/689419

Aziz N, Faraz M, Pandey R, Sakir M, Fatma T, Varma A, Barman I, Prasad R (2015) Facile algae-derived route to biogenic silver nanoparticles: synthesis, antibacterial and photocatalytic properties. Langmuir 31:11605–11612. https://doi.org/10.1021/acs.langmuir.5b03081

Aziz N, Pandey R, Barman I, Prasad R (2016) Leveraging the attributes of mucor hiemalis-derived silver nanoparticles for a synergistic broad-spectrum antimicrobial platform. Front Microbiol 7:1984. https://doi.org/10.3389/fmicb.2016.01984

Aziz N, Faraz M, Sherwani MA, Fatma T, Prasad R (2019) Illuminating the anticancerous efficacy of a new fungal chassis for silver nanoparticle synthesis. Front Chem 7:65. https://doi.org/10.3389/fchem.2019.00065

Ball AS, Patil S, Soni S (2019) Introduction into nanotechnology and microbiology. In: Methods in microbiology, vol 46. Academic Press, London, pp 1–18

Bhattacharyya A, Duraisamy P, Govindarajan M, Buhroo AA, Prasad R (2016) Nano-biofungicides: emerging trend in insect pest control. In: Prasad R (ed) Advances and applications through fungal nanobiotechnology. Springer International Publishing Switzerland, pp 307–319

Begum SJP, Pratibha S, Rawat JM, Venugopal D, Sahu P, Gowda A, Qureshi KA, Jaremko M (2022) Recent advances in green synthesis, characterization, and applications of bioactive metallic nanoparticles. Pharmaceuticals 15:455. https://doi.org/10.3390/ph15040455

Benzerara K, Miot J, Morin G, Ona-Nguema G, Skouri-Panet F, Ferard C (2011) Significance, mechanisms and environmental implications of microbial biomineralization. Compt Rendus Geosci 343(2–3):160–167

Borah SN, Koch N, Sen S, Prasad R, Sarma H (2022) Novel nanomaterials for nanobioremediation of polyaromatic hydrocarbons. In: Dominguez DC, Lee W-Y (eds) Sharma H. Elsevier, Emerging Contaminants in the Environment, pp 643–667

Boroumand Moghaddam A, Namvar F, Moniri M, Md Tahir P, Azizi S, Mohamad R (2015) Nanoparticles biosynthesized by fungi and yeast: a review of their preparation, properties, and medical applications. Molecules 20(9):16540–16565

Celiksoy S, Ye W, Wandner K, Schlapp F, Kaefer K, Guzman A (2020) Plasmonic nanosensors for the label-free imaging of dynamic protein patterns. J Phys Chem Lett 11:4554–4558. https://doi.org/10.1021/acs.jpclett.0c01400

Cheng S, Li N, Jiang L, Li Y, Xu B, Zhou W (2019) Biodegradation of metal complex Naphthol Green B and formation of iron–sulfur nanoparticles by marine bacterium Pseudoalteromonas sp CF10-13. Bioresour Technol 273:49–55

Chisanga M, Muhamadali H, Ellis DI, Goodacre R (2019) Enhancing disease diagnosis: biomedical applications of surface-enhanced Raman scattering. Appl Sci 9:1163. https://doi.org/10.3390/app9061163

Davis TA, Volesky B, Mucci A (2003) A review of the biochemistry of heavy metal biosorption by brown algae. Water Res 37(18):4311–4330

Dhillon GS, Brar SK, Kaur S, Verma M (2012) Green approach for nanoparticle biosynthesis by fungi: current trends and applications. Crit Rev Biotechnol 32(1):49–73

Dhillon GS, Kaur S, Brar SK (2014) Facile fabrication and characterization of chitosan-based zinc oxide nanoparticles and evaluation of their antimicrobial and antibiofilm activity. Int Nano Lett 4(2):1–11

Du L, Jiang H, Liu X, Wang E (2007) Biosynthesis of gold nanoparticles assisted by Escherichia coli DH5α and its application on direct electrochemistry of hemoglobin. Electrochem Commun 9(5):1165–1170

Durán N, Marcato PD, De Souza GI, Alves OL, Esposito E (2007) Antibacterial effect of silver nanoparticles produced by fungal process on textile fabrics and their effluent treatment. J Biomed Nanotechnol 3(2):203–208

Eftekhari A, Khalilov R, Kavetskyy T, Keskin C, Prasad R, Rosic GL (2023) Biological/chemical-based metallic nanoparticles synthesis, characterization, and environmental applications. Front Chem 11:1191659. https://doi.org/10.3389/fchem.2023.1191659

Elahi N, Kamali M, Baghersad MH (2019) Recent biomedical applications of gold nanoparticles: a review. Talanta 184:537–556. https://doi.org/10.1016/j.talanta.2018.02.088

El-Deeb NM, Abo-Eleneen MA, Al-Madboly LA, Sharaf MM, Othman SS, Ibrahim OM, Mubarak MS (2020) Biogenically synthesized polysaccharides-capped silver nanoparticles: immuno-modulatory and antibacterial potentialities against resistant Pseudomonas aeruginosa. Front Bioeng Biotechnol 8:643

El-Sayed A, Kamel M (2020) Advances in nanomedical applications: diagnostic, therapeutic, immunization, and vaccine production. Environ Sci Pollut Res 27(16):19200–19213

Esmail R, Afshar A, Morteza M, Abolfazl A, Akhondi E (2022) Synthesis of silver nanoparticles with high efficiency and stability by culture supernatant of *Bacillus ROM6* isolated from Zarshouran gold mine and evaluating its antibacterial effects. BMC Microbiol 22(97):1–10. https://doi.org/10.1186/s12866-022-02490-5

Fayaz AM, Balaji K, Girilal M, Yadav R, Kalaichelvan PT, Venketesan R (2010) Biogenic synthesis of silver nanoparticles and their synergistic effect with antibiotics: a study against gram-positive and gram-negative bacteria. Nanomedicine 6(1):103–109

Flenniken ML, Uchida M, Liepold LO, Kang S, Young MJ, Douglas T (2009) A library of protein cage architectures as nanomaterials. Viruses Nanotechnol 327:71–93

Gao C, Wang Y, Ye Z, Lin Z, Ma X, He Q (2020) Biomedical micro- /nanomotors: from overcoming biological barriers to in vivo imaging. Adv Mater 33:2000512. https://doi.org/10.1002/adma.202000512

Gericke M, Pinches A (2006) Biological synthesis of metal nanoparticles. Hydrometallurgy 83(1–4):132–140

Ghaffar KA, Marasini N, Giddam AK, Batzloff MR, Good MF, Skwarczynski M, Toth I (2016) Liposome-based intranasal delivery of lipopeptide vaccine candidates against group A streptococcus. Acta Biomater 41:161–168

Ghosh S, Ahmad R, Zeyaullah M, Khare SK (2021) Microbial nano-factories: synthesis and biomedical applications. Front Chem 9:626834. https://doi.org/10.3389/fchem.2021.626834

Gomaa EZ (2017) Silver nanoparticles as an antimicrobial agent: a case study on Staphylococcus aureus and Escherichia coli as models for Gram-positive and Gram-negative bacteria. J Gen Appl Microbiol 63(1):36–43

Gopinath P, Anitha V, Mastani SA (2015) Microcantilever based biosensor for disease detection applications. J Med Bioeng 4(4):34

Govarthanan M, Jeon CH, Jeon YH, Kwon JH, Bae H, Kim W (2020) Non-toxic nano approach for wastewater treatment using Chlorella vulgaris exopolysaccharides immobilized in iron-magnetic nanoparticles. Int J Biol Macromol 162:1241–1249

Gref R, Minamitake Y, Peracchia MT, Trubetskoy V, Torchilin V, Langer R (1994) Biodegradable long-circulating polymeric nanospheres. Science 263(5153):1600–1603

Gurunathan S, Lee KJ, Kalishwaralal K, Sheikpranbabu S, Vaidyanathan R, Eom SH (2009) Antiangiogenic properties of silver nanoparticles. Biomaterials 30(31):6341–6350

He S, Guo Z, Zhang Y, Zhang S, Wang J, Gu N (2007) Biosynthesis of gold nanoparticles using the bacteria Rhodopseudomonas capsulata. Mater Lett 61(18):3984–3987

Helmke BP, Minerick AR (2006) Designing a nano-interface in a microfluidic chip to probe living cells: challenges and perspectives. Proc Natl Acad Sci 103(17):6419–6424

Husseiny MI, Abd El-Aziz M, Badr Y, Mahmoud MA (2007) Biosynthesis of gold nanoparticles using Pseudomonas aeruginosa. Spectrochim Acta A Mol Biomol Spectrosc 67(3–4): 1003–1006

Ingale AG, Chaudhari AN (2013) Biogenic synthesis of nanoparticles and potential applications: an eco-friendly approach. J Nanomed Nanotechol 4(165):1–7

Iravani S (2014) Bacteria in nanoparticle synthesis: current status and future prospects. Int Scholar Res Notice 2014:359316

Jassal PS, Kaur D, Prasad R, Singh J (2022) Green synthesis of titanium dioxide nanoparticles: development and applications. J Agriculture Food Res 10:100361. https://doi.org/10.1016/j.jafr.2022.100361

Kalishwaralal K, Deepak V, Ramkumarpandian S, Nellaiah H, Sangiliyandi G (2008) Extracellular biosynthesis of silver nanoparticles by the culture supernatant of Bacillus licheniformis. Mater Lett 62(29):4411–4413

Kalishwaralal K, Banumathi E, Pandian SRK, Deepak V, Muniyandi J, Eom SH, Gurunathan S (2009) Silver nanoparticles inhibit VEGF induced cell proliferation and migration in bovine retinal endothelial cells. Colloids Surf B: Biointerfaces 73(1):51–57

Karlo J, Prasad R, Singh SP (2023) Biophotonics in food technology: quo vadis ? J Agriculture Food Res. https://doi.org/10.1016/j.jafr.2022.100482

Kavitha A, Doss A, Pole RPP, Pushpa Rani TPK, Prasad R, Satheesh S (2023) A mini review on plant-mediated zinc oxide nanoparticles and their antibacterial potency. Biocatal Agric Biotechnol. https://doi.org/10.1016/j.bcab.2023.102654

Kim HJ, Jeong H, Lee SJ (2018) Synthetic biology for microbial heavy metal biosensors. Anal Bioanal Chem 410(4):1191–1203

Kisimba K, Krishnan A, Faya M, Byanga K, Kasumbwe K, Vijayakumar K, Prasad R (2023) Synthesis of metallic nanoparticles based on green chemistry and their medical biochemical applications: synthesis of metallic nanoparticles. J Renewable Mater 11(6):2575–2591. 10.32604/jrm.2023.026159

Koch N, Sonowal S, Prasad R (2023) Elucidate the smart tailored biogenic nanoparticles and their applications in remediation. Biotechnol Genet Eng Rev. https://doi.org/10.1080/02648725.2023.2219942

Konishi Y, Tsukiyama T, Tachimi T, Saitoh N, Nomura T, Nagamine S (2007) Microbial deposition of gold nanoparticles by the metal-reducing bacterium Shewanella algae. Electrochim Acta 53(1):186–192

Kuchibhatla SVNT, Karakoti AS, Baer DR (2012) Influence of aging and environment on nanoparticle chemistry: implication to confinement effects in nanoceria. J Phys Chem C 116(26): 14108–14114

Kumar RMP, Venkatesh A, Moorthy VHS (2019) Nanopits based novel hybrid plasmonic nanosensor fabricated by a facile nanofabrication technique for biosensing. Mater Res Express 6:1150b6. https://doi.org/10.1088/2053-1591/ab33b9

Lamprecht A, Saumet JL, Roux J, Benoit JP (2004) Lipid nanocarriers as drug delivery system for ibuprofen in pain treatment. Int J Pharm 278(2):407–414

Lengke MF, Fleet ME, Southam G (2006a) Morphology of gold nanoparticles synthesized by filamentous cyanobacteria from gold (I)–thiosulfate and gold (III)–chloride complexes. Langmuir 22(6):2780–2787

Lengke MF, Ravel B, Fleet ME, Wanger G, Gordon RA, Southam G (2006b) Mechanisms of gold bioaccumulation by filamentous cyanobacteria from gold (III)–chloride complex. Environ Sci Technol 40(20):6304–6309

Li X, Xu H, Chen ZS, Chen G (2011a) Biosynthesis of nanoparticles by microorganisms and their applications. J Nanomater 2011:270974

Li X, Huizhong X, Chen Z-S, Chen G (2011b) Review Article: Biosynthesis of nanoparticles by microorganisms and their applications. J Nanomater 270974:16. https://doi.org/10.1155/2011/270974

Liu WT (2006) Nanoparticles and their biological and environmental applications. J Biosci Bioeng 102(1):1–7

Løver T, Henderson W, Bowmaker GA, Seakins JM, Cooney RP (1997) Functionalization and capping of a CdS nanocluster: a study of ligand exchange by electrospray mass spectrometry. Chem Mater 9(8):1878–1886

Lu H, Wang J, Stoller M, Wang T, Bao Y, Hao H (2016) An overview of nanomaterials for water and wastewater treatment. Adv Mater Sci Eng 2016:4964828

Maddela NR, Chakraborty S, Prasad R (2021) Nanotechnology for advances in medical microbiology. Springer Singapore. (ISBN 978-981-15-9915-6) https://www.springer.com/gp/book/9789811599156

Maddela NR, Eller LKW, Prasad R (2023) Microbiology for cleaner production and environmental sustainability. CRC Press. (ISBN-13: 9781032496061)

Mahanty S, Chatterjee S, Ghosh S, Tudu P, Gaine T, Bakshi M, Das S, Das P, Bhattacharyya S, Bandyopadhyay S, Chaudhuri P (2020) Synergistic approach towards the sustainable management of heavy metals in wastewater using mycosynthesized iron oxide nanoparticles: biofabrication, adsorptive dynamics and chemometric modeling study. J Water Process Eng 37:101426

Mergeay M, Monchy S, Vallaeys T, Auquier V, Benotmane A, Bertin P, Taghavi S, Dunn J, van der Lelie D, Wattiez R (2003) Ralstonia metallidurans, a bacterium specifically adapted to toxic metals: towards a catalogue of metal-responsive genes. FEMS Microbiol Rev 27(2–3):385–410

Morganti P (2010) Use and potential of nanotechnology in cosmetic dermatology. Clin Cosmet Investig Dermatol 3:5

Nile SH, Baskar V, Selvaraj D, Nile A, Xiao J, Kai G (2020) Nanotechnologies in food science: applications, recent trends, and future perspectives. Nano-Micro Lett 12(1):1–34

Noah NM, Ndangili PM (2022) Green synthesis of nanomaterials from sustainable materials for biosensors and drug delivery. Sensors Int 3:100166. https://doi.org/10.1016/j.sintl.2022.100166

Noman M, Shahid M, Ahmed T, Niazi MBK, Hussain S, Song F, Manzoor I (2020) Use of biogenic copper nanoparticles synthesized from a native Escherichia sp. as photocatalysts for azo dye degradation and treatment of textile effluents. Environ Pollut 257:113514

Noori R, Ahmad R, Sardar M (2020) Nanobiosensor in health sector: the milestones achieved and future prospects. In: Mohsin M, Naz R, Ahmad A (eds) Nanobiosensors for agricultural, medical and environmental applications. Springer, Singapore, pp 63–90. https://doi.org/10.1007/978-981-15-8346-9_4

Oh SY, Seo YD, Kim B, Kim IY, Cha DK (2016) Microbial reduction of nitrate in the presence of zero-valent iron and biochar. Bioresour Technol 200:891–896

Osherov A, Prasad R, Chrzanowski W, New EJ, Brazaca L, Sadik O, Haynes CL, Maine E (2023) Responsible nanotechnology for a sustainable future. One Earth 6(7):763–766. https://doi.org/10.1016/j.oneear.2023.06.010

Ozturk B, Argin S, Ozilgen M, McClements DJ (2015) Formation and stabilization of nanoemulsion-based vitamin E delivery systems using natural biopolymers: whey protein isolate and gum arabic. Food Chem 188:256–263

Pantidos N, Horsfall LE (2014) Biological synthesis of metallic nanoparticles by bacteria, fungi and plants. J Nanomed Nanotechnol 5(5):1

Pastorino F, Brignole C, Di Paolo D, Perri P, Curnis F, Corti A (2019) Overcoming biological barriers in neuroblastoma therapy: the vascular targeting approach with liposomal drug nanocarriers. Small 15:1804591. https://doi.org/10.1002/smll.201804591

Patel V, Berthold D, Puranik P, Gantar M (2015) Screening of cyanobacteria and microalgae for their ability to synthesize silver nanoparticles with antibacterial activity. Biotechnol Rep 5:112–119

Patra JK, Baek K-H (2014) Green nanobiotechnology: factors affecting synthesis and characterization techniques. Rev J Nanomater 417305:12. https://doi.org/10.1155/2014/417305

Pedrosa P, Baptista PV (2015) Gold and silver nanoparticles for diagnostics of infection. In: Nanotechnology in diagnosis, treatment and prophylaxis of infectious diseases. Academic Press, London, pp 1–18

Perez-Gonzalez T, Jimenez-Lopez C, Neal AL, Rull-Perez F, Rodriguez-Navarro A, Fernandez-Vivas A, Iañez-Pareja E (2010) Magnetite biomineralization induced by Shewanella oneidensis. Geochim Cosmochim Acta 74(3):967–979

Pradhan N, Singh S, Ojha N, Shrivastava A, Barla A, Rai V, Bose S (2015) Facets of nanotechnology as seen in food processing, packaging, and preservation industry. Biomed Res Int 2015: 365672

Prasad R (2014) Synthesis of silver nanoparticles in photosynthetic plants. J Nanoparticles., Article ID 963961:2014. https://doi.org/10.1155/2014/963961

Prasad R (ed) (2017) Fungal nanotechnology: applications in agriculture, industry, and medicine. Springer, Cham

Prasad R, Kumar V, Prasad KS (2014) Nanotechnology in sustainable agriculture: present concerns and future aspects. Afr J Biotechnol 13(6):705–713

Prasad R, Pandey R, Barman I (2016) Engineering tailored nanoparticles with microbes: quo vadis. WIREs Nanomed Nanobiotechnol 8:316–330. https://doi.org/10.1002/wnan.1363

Prasad R, Kumar M, Kumar V (2017a) Nanotechnology: an agriculture paradigm. Springer Nature Singapore Pte Ltd. (ISBN: 978-981-10-4573-8)

Prasad R, Kumar V, Kumar M (2017b) Nanotechnology: food and environmental paradigm. Springer Nature Singapore Pte Ltd. (ISBN 978-981-10-4678-0)

Prasad R, Bhattacharyya A, Nguyen QD (2017c) Nanotechnology in sustainable agriculture: recent developments, challenges, and perspectives. Front Microbiol 8:1014. https://doi.org/10.3389/fmicb.2017.01014

Prasad R, Jha A, Prasad K (2018) Exploring the realms of nature for nanosynthesis. Springer International Publishing. (ISBN 978-3-319-99570-0) https://www.springer.com/978-3-319-99570-0

Prasad R (2019a) Microbial nanobionics: basic research and applications. Springer International Publishing. (ISBN 978-3-030-16534-5) https://www.springer.com/gp/book/9783030165338
Prasad R (2019b) Microbial nanobionics: state of art. Springer International Publishing. (ISBN 978-3-030-16383-9) https://www.springer.com/gp/book/9783030163822
Purohit J, Chattopadhyay A, Singh NK (2019) Green synthesis of microbial nanoparticle: approaches to application. In: Microbial nanobionics. Springer, Cham, pp 35–60
Raj S, Jose S, Sumod US, Sabitha M (2012) Nanotechnology in cosmetics: opportunities and challenges. J Pharm Bioall Sci 4(3):186
Reddy BL, Jatav HS, Rajput VD, Minkina T, Ranjan A, Harikrishnan A, Veena VK, Chauhan A, Kumar S, Prakash A, Prasad R (2022) Nanomaterials based monitoring of food- and water-borne pathogens. J Nanomater. https://doi.org/10.1155/2022/9543532
Ribeiro BD, Coelho MAZ, de Castro AM (2015) Principles of green chemistry and white biotechnology. RSC, London
Rizwan M, Singh M, Mitra CK, Morve RK (2014) Ecofriendly application of nanomaterials: nanobioremediation. J Nanoparticles 2014:431787
Ruckenstein E, Kong XZ (1999) Control of pore generation and pore size in nanoparticles of poly (styrene-methyl methacrylateacrylic acid). J Appl Polym Sci 72(3):419–426
Sanghi R, Verma P (2009) A facile green extracellular biosynthesis of CdS nanoparticles by immobilized fungus. Chem Eng J 155(3):886–891
Sanyasi S, Majhi RK, Kumar S, Mishra M, Ghosh A, Suar M, Satyam PV, Mohapatra H, Goswami C, Goswami L (2016) Polysaccharide-capped silver Nanoparticles inhibit biofilm formation and eliminate multi-drug-resistant bacteria by disrupting bacterial cytoskeleton with reduced cytotoxicity towards mammalian cells. Sci Rep 6(1):1–16
Sarma H, Joshi S, Prasad R, Jampilek J (2021) Biobased nanotechnology for green applications. Springer International Publishing. (ISBN 978-3-030-61985-5) https://www.springer.com/gp/book/9783030619848
Sastry M, Ahmad A, Khan MI, Kumar R (2003) Biosynthesis of metal nanoparticles using fungi and actinomycete. Curr Sci 85:162–170
Selvakumar R, Seethalakshmi N, Thavamani P, Naidu R, Megharaj M (2014) Recent advances in the synthesis of inorganic nano/microstructures using microbial biotemplates and their applications. RSC Adv 4(94):52156–52169
Shah M, Fawcett D, Sharma S, Tripathy SK, Poinern GEJ (2015) Green synthesis of metallic nanoparticles via biological entities. Materials 8(11):7278–7308
Shash S, Ramanan VV, Prasad R (2019) Sustainable green technologies for environmental management. Springer Singapore. (ISBN: 978-981-13-2772-8) https://www.springer.com/la/book/9789811327711
Shukla P (2020) Microbial nanotechnology for bioremediation of industrial wastewater. Front Microbiol 11:590631
Siddiqi KS, Husen A (2016) Fabrication of metal and metal oxide nanoparticles by algae and their toxic effects. Nanoscale Res Lett 11(1):1–11
Singh P, Kim YJ, Zhang D, Yang DC (2016) Biological synthesis of nanoparticles from plants and microorganisms. Trends Biotechnol 34(7):588–599
Singh T, Shukla S, Kumar P, Wahla V, Bajpai VK, Rather IA (2017) Application of nanotechnology in food science: perception and overview. Front Microbiol 8:1501
Sneha K, Sathishkumar M, Mao J, Kwak IS, Yun YS (2010) Corynebacterium glutamicum-mediated crystallization of silver ions through sorption and reduction processes. Chem Eng J 162(3):989–996
Songara J, Shanker R, Singh NK (2018) Transformation of benzyl butyl phthalate by Pseudomonas putida and photocatalytic ZnO nanoparticles. Int J Chem Stud 6(4):1334–1340
Soni N, Prakash S (2011) Factors affecting the geometry of silver nanoparticles synthesis in Chrysosporium tropicum and Fusarium oxusporum. Am J Nanotechnol 2(1):112–121

Srivastava S, Usmani Z, Atanasov AG, Singh VK, Singh NP, Abdel-Azeem AM, Prasad R, Gupta G, Sharma M, Bhargava A (2021) Biological nanofactories: using living forms for metal nanoparticle synthesis. Mini-Rev Med Chem 21(2):245–265

Stillman NR, Kovacevic M, Igor B, Sabine H (2020) In silico modelling of cancer nanomedicine, across scales and transport barriers. NPJ Comput Mater 6:1–10. https://doi.org/10.1038/s41524-020-00366-8

Suresh AK, Pelletier DA, Wang W, Broich ML, Moon JW, Gu B, Allison DP, Joy DC, Phelps TJ, Doktycz MJ (2011) Biofabrication of discrete spherical gold nanoparticles using the metal-reducing bacterium Shewanella oneidensis. Acta Biomater 7(5):2148–2152

Tang H, Yan M, Zhang H, Xia M, Yang D (2005) Preparation and characterization of water-soluble CdS nanocrystals by surface modification of ethylene diamine. Mater Lett 59(8–9):1024–1027

Tanwar S, Paidi SK, Prasad R, Pandey R, Barman I (2021) Advancing raman spectroscopy from research to clinic: translational potential and challenges. Spectrochim Acta A Mol Biomol Spectrosc 260:119957. https://doi.org/10.1016/j.saa.2021.119957

Thakkar KN, Mhatre SS, Parikh RY (2010) Biological synthesis of metallic nanoparticles. Nanomedicine 6(2):257–262

Thota R, Ganesh V (2016) Selective and sensitive electrochemical detection of methyl parathion using chemically modified overhead projector sheets as flexible electrodes. Sensors Actuators B Chem 227:169–177

Ubbink J, Krüger J (2006) Physical approaches for the delivery of active ingredients in foods. Trends Food Sci Technol 17(5):244–254

Vadlapudi V, Kaladhar DSVGK (2014) Review: green synthesis of silver and gold nanoparticles. Middle-East J Sci Res 19(6):834–842

Wang L, Chen W, Xu D, Shim BS, Zhu Y, Sun F, Liu L, Peng C, Jin Z, Xu C, Kotov NA (2009) Simple, rapid, sensitive, and versatile SWNT–paper sensor for environmental toxin detection competitive with ELISA. Nano Lett 9(12):4147–4152

Weiss J, Takhistov P, McClements DJ (2006) Functional materials in food nanotechnology. J Food Sci 71(9):R107–R116

Willner MR, Vikesland PJ (2018) Nanomaterial enabled sensors for environmental contaminants. J Nanobiotechnol 16(1):1–16

Xiang L, Wei J, Jianbo S, Guili W, Feng G, Ying L (2007) Purified and sterilized magnetosomes from Magnetospirillum gryphiswaldense MSR-1 were not toxic to mouse fibroblasts in vitro. Lett Appl Microbiol 45(1):75–81

Yang R, Zhou Z, Sun G, Gao Y, Xu J, Strappe P, Blanchard C, Chenga Y, Ding X (2015) Synthesis of homogeneous protein-stabilized rutin nanodispersions by reversible assembly of soybean (Glycine max) seed ferritin. RSC Adv 5(40):31533–31540

Yuan C, Zhang T (2013) Environmental implications of nano-manufacturing. In: Green manufacturing. Springer, Boston, MA, pp 179–202

Zhang T, Lv C, Chen L, Bai G, Zhao G, Xu C (2014) Encapsulation of anthocyanin molecules within a ferritin nanocage increases their stability and cell uptake efficiency. Food Res Int 62: 183–192

Zhou Y, Yang Y, Deng X, Zhang G, Zhang Y, Zhang C, Sun W (2018) Electrochemical sensor for determination of ractopamine based on aptamer/octadecanethiol Janus particles. Sensors Actuators B Chem 276:204–210

Microbial Synthesis of Gold Nanoparticles

2

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Abstract

Due to their nanoscopic size and notable structural variations from many of their counterparts, nanoparticles exhibit qualities that make them sustainable building materials. Owing to this fact, they have become a key focus of research and possess numerous applications in biology and as well as in agriculture. One such notable example of nanoparticles is gold nanoparticles. In the domain of healthcare, these particles have also been applied in a variety of ways. They have recently been used in biological research as well because of their distinctive photothermal and surface plasmon resonance capabilities. In addition, they also possess optoelectronic properties, i.e., produce vivid colors on interaction with visible light. These properties make them highly beneficial in certain high-tech applications such as therapeutic agents, sensory probes, and drug administration in medical as well as biological uses among others. By changing the form, the gold nanoparticles (AuNPs) surface chemistry and structure traits can be modified to fit certain requirements. There are countless applications for AuNPs in the production of pharmaceuticals including antibacterial and anti-biofilm compounds, biosensors, biocatalysis, bioremediation, modification of hazardous substances exposed to the soil and atmosphere, etc. Different physiological, chemical, and biological methods can be employed to synthesize AuNPs. Of these, the most popularly used method is the usage of microorganisms. The major objective of the current chapter is to discuss the new advancements in the process of synthesizing AuNPs using bacterial, algal, and fungal sources. This chapter

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also emphasizes the categorization of AuNPs, their architecture, and their usage in the creation of diverse products.

Keywords

Nanoparticles · Surface plasmon resonance · Gold nanoparticles (AuNPs) · Photothermal properties · Optoelectronic properties · Biocatalysis · Bioremediation

2.1 Introduction

Metal nanotechnology research has gained prominence over the past 10 years and has become a revolution due to its novel system in many industrial domains (Thakkar et al. 2010). A branch of research known as nanotechnology creates microscopic particles with specific functions by combining biological, physiological, and chemical principles (Suresh et al. 2011). Due to their distinctive electrical, structural, optical, biochemical, and magnetic characteristics, noble-metallic nanoparticles such as gold, rhodium, palladium, silver, etc., and non-metallic inorganic oxides, namely, oxides of titanium and zinc have been extensively used for specific purposes (Abdel-Mohsen et al. 2012; Nalawade et al. 2014). Chemical, physical, and biological processes can all be used to synthesize nanomaterials. Industries often choose physical and chemical approaches, despite the fact that the disadvantages outweigh their benefits. They frequently require difficult operations, are expensive, and time-consuming, the labor force is required, and produce harmful by-products (Castro et al. 2014; Ngoepe et al. 2020). The development of safe, environmentally friendly processes that don't depend on using hazardous chemicals has increased to produce nanoparticles (Thangadurai et al. 2020a, b). Utilizing enzymes that are found in microorganisms or plants makes it simple to break down the toxic elements created during the nanoparticle production process. Utilizing fungus for nanoparticle synthesis has further advantages including downstream processing, manageable biomass, and economic feasibility. Additionally, fungi are highly effective secretors of extracellular enzymes. For instance, nitrate reductase primarily takes part in the reduction of nanoparticles in the context of fungus (Rajeshkumar et al. 2014; Yasmin et al. 2014; Prasad 2016, 2017, 2019a, b). One effective use of nanoparticles is in the form of nanocapsules that enclose food items. These nanocapsules hasten the absorption of nutrients from a source. Vitamins are added to food and drink using organic and polymeric nanoparticles, which don't alter the flavor or appearance (Hammami and Alabdallah 2021).

In general, there are two methods used to synthesize nanoparticles: a top-down (top-to-bottom) approach and a bottom-up (bottom-to-top) approach. Nanoparticles can be created by chemical (say, chemical reduction) and natural processes (by using plants, microbes, etc.) in a bottom-up manner by the formation of new nuclei through self-assembly of atoms that eventually evolve into tiny particles (Tran et al. 2013). The top-down strategy involves shrinking acceptable solid materials to a smaller size

by utilizing a variety of lithographic techniques, including milling, grinding, sputtering, laser ablation, etc. (Ahmed et al. 2016). Materials from a wide range are utilized to create nanoparticles and most of these pose biological hazards and are highly expensive. Also, the different techniques (physical and chemical) employed to create nanoparticles are extremely dangerous (Mittal et al. 2013). In addition, the processes used to create nanoparticles by chemical methods need maintenance of conditions like high pressure and high temperature, have a requirement of both strong and mild chemical reduction compounds, as well as protective agents like sodium borohydride, sodium citrate, and alcohols. Most of these compounds are dangerous, flammable, hard to release, and have limited production rates (Khan et al. 2015).

However, the biological method of nanoparticle synthesis makes use of living things which include bacteria, yeast, fungi, actinomycetes, plants, and algae (Thakkar et al. 2010; Prasad et al. 2016, 2018a, b; Srivastava et al. 2021; Kisimba et al. 2023; Koch et al. 2023). It is discovered that biological agents significantly speed up the rate of metal ion reduction when operating at ambient pressure and temperature levels. Recently, a unique method of synthesizing metal nanoparticles called the exploitation of microbial cells aimed at producing nanosized materials has been developed. Cells from microorganisms or plant extracts can be used in the biosynthesis process to create nanoparticles (Prasad 2014). Nanoparticles have entered an era of economic investigation, and their biosynthesis is a fascinating recent addition to the vast arsenal of different ways of synthesis (Tikariha et al. 2012). One of the topics that have been explored the most is Gold Nanoparticles (AuNPs). With 79 atoms and an atomic weight of 196.967, gold is a bright yellow valuable metal that belongs to the group of 11. It is represented by the symbol Au. Currently, much research is being done on the usage of AuNPs as catalysts, super-sensitive biological and chemical sensors, and optoelectronic devices (Villaverde 2010). These are simple to produce, show strong surface plasmon resonance, and have great chemical and thermal stability (Sau and Rogach 2010). Owing to their characteristics including oxidation resistance, biocompatibility, and more atmospheric stability, AuNPs are particularly beneficial. Their diverse capabilities have allowed them to function in a variety of industries, including pharmaceutical manufacturing, drug delivery, biosensors, and bio-meditation (Elahi et al. 2018). In sensors, its surface plasmon resonance (SPR) ability was employed to detect a variety of objects, including environmental, physiological, and military compounds. However, by adjusting the structure and size of the nanoparticles, their distinctive features may be tuned for possible applications. By suitable adjustments, the characteristics of AuNPs may be fine-tuned to increase their adaptability. So, for the advancement of nanotechnology, novel strategies for creating a morphology-controlled synthesis of AuNPs are essential.

The need to produce novel nanoparticles is growing as a result of the expanding demand for gold across numerous industries that are both cost-effective and employ green chemistry (Lengke et al. 2011). Given their numerous potential uses in recent years, including anticancer, antibacterial, antioxidant, and agricultural, AuNPs have attracted immense interest (Dorosti and Jamshidi 2016; Muthuvel et al. 2014).

AuNPs are utilized in biomedicine for a multitude of purposes, including leukemia treatment, biomolecular encapsulation, and biosensor development (Kalishwaralal et al. 2010). AuNPs, as opposed to metallic nanoparticles, have characteristics like single electron conductivity, high conductivity, dielectric function, and neutral oxidation properties, and applications for them include sinter inks, data storage, selective coatings, and quantum devices (Hughes et al. 2013). In this context, we explore the characteristics of AuNPs, how they are synthesized from different microbiological sources, how they are characterized, and what the future holds for them.

2.2 Properties of Gold Nanoparticles (AuNPs)

AuNPs are commonly used in bionanotechnology for their specific properties and range of surface functionalities. For nano-biological assemblies containing oligonucleotides, antibodies, and proteins, the simplicity of AuNP functionalization offers a flexible platform. The high surface area of AuNPs allows for a dense distribution of multifunctional moieties, making them useful platforms for medicinal medicines (Yeh et al. 2012).

AuNPs are gold-containing colloidal or aggregated particles that are encapsulated in a nontoxic, inert substance. One benefit of these particles is their synthetic versatility, which enables them to have different sizes, surfaces, and shapes. The particle's coating can also affect the solubility and stability of the particle during environmental interactions. By attaching thiols and amines to their surface, the AuNPs offer functional groups for pharmaceutical molecule labeling, targeting, and conjugation (Gerber et al. 2013; Her et al. 2017).

Considering their large specific surface area ratio, excellent biocompatibility, size, structure-related optoelectronic properties, and low toxicity, spherical AuNPs are desirable (Sau et al. 2010; Khlebtsov and Dykman 2011). The properties of AuNPs significantly differ from those of bulk gold due to the nano-scale regimen's constraint on quantum size. The electrical, magnetic, and catalytic characteristics of AuNPs are largely governed by their shape and size. For instance, spherical AuNPs exhibit a strong absorbance peak in the visible region of the electromagnetic spectrum (approximately 520 nm), but bulk gold and extremely tiny gold particles (less than 2 nm) lack this band (Tikariha et al. 2012). Important physiological properties of AuNPs include their ability to suppress or extinguish fluorescence and their surface plasmon resonance (SPR) (Yeh et al. 2012). In Fig. 2.1, some crucial characteristics of gold nanoparticles have been outlined.

2.2.1 Physical Properties of AuNPs

Localized surface plasmon resonance (LSPR), high X-ray adsorption coefficient, and radioactivity are some of the physical characteristics of AuNPs. These exceptional qualities have been extensively used in applications such as photo-thermal

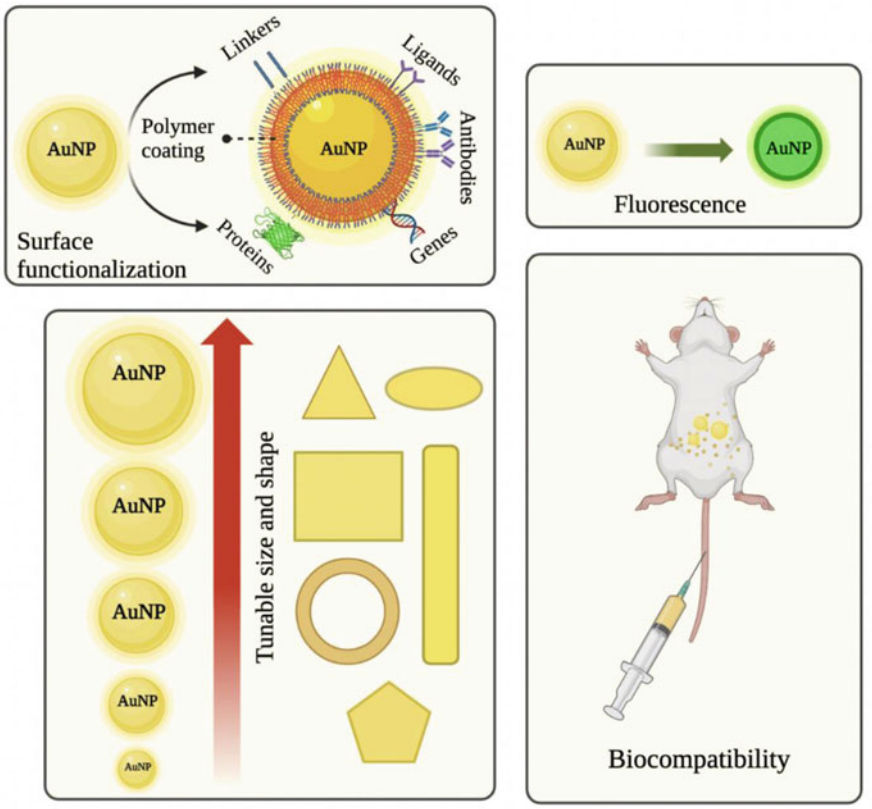

Fig. 2.1 Some important properties of gold nanoparticles (AuNPs)

treatment (PTT), imaging, photodynamic therapy (PDT), in vitro diagnostics (IVD) as well as noninvasive detection in in vivo and in situ. Their radioactivity can also be employed for radionuclide imaging (RNI) and treatment (Bai et al. 2020).

2.2.1.1 Localized Surface Plasmon Resonance (LSPR)

Electrons on a noble metal with conductive properties collectively vibrate or oscillate when they are stimulated by light; this is referred to as a "plasmon" (Qian and Nie 2010). When the input photon frequency resonates with the collective oscillation of the conduction electrons, a zone of absorption called the plasmon resonance (PR) is created (Jauffred et al. 2019). The amplification effect of the local electromagnetic field and an extinction coefficient are two significant impacts that AuNPs present with the aid of LSPR. The photo-thermal conversion efficiency, light energy absorption, and photo-chemistry conversion of AuNPs are all greatly increased as a result. These characteristics can be used in tumor diagnosis and treatment facilities for the PTT, PDT, and colorimetric assays (De Puig et al. 2015).

Surface-Enhanced Raman Spectroscopy (SERS)

SERS is a technology that is surface sensitive and makes use of molecules adsorbed on the surface of rough metals to increase Raman scattering. The SERS properties of metal nanoparticles, especially those of Au and Ag nanoparticles have greatly influenced the production of biocatalysts and biosensors. For instance, it was demonstrated that AuNPs had excellent SERS properties for identifying oral cancer cells (Quester et al. 2013; Tanwar et al. 2021; Liu et al. 2021).

Surface-Enhanced Fluorescence (SEF)

Fluorescence quenching and fluorescence enhancement are two fundamentally different outcomes of AuNPs LSPR on the signal strength of fluorescent molecules. The proximity of the fluorescence molecules to the AuNPs affects SEF (Bai et al. 2020). Due to their great stability and well-understood surface chemistry, gold nanoparticles were chosen as the SEF functional species. It is standard procedure to use various linkers to connect fluorescent molecules and AuNPs. The substance and the linker engage to alter the substance's structure, which also alters the distance between the AuNPs and the fluorescent molecules.

Photothermal Conversion

AuNPs transform the light energy of the electrons into kinetic energy upon absorbing photons. When the lattice/phonon scatters the moving electrons, some of their kinetic energy is converted into the vibrational energy of the lattice. The vibrational energy of the lattice eventually manifests as heat. This would be the alleged "Photothermal effect" (Bai et al. 2020). Plasmon-photothermal therapy, or surface plasmon absorption maxima of AuNPs, may be altered to the near-infrared region to create efficient photothermal conversion (Huang and El-Sayed 2011).

Colorimetric Responses

The detection responsiveness of colorimetric analysis for these nanoparticles reaches the nanomole level because gold nanoparticles have a high molar absorption coefficient that is substantially lower than that of the traditional colorimetric method. AuNP-based colorimetric biosensing experiments make use of the color shift of the AuNP-induced plasmon from red to blue, purple, or gray when these AuNPs are twisted to cluster the analytes (such as proteins associated with tumors, nucleic acids, or cytokines) (Zhou et al. 2015).

2.2.1.2 Radioactivity

Gold, as a metal, is a radionuclide with nuclear characteristics. Because of their advantageous nuclear characteristics, ^{198}Au and ^{199}Au can be eliminated in their entirety in the urine or liver and are commonly utilized in biomedicine. The potential of ^{199}Au to selectively attach to monoclonal antibodies piqued researchers' interest at first. This makes it possible to add more tumor-targeted monoclonal antibodies to ^{199}AuNPs, which could improve their specific activity and boost the delivery of the therapeutic payload to tumors (Bai et al. 2020). Due to the high concentration of

these radioactive atoms in AuNPs, less amount of NPs is needed to provide the desired level of radioactivity for therapy and imaging (Cutler et al. 2013).

2.2.1.3 High Atomic Number

The amount of X-ray that is absorbed rises as the atomic number approaches 53.0. This has the potential to lessen X-ray damage to healthy tissues and is an effective radiation sensitizer for oncotherapy (Hernández-Rivera et al. 2017).

2.2.1.4 Tunability

By altering the size, shape, surface chemistry, or aggregation state of gold nanoparticles, it is possible to control their optical and electrical properties.

2.2.2 Biochemical Properties of AuNPs

There are many properties that are needed to be discussed under the biochemical properties of gold nanoparticles like biocompatibility, targeting, delivery, etc. A few of them are defined and explained below.

2.2.2.1 Biocompatibility

Despite the fact that AuNPs have demonstrated potential in several biological applications, their wider use is dependent on the evaluation of their biosafety. The biological outcome of AuNPs in vivo may be evaluated by utilizing pharmacokinetics, tissue distribution, cytotoxicity, and clearance. All AuNP applications in vivo require biocompatibility, which can be intensified by surface alterations (Bai et al. 2020). Also, the notion of biocompatibility is based on the material's ability to interact appropriately with its biological environment, i.e., without causing a toxic or immunological reaction in the treated biomaterial (Kohane and Langer 2010). The size of AuNPs influences their absorption by cells as well as their cytotoxicity (Carnovale et al. 2019). Because small-sized AuNPs have a significant surface area compared to their volume, this is a hypothesis that might explain their toxicity. This increases absorption capacity and also improves the likelihood of interacting with biomolecules hence being more biocompatible (Adewale et al. 2019).

2.2.2.2 Ease of Coupling

AuNPs differ from many other nanoparticles in that they can create chemically stable interactions with groups comprising S and N. Thus, a variety of chemical ligands or polymers with specific functionalities can bind to AuNPs. AuNPs have remarkable biocompatibility, selectivity, and drug transport properties as a result of these surface modifications (Jans and Huo 2012).

2.2.2.3 Targeting

There are two approaches to targeting AuNPs: inactively (via the enhanced permeability and retention (EPR) effect) and proactively (by MPS escape) (stimuli-response and tumor cell targeting) (Bai et al. 2020). For example, the internal

blood arteries and lymphatic vessels of the tumor are damaged as a result of its rapid growth. Due to their effectiveness in passing through the tumor arteries and concentrating therein, AuNPs of a given range have been employed for tumor imaging and treatment (Zhang et al. 2012).

2.2.2.4 Delivery

Drug and gene delivery approaches can use AuNPs since they are nontoxic carriers. Recently, AuNPs have become a desirable alternative for delivering a variety of payloads to their destinations. Small drug molecules or huge macromolecules like DNA, RNA, or proteins could be the payloads. To deliver and unload drugs, AuNPs take advantage of their special chemical and physical capabilities. First, the gold core is basically inert and nontoxic. The ability to create monodisperse nanoparticles with core diameters ranging from 1 to 150 nm is another benefit. Their easy functionalization, typically through thiol connections, adds even more versatility. Additionally, their photo-physical capabilities could cause medication delivery at a distant location (Ghosh et al. 2008).

2.3 Microbial Synthesis of AuNPs

AuNPs offer promise as a crucial element and fundamental building block for cutting-edge technology in the twenty-first century since they are the most stable mono-metallic nanoparticles. Because of its fully filled d-band, gold is classified as a noble metal and is very inert in its bulk condition. It is proven to be a useful substance for catalysis nevertheless, because of its size, shape, and nanoscale crystalline structure. It has found extensive use in optics, electronics, catalysis, manufacturing, and biological utility because of these novel features (Srivastava et al. 2013). Typically, chemical synthesis demands the addition of a stabilizing agent once a reducing agent (often citrate) has been added, whereas physical techniques of generating gold nanoparticles typically include burning Au at decreased pressure to form Au vapor (Genç et al. 2011). These chemical methods are effective, but they come at a cost of expensive reduction and capping agents, dangerous solvents, and time-consuming process control. Microbial systems have found a remarkable role in the creation of nanoparticles due to their innate ability to detoxify metal salts via reduction, which may be carried out in the extracellular environment or intercellular by biomagnification, precipitation, biosorption, and biomineralization (Srivastava et al. 2013). Numerous enzymes are released by microorganisms, and all these enzymes are essential for the production of nanoparticles (Tomar and Shrivastava 2014). Therefore, it is essential to improve this environmental synthesis method in order to understand the underlying process and develop a useful prototype for the bio-inspired manufacture of AuNPs.

Microorganisms can be used as promising biofactories to synthesize AuNPs, and it has a lot of potential for being a relatively new topic of study. Furthermore, it can be easily scaled up for large-scale synthesis and is economical, time-saving, and

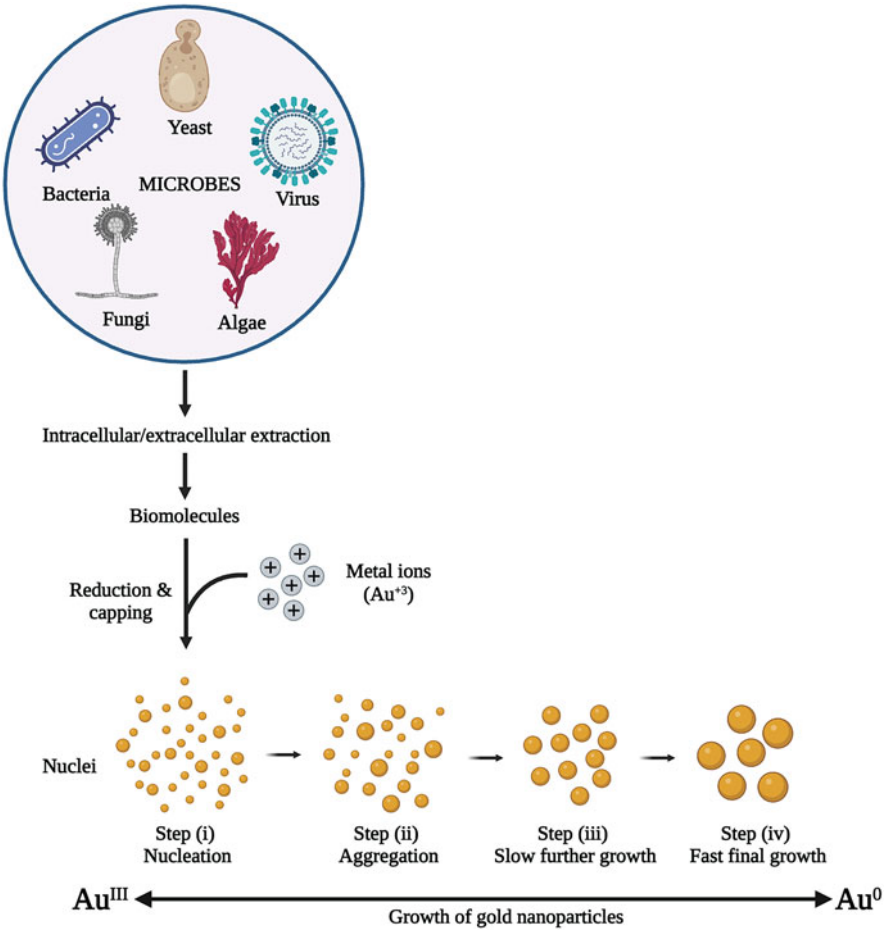

Fig. 2.2 Synthesis of AuNPs using microbial sources. The formation of NPs by this method includes capturing the metal either internally or externally followed by enzymatic reduction and capping. The enzyme acts as the metal's nucleation site, supplying electrons for reduction

environmentally benign. The synthesis of AuNPs from microbes has been discussed below and has also been depicted in Fig. 2.2.

2.3.1 Synthesis of AuNPs from Bacteria

Prokaryotes have drawn the greatest attention among microorganisms in the field of AuNP production. *Bacillus subtilis* 168 was the first microbe to synthesize AuNPs, and the results showed that the cell wall of this organism contained octahedral NPs measuring 5–25 nm in size (Beveridge and Murray 1980). Prokaryotic microbes

Rhodopseudomonas capsulata, which is known to be among the ecologically and environmentally significant microorganisms typically found in the natural environment, was researched for its ability to reduce Au^{3+} ions in a single step at ambient temperature. Under the lower initial pH, gold nanoplates in particular were created (He et al. 2007). Recent studies have attempted to assess and compare the nanotoxicity of AuNPs generated in vitro by two distinct bacterial species. *Bacillus cereus* and *Fusarium oxysporum* are used to generate AuNPs, and X-ray diffraction (XRD) and transmission electron microscopy, with visual spectral investigations, were used to corroborate this (Pourali et al. 2017). The thermophilic bacteria *Geobacillus* strain ID17 has been reported to produce gold nanoparticles. Cells exposed to Au^{3+} changed from being colorless to having a deep purple hue. The build-up of intracellular gold nanoparticles is shown by this shift in color (Correa-Llantén et al. 2013). Table 2.1 gives an overview of the bacterial production of AuNPs.

2.3.2 Synthesis of AuNPs from Fungi

Since they are easier to cultivate in the lab and on an industrial scale and produce a significant amount of proteins, fungi are thought to be more feasible for synthesizing NPs in large quantities (Das and Marsili 2010; Aziz et al. 2016). It is stated that the plant pathogenic fungus, namely, *Fusarium oxysporum* f. sp. *cubense* JT1 (FocJT1) may produce gold nanoparticles quickly and extracellularly (Thakker et al. 2013). It has been reported that fungi like *Verticillium* sp. can be used to synthesize AuNPs. In the same way, the endophytic fungus *Colletotrichum* from geranium leaves also produced AuNPs. Various shapes and sizes of AuNPs are produced from different species of fungi such as *Trichothecium*, *Aspergillus niger*, *Volvariella volvacea*, *Rhizopus stolonifer*, and so on (Iranmanesh et al. 2020). A summary of the fungal production of AuNPs is provided in Table 2.1.

2.3.3 Synthesis of AuNPs from Algae

Researchers are working on algae, a photoautotrophic, eukaryotic, aquatic, oxygenic microbe that can collect heavy metals, to develop more environmentally friendly methods to synthesize nanoparticles (Castro et al. 2013). Fucoidans are polysaccharides that marine brown algae discharge from their cell walls. These fucoidans are used to successfully synthesize gold NPs as a substitute for chemical processes (Soisuwan et al. 2014). The utilization of the marine alga *Sargassum wightii* has been described as a systematic way to quickly produce extracellular gold nanoparticles that are extremely stable (Singaravelu et al. 2007). The processes through which *Chlorella vulgaris* biomass reduces gold in gold (III) chloride solutions in the algal system and XAS have been used (Tikariha et al. 2012). Using *Galaxaura elongata* (genus of thalloid red algae) extract in an aqueous

Table 2.1 Synthesis of gold nanoparticles using various microbial sources

S. No.	Source	Intracellular/ extracellular	Size (nm)	Characterization methods	Shape of AuNPs	Potential applications	References
1.	*Escherichia coli K12*	Extracellular	50	UV—Vis spectrophotometry, AFM, TEM, XRD, FTIR, and SDS-PAGE	Circular with catalytic activity during reduction of 4-nitrophenol	Catalysis and bioremediation studies	Srivastava et al. (2013)
2.	*Lactobacillus casei*	Extracellular	29.6	SEM, TEM, and EDS	Various shapes	Rheumatology, drug delivery, and other medical applications	Kato et al. (2019)
3.	*Shewanella algae*	Intracellular	9.6	TEM, SAED FTIR, UV—Vis spectrophotometry	Spherical in shape, crystalline	Optical applications, surface-enhanced Raman spectroscopy, or cancer hyperthermia.	Ogi et al. (2010)
4.	*Shewanella oneidensis*	Extracellular	2–50	UV-vis spectroscopy, FTIR, XRD, EDX, TEM	Spherical in shape	Medical research and catalysis	Suresh et al. (2011)
5.	*Stenotrophomonas maltophilia*	Intracellular	40	Electrophoresis, UV-vis spectroscopy, TEM, and FTIR	Spherical in shape	Drug delivery and gene transfer	Nangia et al. (2009)
6.	*Sargassum* myriocystum	Extracellular	15	FTIR, TEM, SEM–EDAX, and XRD analysis	Stable, triangular, or spherical in shape and highly crystalline	Treatment of cardiovascular disorders	Dhas et al. (2012)
7.	*Rhodopseudomonas capsulata*	Extracellular	10–20	UV-vis spectroscopy, TEM, FTIR, EDX, SDS-PAGE	Spherical in shape with a polycrystalline structure	Microelectronics, optoelectronics, and nanoscale electronic devices	He et al. (2008)
8.	*Pseudomonas aeruginosa*	Extracellular	20–80	TEM and UV-vis spectroscopy	Spherical in shape	Good labels for sensors, ultrasound treatment	Singh and Kundu (2014)

(continued)

Table 2.1 (continued)

S. No.	Source	Intracellular/ extracellular	Size (nm)	Characterization methods	Shape of AuNPs	Potential applications	References
9.	*Azospirillum brasilense*	Extracellular	5–300	TEM and UV-vis spectroscopy	Nanospheres and nanoprisms	Biomedical applications	Kupryashina et al. (2013)
10.	*Pseudomonas fluorescens*	Extracellular	50–70	TEM, Ultraviolet spectroscopy, SEM, FTIR	Uniform size and stability	Wound healing, medical and electronic applications	Rajasree and Suman (2012)
11.	*Pseudomonas denitrificans*	Extracellular	25–30	UV–vis spectroscopy, FTIR, TEM, and XRD	Face centered cubic	Biosensors and optoelectronics	Mewada et al. (2012)
12.	*Pseudomonas veronii*	Extracellular	5–25	UV–vis spectroscopy, TEM, FTIR, and XRD	Various shapes	Antibacterial activity against most human pathogens	Baker and Satish (2015)
13.	*Geobacillus sp. strain ID17*	Intracellular	5–50 and 10–20	TEM, EDX, FTIR, UV-vis spectroscopy	Quasi-hexagonal with good surface bioactivity	Biomedical and healthcare applications	Correa-Llantén et al. (2013)
14.	*Geobacillus stearothermophilus*	Extracellular	6–14	UV–vis spectroscopy, FTIR, TEM, and XRD	Spherical in shape	Improving the efficiency of PCR (Polymerase Chain Reaction)	Fayaz et al. (2011), Girilal et al. (2013)
15.	*Marinobacter pelagius*	Extracellular	10	UV–vis spectroscopy, TEM, DLS, FTIR	Spherical in shape with occasional nano-triangles		Sharma et al. (2012)
16.	*Vibrio alginolyticus*	Extracellular	100–150	SEM, TEM, and FTIR	Irregular shapes	Cancer therapy and other biomedical applications	Shunmugam et al. (2021)
17.	*Streptomyces fulvissimus*	Extracellular	20–50	UV-Visible spectroscopy, TEM, XRD and EDX		Offers an environmentally safe industrial production of AuNPs	Soltani et al. (2015)

18.	*Streptomyces viridogens strain HM10*	Intracellular	18–20	TEM, XRD, UV-Visible spectroscopy	Spherical and rod-shaped		Balagurunathan et al. (2011)
19.	*Klebsiella pneumoniae*	Extracellular	35–65	UV–vis spectroscopy, XRD, FTIR, TEM, and SEM	Spherical in shape	Medical and pharmaceutical applications	Kumar et al. (2014), Malarkodi et al. (2013)
20.	*Spirulina platensis*	Extracellular	5	UV–vis spectroscopy, TEM, EDX, FTIR, Raman Spectroscopy, and Fluorescence Spectroscopy	Uniform shape with antibacterial activity against *Staphylococcus aureus* and *Bacillus subtilis*.	Possess antibacterial activity and hence can be used in antibiotics and while treating infectious disorders caused by gram-positive bacteria.	Suganya et al. (2015)
21.	*Magnetospirillum gryphiswaldense* MSR-1	Intracellular		TEM, XRD and XPS	Spherical in shape		Cai et al. (2011)
22.	*Micrococcus luteus*	Extracellular	6–50	UV–vis spectroscopy, TEM, FTIR, DLS	Spherical in shape	Immunological studies	Arunkumar et al. (2013)
23.	*Acanthella elongata*	Extracellular	7–20	UV–vis spectroscopy, TEM, FTIR, and XRD	Polydispersed spherical nanoparticles	Applications in biomedicine and pharmaceuticals, as well as for extensive commercial manufacturing	Inbakandan et al. (2010)
24.	*Stoechospermum marginatum*	Extracellular	18.7–93.7	FTIR, SEM, TEM, XRD, UV–vis spectroscopy	Mostly spherical, occasionally triangular and hexagonal	Effective against bacterial pathogens	Rajathi et al. (2012)
25.	*Candida albicans*	Extracellular	20–80	TEM and AFM	Spherical and non-spherical in shape	Differentiating between malignant and normal cells in cases of liver cancer	Chauhan et al. (2011)

media under normal air conditions, it has been discovered that stable Au nanoparticles develop quickly (Abdel-Raouf et al. 2017).

2.3.4 Synthesis of AuNPs from Viral Templates

Recently, viruses were employed as a restricted template to regulate the synthesis of nanoparticles. In addition to their high symmetry, confined cages, robust functioning protein capsids, distinctive structural designs, recurring patterns, and ability to be modified by molecular biology, viruses provide excellent templates. The wild-type *tobacco mosaic virus* (TMV) and *cowpea chlorotic mottle* virus are typical examples of viral templates (CCMV). These models offer great beginning points for the bioinspired synthesis of various nanoparticles (Wnęk et al. 2012).

2.4 Characterization of Gold Nanoparticles (AuNPs)

Numerous ways have been employed to characterize gold nano-alloys and AuNPs produced by microbes. But to characterize something, a set of procedures rather than a single methodology is required (Shedbalkar et al. 2014). Some of the techniques for characterization are discussed below.

2.4.1 Visual Color and UV-Visible Spectroscopy

The surface plasmon resonance principle (SPR) is used to characterize these gold nanoparticles by changing their color visibly. In the instance of gold, the color shifts from a deep red to a purplish color as the particle size increases. They exhibit LSPR, a phenomenon in which certain wavelengths in the visible range of the electromagnetic spectrum are absorbed while others are reflected, causing the wavelength that is released to mirror its color. This causes varied color changes. UV-visible spectroscopy can be utilized to detect the absorbance of these color shifts (Zhang et al. 2016). The resulting peaks also show how the nanoparticles' stability grows with time (Soltani et al. 2015).

2.4.2 SEM Analysis

Scanning electron microscopy (SEM) was used to validate the formation of AuNPs and analyze the morphology of the generated AuNPs (Dzimitrowicz et al. 2019). Different shapes of the gold nanoparticles, including rectangles, squares, cubic shapes, and triangles, have been identified (Rajeshkumar 2016). Purified AuNPs were added to solutions containing DDW, which were then placed on carbon-sticky conductive tape and allowed to evaporate. The magnification range for the SEM

pictures was 15,000 to 18,000 times. A 20–25 kV accelerating voltage was used (Dzimitrowicz et al. 2019).

2.4.3 TEM Analysis

As part of the sample preparation for TEM examination, a drop of AuNP solution is put into a carbon-coated copper grip, after which it is cooled at ambient temperature, whereas the resulting mixture is wiped away using paper towels. By using TEM, the size, particle shape distribution, and elemental makeup of the AuNPs were measured (Montes et al. 2011). Centrifugation-based AuNP purification before measurements was unnecessary because of the excellent resolution of TEM. The length of nanorods, the diameter of nanostars, the height of triangular NPs, and the diameter of spherical NPs were all calculated to estimate the size of the AuNPs (Dzimitrowicz et al. 2019).

2.4.4 EDX/EDS Analysis

Energy-dispersive X-ray spectroscopy (EDX) is a technique for determining the components in a sample or characterizing its chemical composition. It may be used to calculate how many gold nanoparticles were made from a thin layer of bacterial biomass (Rajeshkumar et al. 2013). The present AuNPs approach is simple and appropriate; it permits mono-crystalline gold nanoparticles, practically narrows diameter, and makes it simple to assess the dispersion of nanoparticles using EDX (TYAl-Abdullah et al. 2020).

2.4.5 AFM Analysis

Sub-nanometer resolution 3D characterization of nanoparticles is possible using the atomic force microscope (AFM). The nanoparticles obtained on bioreduction were dissolved in either water or ethanol to create the sample, which was then dropped onto a previously cleaned silicon substrate. The AFM imaging was carried out using phosphorus-doped silicon probes. It was given time to gradually dry. The sample's Si- substrate was employed for AFM imaging and further experiments (Philip and Unni 2011).

2.4.6 FTIR Analysis

The existence of various functional groups in the generated AuNPs was determined using Fourier transform infrared (FTIR) analysis. The potential biomolecules that would be in charge of capping, which would effectively stabilize the gold nanoparticles, were further identified using FTIR measurements (Elavazhagan and

Arunachalam 2011). After being thoroughly dried and powdered with KBr pellets, the improved suspension which contains the nanoparticles was studied (Jayaseelan et al. 2013).

2.4.7 XRD Analysis

Gold nanoparticle crystalline structure was ascertained using X-ray diffraction (XRD) analysis. The apparatus used to prepare the samples operated with Cu Kα radiations at a voltage of 20 mA and was effective at a voltage of 40 kV. On a glass surface, a drop-coating of the reducing gold nanoparticle solution had to be performed (Bennur et al. 2016).

2.4.8 DLS Analysis

Dynamic light scattering (DLS) is a popular method of analyzing colloids and nanoparticles to determine their hydrodynamic size in a liquid environment. For research on bioconjugation and biomolecular binding involving gold nanoparticles, DLS can be a very useful and effective method. DLS carefully evaluated and monitored the stability and quality of the manufactured conjugates, as well as the process of conjugation between a protein and gold nanoparticles under various experimental circumstances (Jans et al. 2009).

2.4.9 XPS Analysis

An approach for examining the surface chemistry of a nanoparticle is called X-ray photoelectron spectroscopy (XPS), often known as electron spectroscopy for chemical analysis (ESCA). A material's atomic state, chemical composition, and electronic state can all be determined using XPS. Since the binding affinity and strength of the photoemission peak, the XPS is largely used to analyze the superficial properties of nanoparticles, including elemental identification, chemical state, and amount of a detected element (Rani and Shanker 2022).

2.5 Mechanism of Synthesis of AuNPs

Depending on where they are produced, microbes can produce either intracellular or extracellular nanoparticles. The intracellular mechanism enables certain ions to be carried into the cell wall which is negatively charged, where they are electrostatically attracted to the positively charged metals and diffuse through the negatively charged cell wall. The poisonous metals are then changed to nontoxic metal nanoparticles by enzymes found in the cell walls of microbes. The extracellular method transforms the metallic ions into metallic nanoparticles with the use of enzymes such as nitrate

reductase or hydroquinone, which are produced by various fungi or prokaryotic organisms. The phenomenon known as "biosynthesis" occurs through enzymatic or biological mechanisms. These environmentally friendly procedures are known as green and clean technology, and they may be utilized to produce metal nanoparticles from microbial cells more effectively (Shedbalkar et al. 2014). Because of their capacity to handle stress, microorganisms may thrive and live in environments with high metal ion concentrations (Moghaddam 2010). Metal binding, vacuole compartmentalization, or volatilization (tuning metals into volatile forms) are some of the detoxifying mechanisms used by bacteria. When bacteria are exposed to metal stresses, they employ a variety of mechanisms to get rid of the poisonous heavy metals to survive. In addition to reducing hazardous metal ions to nontoxic ions and accumulating the metal ions inside the cells, it entails an active efflux of metallic ions across the cell membrane. Ion channels, endocytosis, carrier-mediated transport, ion pumps, or lipid penetration all play a role in the inflow of heavy metals like gold, silver, lead, nickel, and other metals (Issazadeh et al. 2013).

Owing to their resistance to oxidation, immunogenicity, and stability, gold nanoparticles (AuNPs) are a popular research tool. When AuNP is synthesized chemically, hazardous residues are frequently left behind, raising environmental concerns. However, the natural synthesis of AuNPs in living microorganisms and associated cell-free extracts is a low-cost and ecologically beneficial procedure (Kitching et al. 2015). The large surface area of AuNPs enables a robust distribution of multifunctional moieties, making them useful platforms for therapeutic medicines (Yeh et al. 2012). A new and environmentally acceptable practice for the synthesis of metal NPs is the exploitation of microbial cells. Growing microorganisms in culture media, collecting biomass from the medium, and then incubating the biomass with subinhibitory concentrations of target metal salts are all steps in the biosynthetic process of metal nanoparticles. The demand for environmentally acceptable and cost-effective strategies for nanoparticle synthesis is gaining demand in biological systems that do not require toxic chemicals as by-products (Barabadi et al. 2014).

There are several techniques for producing gold nanoparticles, involving chemical, sonochemical, and photochemical methods. The most popular chemical process involves a reducing agent like sodium citrate, sodium borohydride, ascorbic acid, or block copolymers to precipitate the AuNPs in an aqueous solution from a dissolved gold precursor, such as $HAuCl_4$. Certain reducing agents (e.g., sodium citrate and block copolymers) also function as stabilizers, even though additional stabilizing agents are typically needed to avoid agglomeration or continued expansion of the particles. Different chemical components included in biogenic compounds may operate as reducing agents, interacting with metal ions to reduce them and synthesize metal nanoparticles (Hulkoti and Taranath 2014). For example, Song et al. (2011) generated thiol-capped AuNPs in the 1–6 nm range in various organic solvent polarities. *Rhodopseudomonas capsulata* was used to synthesize AuNPs extracellularly, and a mechanism for this process was also described (Tikariha et al. 2012). It is well known that the bacterium *R. capsulata* secretes the cofactor NADH and NADH-dependent enzymes. It was discovered that the NADH-dependent reductase served as the electron carrier and that the bioreduction of gold ions was started by the

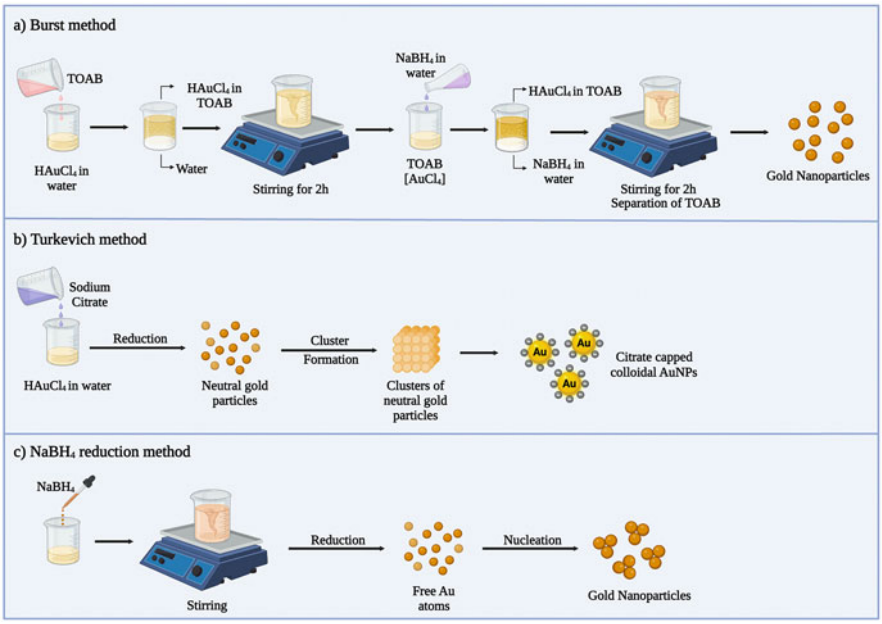

Fig. 2.3 A thorough schematic depiction of the steps needed to produce AuNPs through. (**a**) Burst method (**b**) Turkevich method and (**c**) $NaBH_4$ method

transfer of electrons from the NADH. The next step involves the reduction of the gold ions (Au^{3+}) to elemental gold (Au^0), which produces AuNPs.

Turkevich technique is a promising technique when compared to others in the chemical synthesis of GNPs. In the Turkevich technique, a moderate reducing agent for instance citrate, tannic acid (Ahmad 2014), and ascorbic acid (Larm et al. 2018) decreases Au^{3+} ions in an aqueous solution. This technique results in AuNPs that are biocompatible and of relatively modest size (Fig. 2.3). The primary disadvantage of this technique is the stringent adherence to a highly regulated manufacturing protocol (temperature, pH, and concentration) required to generate monodisperse particles with the desired sizes (Hussain et al. 2020). A modified Turkevich method using ascorbic acid was used to synthesize colloidal GNPs (Malassis et al. 2016).

The Burst method converts $HAuCl_4$ into AuNPs in a nonaqueous solution utilizing tetraoctyl ammonium bromide as a catalyst for the phase-transfer reaction and sodium borohydride to transform Au(III) into Au(0) as shown in Fig. 2.3. Without a doubt, the Burst procedure for synthesizing gold nanoparticles with thiol stabilization is a useful method; however, the functional groups are constrained by the stability of thiols. Since these alkanethiol-protected AuNPs have stronger thiol-gold linkages and van der Waals attractions between the nearby ligands, they are more stable than most other AuNPs. For the synthesis of each functionalized target, it is frequently necessary to identify a specific set of reaction circumstances, and most of the methods in these studies are always associated with dangerous

synthesis processes (Sharon et al. 2017). The Faraday two-phase system served as a model for the Brust approach. In the $NaBH_4$ reduction method, citrate solely serves as a stabilizing agent, with $NaBH_4$ serving as the reducing agent (Fig. 2.3). The reaction conditions in a single aqueous system regulate the rate of the reaction. To obtain AuNPs with homogeneous size distribution, several reaction parameters are being examined (such as reaction temperature, reactant concentration, and addition rate for $NaBH_4$) (Fountoulaki et al. 2014).

While spherical AuNPs may be produced using the Turkevich and Brust procedures, AuNPs can also be found in a variety of nanostructures, including rods, cubes, tubes, and more. Seed-mediated growth is a frequently used method for producing AuNPs in different forms (Ziegler and Eychmuller 2011). The basic idea behind this procedure is to start with the reduction of Au salts with a strong reducing agent, like sodium borohydride, to produce seed particles. The seed particles will be then introduced to a metal salt solution together with a mild reducing agent (ascorbic acid) and a structure-directing agent to stop additional nucleation and speed up the development of AuNPs in an anisotropic state. The morphology of gold nanostructures may be changed by adjusting the concentration of seeds, reducing agents, and structure-guiding agents.

It was discovered that physicochemical factors including temperature, pH, and the concentration of substrate had an impact on the intracellular synthesis of AuNPs (Castro et al. 2014). By further adjusting these characteristics, monodispersity can be attained. However, in-depth research on optimization has not yet been carried out. It has been proposed that the creation and stability of AuNPs depend on proteins and the amino acid residues found in proteins, such as cysteine, tyrosine, and tryptophan (Xia et al. 2010). Proteins with free amino or cysteine groups can be attached to the AuNPs to stabilize them as a response (Bonomi et al. 2011). Tyrosine can sometimes attach to the surface of gold through amine groups and the reduction of silver ions takes place at high pH, resulting in the formation of gold core–silver shell nanostructures (Zhou et al. 2018). By understanding the metabolic processes that result in the biomineralization of gold, a reasonable method for AuNPs synthesis may be developed (Das and Marsili 2010).

In *Trichothecium* sp., different growth conditions including static, and shaking were used to regulate the synthesis of AuNPs. AuNPs were produced extracellularly and intracellularly under shaking and static conditions, respectively (Shivaji et al. 2014). Controlling yeast strain activity and cellular development conditions leads to the synthesis of AuNPs (Kalaivani et al. 2020). The bioreduction of Au^{3+} ions to produce the AuNPs in *F. oxysporum* and *R. capsulata* is thought to be carried out by species-specific NADH-dependent reductases (Kang et al. 2017). *Pseudomonas aeruginosa* bacterial cell supernatants have been employed for the extracellular synthesis of AuNPs and the reduction of Au ions (Srivastava and Constanti 2012). It has been discovered that *Bacillus subtilis* 168 can convert water-soluble Au^{3+} ions to Au^0 and create 5–25 nm octahedral nanoparticles inside cell walls (Afifudin et al. 2011).

2.6 Applications of AuNPs

There have been several applications for gold nanoparticles over the past few decades, including drug delivery, biosensors, cosmetics, and various medicinal applications. A wide variety of microorganisms are susceptible to the bactericidal effects of gold nanoparticles, which act as powerful antibacterial agents (Sathiyaraj et al. 2021). Pharmaceutical products including antibacterial agents, the creation of biosensors, delivery of specific drugs for the treatment of cancer, bioremediation, etc. all employ gold nanoparticles. However, these techniques are overpriced and at odds with the natural environment. Pure microorganisms recently underwent a quick shift that made them nontoxic, eco-friendly, and biocompatible. These properties enable them to be utilized in the physiological and chemical procedures for the creation of gold nanoparticles. The following are some of the major applications of AuNPs in diverse fields:

1. AuNPs are extensively used in photodynamic therapy, a treatment for oncological diseases, owing to their tendency of binding to amines, disulfides as well as cells. Thus, they promote effective penetration into tumor cells (Shedbalkar et al. 2014).
2. AuNPs play a noteworthy role in the therapy of cancer because of their biocompatibility and potent interaction with soft bases like thiols. For instance, AuNPs may be used to treat epithelial ovarian carcinoma, a frequent condition affecting the female reproductive system. Vascular endothelial growth factor (VEGF) is essential for the formation of tumors and the advancement of ovarian cancer, and AuNPs have the power to stop the spread of ovarian growth and metastasis (Rai et al. 2011; Arvizo et al. 2011).
3. The high-intensity β-emission given by AuNPs makes them effective at destroying tumor cells and tissue. To have the same therapeutic impact with less AuNP injection, target-specific AuNPs were produced. The accumulation in tumor tissue was boosted using nanocomposite technology or tumor-specific antibodies (Chanda et al. 2017).
4. For a very long period, drug molecules have been delivered into cells using gold nanoparticles. Utilizing particle ingestion or gene guns, the molecules are first adsorbed on the surface of AuNPs before being delivered to the cells. Drug delivery is one of the most notable benefits of AuNPs, along with their unique optical and physicochemical properties, biocompatibility, and adaptability. They offer controlled distribution of drugs and serve as high-density drug reserves (Siddique and Chow 2020; Wang et al. 2020).
5. They also serve as efficient nanocarriers of plasmid DNA (pDNAs), peptides, proteins, and short RNAs (siRNAs). Stable gold nanorods are chosen as more effective drug delivery systems when compared to circular nanoparticles (Zhang et al. 2011).
6. Due to their capability for adsorptive behavior and electron transmission, biosensors have also been created using AuNPs (Yu et al. 2016).

7. AuNPs have been used to identify dangerous environmental contaminants. For instance, the use of AuNPs in the identification of copper, which is normally essential for physiological functions in the body but when present at levels above normal, becomes toxic and results in Wilson's disorder, a hereditary condition (Wang and Yu 2013).
8. AuNP-based technologies are also developed for environmental remediation like water purification and pollution control. According to research, bimetallic gold-palladium nanoparticles can be utilized as an active catalyst to transform the primary groundwater pollutant trichloroethene (TCE) into a nontoxic form (Bansal et al. 2020).
9. AuNPs show excellent catalytic activity. For instance, AuNPs synthesized from *Pogestemon benghalensis* and *Sesbania grandiflora* extract served as efficient photocatalysts in the reduction of methylene blue (Das and Velusamy 2014; Paul et al. 2015).
10. Due to their superior labeling properties and the fact that several methods, including electric conductivity, and optical absorption luminescence, can be used to detect them, AuNPs have been employed largely for labeling and bioimaging applications for biosensors. AuNPs are excellent contrast agents (Cole et al. 2015). To find and monitor AuNPs in dissected tissues and living animals, Chen and colleagues developed a PEGylated AuNP system (Chen et al. 2015).
11. In technological applications, AuNPs were created to enhance computer memory (Draz and Shafiee 2018). A 3D computer memory device has been made using layers of AuNPs to expand the memory on a single chip's capacity. An organic nonvolatile switchable memory is yet another advancement in computer memory employing AuNPs which are constructed of plastic and gold (Lee 2010).

2.7 Challenges and Future Prospects

Nanomaterials are being employed more and more in industry, and soon they will take the place of poisonous or harmful chemicals that are currently used as antimicrobial agents. The creation of quick, affordable, biocompatible, and environmentally friendly processes has shown great promise for producing biogenic colloidal gold nanoparticles. Many of the underlying chemical mechanisms that result in the production of biologically active nanoparticles are probably present, regardless of the fact that they are not yet fully understood. The changed synthesis and higher production of these NPs can both benefit from the investigation of these routes (Ovais et al. 2018).

- Future studies on microorganism-produced AuNPs should work to establish trustworthy experimental methodologies for the creation of monodispersed AuNPs of a certain concentration.

- The research should also concentrate on improving the conditions under which microorganisms may grow and the physicochemical variables, including pH, culture age, temperature, biomass production, salt content, etc., that have an impact on synthesis. The massive microbial production of monodispersed AuNPs requires more investigation.
- Clarifying the mechanism of AuNPs produced by microbes is one of the complex challenges in nanotechnology. But it is important to investigate the precise function of the biomolecules and reductases involved in the reduction of the gold ions.
- Currently, AuNPs are utilized as labeling material in therapeutic and diagnostic tools for a wide range of diseases. PPR diagnostic strips were successfully created by combining the peste des petits ruminants (PPR) antibody with the colloidal AuNPs production (Verma et al. 2014).
- Recently, *Woodfordia fruticose*-produced gold nanoparticles were copolymerized with carbopol to create an ointment. The results revealed that collagen fibers had a high quantity of hydroxyproline, which increased their tensile strength and increased the healing process (Raghuwanshi et al. 2017).
- Indeed, as innovative nano-systems with decreased systemic toxic effects and greater therapeutic effectiveness, gold nanoparticles have surpassed the standard biochemically generated AuNPs. By acquiring the methods used in the production of AuNPs, tremendously innovative possibilities and fresh insights into green chemistry enabled tuning and improvement (Asiya et al. 2020).
- The manufacture of microbiologically derived gold nanoalloys and nanoconjugates is an intriguing area to investigate, as is the analysis of their symbols and structures. The synthesis of viral AuNPs should be carried out utilizing a variety of anti-toxins, antibodies, peptides, proteins, and biomolecules with equal emphasis being placed on the coupling of bimetallic and trimetallic gold amalgams via microbial origin (Chowdhury et al. 2022).
- The diameter of AuNPs is highly scrutinized, and smaller ones, within certain boundaries, have stronger antibacterial activity. The shape of AuNPs is still important to research, nevertheless. Spherical AuNPs have the ability for drug adsorption which is significantly influenced by the proportion of surface area and volume (Tian et al. 2021).
- Algae may be employed to develop organic nano factories for synthesizing gold nanoparticles. Algae may be utilized to create organic nano factories for making gold nanoparticles. Metal nanoparticle synthesis is the only type of nanomaterial that can currently be produced with algal assistance (Khan et al. 2019).
- AuNPs have indeed recently been employed to observe a chlorophyll fluorescence quenching effect in vivo (Falco et al. 2011). Chlorophyll fluorescence is a measurement of plant photosynthetic efficiency that may be used to identify plants, quantify chlorophyll levels, and evaluate how environmental stresses and stimuli affect plant development.
- The fabrication of gold nanoparticles using organic elements is thought to improve their therapeutic qualities, including their anti-microbial and anti-cancer properties as well as their role as reducing and stabilizing agents for the creation

of nanoparticles. This method of gold nanoparticle synthesis is thought to be more economical and may produce AuNPs with fewer or no adverse effects due to the reduced need for residual chemicals in the manufacture of AuNPs (Vines et al. 2019).

- The next decade is expected to see a revolution in nanomedicine as cancer theranostics is made possible by biosynthesized multifunctional gold nanoparticles. Due to their great biocompatibility and biodegradability, gold nanoparticles produced by biosynthesis are becoming increasingly effective in the treatment of malignancies (Ovais et al. 2017).
- Both early stage breast cancer therapy and palliative care for more progressed breast tumors can benefit from the use of AuNPs as most breast cancers are found very close to the skin's surface, where they are easily reached (Zhang 2015).

2.8 Conclusion

In the present chapter, a full explanation of the process for producing gold nanoparticles using microorganisms such as fungi, bacteria, yeast, and algae has indeed been provided. It is known that a number of microbe species can absorb metals in their natural environments, turn them into constituent nanoparticles, and clean the surrounding area at the same time. The majority of the metals, chiefly gold, are toxic to microbial cells as a result of which, it has been commonly documented that a stress reaction causes metals to transform into their fundamental nano-forms of the organism to either eliminate or alleviate the harmful effect of these metals. Bacteria secrete functional reducing agents and enzymes that convert hazardous ions into benign substances and this characteristic could be crucial in the creation of nanoparticles. Though it cannot be ruled out, precipitation may have contributed to the formation of the nanoparticles. Measures to acquire better control over particle size, properties, and monodispersity of AuNPs are still under development. AuNPs possess a variety of qualities that make them effective instruments for use in bionanotechnology. These systems are advantageous for numerous applications due to the extensive range of surface functionality and bioconjugates, as well as the exceptional physical characteristics of AuNPs. Furthermore, highly sensitive and focused diagnostic devices may also be developed by modifying the surface monolayer of the target analytes. Due to the regulated release of the medications deposited on their surfaces and the high surface loading of pharmaceuticals and genes, AuNP-based delivery vectors have also demonstrated immense potential in therapeutics. The green synthesis of AuNPs using microbes serves as a remarkable alternative to a nontoxic, clean, and environmentally friendly procedure for AuNP synthesis and has a multitude of advantages over conventional techniques. The majority of the research on AuNP biosynthesis is currently in the discovery phase. A large focus on the biosynthesis of AuNPs with adjustable size and shape is still not being focused, despite the widespread commercial application of AuNPs that is predicted. In all, AuNPs have the potential to serve as incredible materials for most cutting-edge biological applications.

References

Abdel-Mohsen AM, Hrdina R, Burgert L, Krylová G, Abdel-Rahman RM, Krejčová A, Steinhart M, Beneš L (2012) Green synthesis of hyaluronan fibers with silver nanoparticles. Carbohydr Polym 89(2):411–422

Abdel-Raouf N, Al-Enazi NM, Ibraheem IB (2017) Green biosynthesis of gold nanoparticles using *Galaxaura elongata* and characterization of their antibacterial activity. Arab J Chem 10:S3029–S3039

Adewale OB, Davids H, Cairncross L, Roux S (2019) Toxicological behavior of gold nanoparticles on various models: influence of physicochemical properties and other factors. Int J Toxicol 38(5):357–384

Afifudin H, Nadzarah W, Hamidah MS, Hana HN (2011) Microbial participation in the formation of calcium silicate hydrated (CSH) from *Bacillus subtilis*. Proc Eng 20:159–165

Ahmad T (2014) Reviewing the tannic acid mediated synthesis of metal nanoparticles. J Nanotechnol 2014:954206

Ahmed S, Ahmad M, Swami BL, Ikram S (2016) A review on plants extract mediated synthesis of silver nanoparticles for antimicrobial applications: a green expertise. J Adv Res 7(1):17–28

Arunkumar P, Thanalakshmi M, Kumar P, Premkumar K (2013) *Micrococcus luteus* mediated dual mode synthesis of gold nanoparticles: involvement of extracellular α-amylase and cell wall teichuronic acid. Colloids Surf B: Biointerfaces 103:517–522

Arvizo RR, Rana S, Miranda OR, Bhattacharya R, Rotello VM, Mukherjee P (2011) Mechanism of anti-angiogenic property of gold nanoparticles: role of nanoparticle size and surface charge. Nanomedicine 7(5):580–587

Asiya SI, Pal K, Kralj S, El-Sayyad GS, De Souza FG, Narayanan T (2020) Sustainable preparation of gold nanoparticles via green chemistry approach for biogenic applications. Mater Today Chem 17:100327

Aziz N, Pandey R, Barman I, Prasad R (2016) Leveraging the attributes of *Mucor hiemalis*-derived silver nanoparticles for a synergistic broad-spectrum antimicrobial platform. Front Microbiol 7:1984. https://doi.org/10.3389/fmicb.2016.01984

Bai X, Wang Y, Song Z, Feng Y, Chen Y, Zhang D, Feng L (2020) The basic properties of gold nanoparticles and their applications in tumor diagnosis and treatment. Int J Mol Sci 21(7):2480

Baker S, Satish S (2015) Biosynthesis of gold nanoparticles by *Pseudomonas veronii* AS41G inhabiting *Annona squamosa* L. Spectrochim Acta A Mol Biomol Spectrosc 150:691–695

Balagurunathan R, Radhakrishnan M, Rajendran RB, Velmurugan D (2011) Biosynthesis of gold nanoparticles by actinomycete *Streptomyces viridogens* strain HM10. Indian J Biochem Biophys 48:331–335

Bansal SA, Kumar V, Karimi J, Singh AP, Kumar S (2020) Role of gold nanoparticles in advanced biomedical applications. Nanosc Adv 2(9):3764–3787

Barabadi H, Honary S, Ebrahimi P, Mohammadi MA, Alizadeh A, Naghibi F (2014) Microbial mediated preparation, characterization and optimization of gold nanoparticles. Braz J Microbiol 45:1493–1501

Bennur T, Khan Z, Kshirsagar R, Javdekar V, Zinjarde S (2016) Biogenic gold nanoparticles from the Actinomycete *Gordonia amarae*: application in rapid sensing of copper ions. Sensors Actuators B Chem 233:684–690

Beveridge TJ, Murray RG (1980) Sites of metal deposition in the cell wall of *Bacillus subtilis*. J Bacteriol 141(2):876–887

Bonomi R, Cazzolaro A, Sansone A, Scrimin P, Prins LJ (2011) Detection of enzyme activity through catalytic signal amplification with functionalized gold nanoparticles. Angew Chem Int Ed 50(10):2307–2312

Cai F, Li J, Sun J, Ji Y (2011) Biosynthesis of gold nanoparticles by biosorption using *Magnetospirillum gryphiswaldense* MSR-1. Chem Eng J 175:70–75

Carnovale C, Bryant G, Shukla R, Bansal V (2019) Identifying trends in gold nanoparticle toxicity and uptake: size, shape, capping ligand, and biological corona. ACS Omega 4(1):242–256

Castro L, Blázquez ML, Muñoz JA, González F, Ballester A (2013) Biological synthesis of metallic nanoparticles using algae. IET Nanobiotechnol 7(3):109–116

Castro L, Blázquez ML, González FG, Ballester A (2014) Mechanism and applications of metal nanoparticles prepared by bio-mediated process. Rev Adv Sci Eng 3(3):199–216

Chanda N, Kan P, Watkinson LD, Shukla R, Zambre A, Carmack TL, Engelbrecht H, Lever JR, Katti K, Fent GM, Casteel SW (2017) Radioactive gold nanoparticles in cancer therapy: therapeutic efficacy studies of GA-198AuNP nanoconstruct in prostate tumor-bearing mice. In: Nanomedicine in cancer. Jenny Stanford Publishing, Singapore, pp 753–774

Chauhan A, Zubair S, Tufail S, Sherwani A, Sajid M, Raman SC, Azam A, Owais M (2011) Fungus-mediated biological synthesis of gold nanoparticles: potential in detection of liver cancer. Int J Nanomedicine 6:2305–2319

Chen CH, Lin FS, Liao WN, Liang SL, Chen MH, Chen YW, Lin WY, Hsu MH, Wang MY, Peir JJ, Chou FI (2015) Establishment of a trimodality analytical platform for tracing, imaging and quantification of gold nanoparticles in animals by radiotracer techniques. Anal Chem 87(1): 601–608

Chowdhury NK, Choudhury R, Gogoi B, Chang CM, Pandey RP (2022) Microbial synthesis of gold nanoparticles and their application. Curr Drug Targets 23(7):752–760

Cole LE, Ross RD, Tilley JM, Vargo-Gogola T, Roeder RK (2015) Gold nanoparticles as contrast agents in x-ray imaging and computed tomography. Nanomedicine 10(2):321–341

Correa-Llantén DN, Muñoz-Ibacache SA, Castro ME, Muñoz PA, Blamey JM (2013) Gold nanoparticles synthesized by *Geobacillus* sp. strain ID17 a thermophilic bacterium isolated from Deception Island, Antarctica. Microb Cell Factories 12(1):1–6

Cutler CS, Hennkens HM, Sisay N, Huclier-Markai S, Jurisson SS (2013) Radiometals for combined imaging and therapy. Chem Rev 113(2):858–883

Das SK, Marsili E (2010) A green chemical approach for the synthesis of gold nanoparticles: characterization and mechanistic aspect. Rev Environ Sci Biotechnol 9(3):199–204

Das J, Velusamy P (2014) Catalytic reduction of methylene blue using biogenic gold nanoparticles from *Sesbania grandiflora* L. J Taiwan Inst Chem Eng 45(5):2280–2285

De Puig H, Tam JO, Yen CW, Gehrke L, Hamad-Schifferli K (2015) Extinction coefficient of gold nanostars. J Phys Chem C 119(30):17408–17415

Dhas TS, Kumar VG, Abraham LS, Karthick V, Govindaraju K (2012) Sargassum myriocystum mediated biosynthesis of gold nanoparticles. Spectrochim Acta A Mol Biomol Spectrosc 99:97–101

Dorosti N, Jamshidi F (2016) Plant-mediated gold nanoparticles by *Dracocephalum kotschyi* as anticholinesterase agent: synthesis, characterization, and evaluation of anticancer and antibacterial activity. J Appl Biomed 14(3):235–245

Draz MS, Shafiee H (2018) Applications of gold nanoparticles in virus detection. Theranostics 8(7): 1985

Dzimitrowicz A, Jamroz P, Sergiel I, Kozlecki T, Pohl P (2019) Preparation and characterization of gold nanoparticles prepared with aqueous extracts of Lamiaceae plants and the effect of follow-up treatment with atmospheric pressure glow micro discharge. Arab J Chem 12(8):4118–4130

Elahi N, Kamali M, Baghersad MH (2018) Recent biomedical applications of gold nanoparticles: a review. Talanta 184:537–556

Elavazhagan T, Arunachalam KD (2011) Memecylon edule leaf extract mediated green synthesis of silver and gold nanoparticles. Int J Nanomedicine 6:1265

Falco WF, Botero ER, Falcão EA, Santiago EF, Bagnato VS, Caires ARL (2011) In vivo observation of chlorophyll fluorescence quenching induced by gold nanoparticles. J Photochem Photobiol A Chem 225(1):65–71

Fayaz AM, Girilal M, Rahman M, Venkatesan R, Kalaichelvan PT (2011) Biosynthesis of silver and gold nanoparticles using thermophilic bacterium *Geobacillus stearothermophilus*. Process Biochem 46(10):1958–1962

Fountoulaki S, Daikopoulou V, Gkizis PL, Tamiolakis I, Armatas GS, Lykakis IN (2014) Mechanistic studies of the reduction of nitroarenes by $NaBH_4$ or hydrosilanes catalyzed by supported gold nanoparticles. ACS Catal 4(10):3504–3511

Genç R, Clergeaud G, Ortiz M, O'Sullivan CK (2011) Green synthesis of gold nanoparticles using glycerol-incorporated nanosized liposomes. Langmuir 27(17):10894–10900

Gerber A, Bundschuh M, Klingelhofer D, Groneberg DA (2013) Gold nanoparticles: recent aspects for human toxicology. J Occup Med Toxicol 8(1):1–6

Ghosh P, Han G, De M, Kim CK, Rotello VM (2008) Gold nanoparticles in delivery applications. Adv Drug Deliv Rev 60(11):1307–1315

Girilal M, Fayaz AM, Balaji PM, Kalaichelvan PT (2013) Augmentation of PCR efficiency using highly thermostable gold nanoparticles synthesized from a thermophilic bacterium, *Geobacillus stearothermophilus*. Colloids Surf B: Biointerfaces 106:165–169

Hammami I, Alabdallah NM (2021) Gold nanoparticles: synthesis properties and applications. J King Saud Univ Sci 33(7):101560

He S, Guo Z, Zhang Y, Zhang S, Wang J, Gu N (2007) Biosynthesis of gold nanoparticles using the bacteria *Rhodopseudomonas capsulata*. Mater Lett 61(18):3984–3987

He S, Zhang Y, Guo Z, Gu N (2008) Biological synthesis of gold nanowires using extract of Rhodopseudomonas capsulata. Biotechnol Prog 24(2):476–480

Her S, Jaffray DA, Allen C (2017) Gold nanoparticles for applications in cancer radiotherapy: mechanisms and recent advancements. Adv Drug Deliv Rev 109:84–101

Hernández-Rivera M, Kumar I, Cho SY, Cheong BY, Pulikkathara MX, Moghaddam SE, Whitmire KH, Wilson LJ (2017) High-performance hybrid bismuth–carbon nanotube based contrast agent for X-ray CT imaging. ACS Appl Mater Interfaces 9(7):5709–5716

Huang X, El-Sayed MA (2011) Plasmonic photo-thermal therapy (PPTT). Alexandria J Med 47(1): 1–9

Hughes SI, Dasary SS, Singh AK, Glenn Z, Jamison H, Ray PC, Yu H (2013) Sensitive and selective detection of trivalent chromium using hyper Rayleigh scattering with 5,5′-dithio-bis-(2-nitrobenzoic acid)-modified gold nanoparticles. Sensors Actuators B Chem 178:514–519

Hulkoti NI, Taranath TC (2014) Biosynthesis of nanoparticles using microbes—a review. Colloids Surf B: Biointerfaces 121:474–483

Hussain MH, Abu Bakar NF, Mustapa AN, Low KF, Othman NH, Adam F (2020) Synthesis of various size gold nanoparticles by chemical reduction method with different solvent polarity. Nanoscale Res Lett 15(1):1–10

Inbakandan D, Venkatesan R, Khan SA (2010) Biosynthesis of gold nanoparticles utilizing marine sponge *Acanthella elongata* (Dendy, 1905). Colloids Surf B: Biointerfaces 81(2):634–639

Iranmanesh S, Shahidi Bonjar GH, Baghizadeh A (2020) Study of the biosynthesis of gold nanoparticles by using several saprophytic fungi. SN Appl Sci 2(11):1–11

Issazadeh K, Jahanpour N, Pourghorbanali F, Raeisi G, Faekhondeh J (2013) Heavy metals resistance by bacterial strains. Annal Biol Res 4(2):60–63

Jans H, Huo Q (2012) Gold nanoparticle-enabled biological and chemical detection and analysis. Chem Soc Rev 41(7):2849–2866

Jans H, Liu X, Austin L, Maes G, Huo Q (2009) Dynamic light scattering as a powerful tool for gold nanoparticle bioconjugation and biomolecular binding studies. Anal Chem 81(22):9425–9432

Jauffred L, Samadi A, Klingberg H, Bendix PM, Oddershede LB (2019) Plasmonic heating of nanostructures. Chem Rev 119(13):8087–8130

Jayaseelan C, Ramkumar R, Rahuman AA, Perumal P (2013) Green synthesis of gold nanoparticles using seed aqueous extract of Abelmoschus esculentus and its antifungal activity. Ind Crop Prod 45:423–429

Kalaivani R, Maruthupandy M, Muneeswaran T, Singh M, Sureshkumar S, Anand M, Ramakritinan CM, Quero F, Kumaraguru AK (2020) Chitosan mediated gold nanoparticles against pathogenic bacteria, fungal strains and MCF-7 cancer cells. Int J Biol Macromol 146: 560–568

Kalishwaralal K, Gopalram S, Vaidyanathan R, Deepak V, Pandian SRK, Gurunathan S (2010) Optimization of α-amylase production for the green synthesis of gold nanoparticles. Colloids Surf B: Biointerfaces 77(2):174–180
Kang F, Qu X, Alvarez PJ, Zhu D (2017) Extracellular saccharide-mediated reduction of Au3+ to gold nanoparticles: new insights for heavy metals biomineralization on microbial surfaces. Environ Sci Technol 51(5):2776–2785
Kato Y, Yoshimura E, Suzuki M (2019) Synthesis of gold nanoparticles by extracellular components of *Lactobacillus casei*. Chem Select 4(24):7331–7337
Khan ST, Al-Khedhairy AA, Musarrat J (2015) ZnO and TiO2 nanoparticles as novel antimicrobial agents for oral hygiene: a review. J Nanopart Res 17(6):1–16
Khan AU, Khan M, Malik N, Cho MH, Khan MM (2019) Recent progress of algae and blue–green algae-assisted synthesis of gold nanoparticles for various applications. Bioprocess Biosyst Eng 42(1):1–15
Khlebtsov N, Dykman L (2011) Biodistribution and toxicity of engineered gold nanoparticles: a review of in vitro and in vivo studies. Chem Soc Rev 40(3):1647–1671
Kisimba K, Krishnan A, Faya M, Byanga K, Kasumbwe K, Vijayakumar K, Prasad R (2023) Synthesis of metallic nanoparticles based on green chemistry and their medical biochemical applications: synthesis of metallic nanoparticles. J Renew Mater 11(6):2575–2591. https://doi.org/10.32604/jrm.2023.026159
Kitching M, Ramani M, Marsili E (2015) Fungal biosynthesis of gold nanoparticles: mechanism and scale up. Microb Biotechnol 8(6):904–917
Koch N, Sonowal S, Prasad R (2023) Elucidate the smart tailored biogenic nanoparticles and their applications in remediation. Biotechnol Genet Eng Rev. https://doi.org/10.1080/02648725.2023.2219942
Kohane DS, Langer R (2010) Biocompatibility and drug delivery systems. Chem Sci 1(4):441–446
Kumar KS, Kumar G, Prokhorov E, Luna-Bárcenas G, Buitron G, Khanna VG, Sanchez IC (2014) Exploitation of anaerobic enriched mixed bacteria (AEMB) for the silver and gold nanoparticles synthesis. Colloids Surf A Physicochem Eng Asp 462:264–270
Kupryashina MA, Vetchinkina EP, Burov AM, Ponomareva EG, Nikitina VE (2013) Biosynthesis of gold nanoparticles by *Azospirillum brasilense*. Microbiology 82(6):833–840
Larm NE, Essner JB, Pokpas K, Canon JA, Jahed N, Iwuoha EI, Baker GA (2018) Room-temperature Turkevich method: formation of gold nanoparticles at the speed of mixing using cyclic oxocarbon reducing agents. J Phys Chem C 122(9):5105–5118
Lee JS (2010) Recent progress in gold nanoparticle-based non-volatile memory devices. Gold Bull 43(3):189–199
Lengke MF, Sanpawanitchakit C, Southam G (2011) Biosynthesis of gold nanoparticles: a review. In: Metal nanoparticles in microbiology. Springer, Berlin, pp 37–74
Liu Z, Parida S, Prasad R, Pandey R, Sharma D, Barman I (2021) Vibrational spectroscopy for decoding cancer microbiome interactions: current evidence and future perspective. Semin Cancer Biol. https://doi.org/10.1016/j.semcancer.2021.07.004
Malarkodi C, Rajeshkumar S, Vanaja M, Paulkumar K, Gnanajobitha G, Annadurai G (2013) Eco-friendly synthesis and characterization of gold nanoparticles using Klebsiella pneumoniae. J Nanostruct Chem 3(1):1–7
Malassis L, Dreyfus R, Murphy RJ, Hough LA, Donnio B, Murray CB (2016) One-step green synthesis of gold and silver nanoparticles with ascorbic acid and their versatile surface post-functionalization. RSC Adv 6(39):33092–33100
Mewada A, Oza G, Pandey S, Sharon M (2012) Extracellular synthesis of gold nanoparticles using *Pseudomonas denitrificans* and comprehending its stability. J Microbiol Biotechnol 2(4):493–499
Mittal AK, Chisti Y, Banerjee UC (2013) Synthesis of metallic nanoparticles using plant extracts. Biotechnol Adv 31(2):346–356
Moghaddam K (2010) An introduction to microbial metal nanoparticle preparation method. J Young Investig 19(19):1–6

Montes MO, Mayoral A, Deepak FL, Parsons JG, Jose-Yacamán M, Peralta-Videa JR, Gardea-Torresdey JL (2011) Anisotropic gold nanoparticles and gold plates biosynthesis using alfalfa extracts. J Nanopart Res 13(8):3113–3121

Muthuvel A, Adavallan K, Balamurugan K, Krishnakumar N (2014) Biosynthesis of gold nanoparticles using Solanum nigrum leaf extract and screening their free radical scavenging and antibacterial properties. Biomed Prevent Nutr 4(2):325–332

Nalawade P, Mukherjee P, Kapoor S (2014) Biosynthesis, characterization and antibacterial studies of silver nanoparticles using pods extract of *Acacia auriculiformis*. Spectrochim Acta A Mol Biomol Spectrosc 129:121–124

Nangia Y, Wangoo N, Goyal N, Shekhawat G, Suri C (2009) A novel bacterial isolate Stenotrophomonas maltophilia as living factory for synthesis of gold nanoparticles. Microb Cell Factories 8(1):1–7

Ngoepe NM, Hato MJ, Modibane KD, Hintsho-Mbita NC (2020) Biogenic synthesis of metal oxide nanoparticle semiconductors for wastewater treatment. In: Photocatalysts in advanced oxidation processes for wastewater treatment. Wiley, New York, NY, pp 1–31

Ogi T, Saitoh N, Nomura T, Konishi Y (2010) Room-temperature synthesis of gold nanoparticles and nanoplates using Shewanella algae cell extract. J Nanopart Res 12(7):2531–2539

Ovais M, Raza A, Naz S, Islam NU, Khalil AT, Ali S, Khan MA, Shinwari ZK (2017) Current state and prospects of the phytosynthesized colloidal gold nanoparticles and their applications in cancer theranostics. Appl Microbiol Biotechnol 101(9):3551–3565

Ovais M, Ahmad I, Khalil AT, Mukherjee S, Javed R, Ayaz M, Raza A, Shinwari ZK (2018) Wound healing applications of biogenic colloidal silver and gold nanoparticles: recent trends and future prospects. Appl Microbiol Biotechnol 102(10):4305–4318

Paul B, Bhuyan B, Purkayastha DD, Dey M, Dhar SS (2015) Green synthesis of gold nanoparticles using *Pogestemon benghalensis* (B) O. Ktz. leaf extract and studies of their photocatalytic activity in degradation of methylene blue. Mater Lett 148:37–40

Philip D, Unni C (2011) Extracellular biosynthesis of gold and silver nanoparticles using Krishna tulsi (*Ocimum sanctum*) leaf. Phys E Low Dimens Syst Nanostruct 43(7):1318–1322

Pourali P, Badiee SH, Manafi S, Noorani T, Rezaei A, Yahyaei B (2017) Biosynthesis of gold nanoparticles by two bacterial and fungal strains, Bacillus cereus and Fusarium oxysporum, and assessment and comparison of their nanotoxicity in vitro by direct and indirect assays. Electron J Biotechnol 29:86–93

Prasad R (2014) Synthesis of silver nanoparticles in photosynthetic plants. J Nanoparticles 2014:963961. https://doi.org/10.1155/2014/963961

Prasad R (2016) Advances and applications through fungal nanobiotechnology. Springer, International Publishing Switzerland. (ISBN: 978-3-319-42989-2)

Prasad R (2017) Fungal nanotechnology: applications in agriculture, industry, and medicine. Springer Nature Singapore Pte Ltd. (ISBN 978-3-319-68423-9)

Prasad R, Pandey R, Barman I (2016) Engineering tailored nanoparticles with microbes: quo vadis. WIREs Nanomed Nanobiotechnol 8:316–330. https://doi.org/10.1002/wnan.1363

Prasad R, Jha A, Prasad K (2018a) Exploring the realms of nature for nanosynthesis. Springer International Publishing. (ISBN 978-3-319-99570-0) https://www.springer.com/978-3-319-99570-0

Prasad R, Kumar V, Kumar M, Wang S (2018b) Fungal nanobionics: principles and applications. Springer Nature Singapore Pte Ltd. (ISBN 978-981-10-8666-3) https://www.springer.com/gb/book/9789811086656

Prasad R (2019a) Microbial nanobionics: basic research and applications. Springer International Publishing. (ISBN 978-3-030-16534-5) https://www.springer.com/gp/book/9783030165338

Prasad R (2019b) Microbial nanobionics: state of art. Springer International Publishing. (ISBN 978-3-030-16383-9) https://www.springer.com/gp/book/9783030163822

Qian X, Nie S (2010) Surface-enhanced raman nanoparticles for in-vivo tumor targeting and spectroscopic detection. AIP Conf Proc 1267(1):81–81

Quester K, Avalos-Borja M, Vilchis-Nestor AR, Camacho-López MA, Castro-Longoria E (2013) SERS properties of different sized and shaped gold nanoparticles biosynthesized under different environmental conditions by Neurospora crassa extract. PLoS One 8(10):e77486

Raghuwanshi N, Kumari P, Srivastava AK, Vashisth P, Yadav TC, Prasad R, Pruthi V (2017) Synergistic effects of Woodfordia fruticosa gold nanoparticles in preventing microbial adhesion and accelerating wound healing in Wistar albino rats in vivo. Mater Sci Eng C 80:252–262

Rai M, Gade A, Yadav A (2011) Biogenic nanoparticles: an introduction to what they are, how they are synthesized and their applications. In: Metal nanoparticles in microbiology. Springer, Berlin, pp 1–14

Rajasree SR, Suman TY (2012) Extracellular biosynthesis of gold nanoparticles using a gram-negative bacterium *Pseudomonas fluorescens*. Asian Pac J Trop Dis 2:S796–S799

Rajathi FAA, Parthiban C, Kumar VG, Anantharaman P (2012) Biosynthesis of antibacterial gold nanoparticles using brown alga, *Stoechospermum marginatum* (kützing). Spectrochim Acta A Mol Biomol Spectrosc 99:166–173

Rajeshkumar S (2016) Anticancer activity of eco-friendly gold nanoparticles against lung and liver cancer cells. J Genet Eng Biotechnol 14(1):195–202

Rajeshkumar S, Malarkodi C, Vanaja M, Gnanajobitha G, Paulkumar K, Kannan C, Annadurai G (2013) Antibacterial activity of algae mediated synthesis of gold nanoparticles from Turbinaria conoides. Der Pharma Chemica 5(2):224–229

Rajeshkumar S, Malarkodi C, Paulkumar K, Vanaja M, Gnanajobitha G, Annadurai G (2014) Algae mediated green fabrication of silver nanoparticles and examination of its antifungal activity against clinical pathogens. Int J Met 2014:692643

Rani M, Shanker U (2022) Green nanomaterials: an overview. In: Green functionalized nanomaterials for environmental applications. Elsevier, Amsterdam, pp 43–80

Sathiyaraj S, Suriyakala G, Gandhi AD, Babujanarthanam R, Almaary KS, Chen TW, Kaviyarasu K (2021) Biosynthesis, characterization, and antibacterial activity of gold nanoparticles. J Infect Public Health 14(12):1842–1847

Sau TK, Rogach AL (2010) Nonspherical noble metal nanoparticles: colloid-chemical synthesis and morphology control. Adv Mater 22(16):1781–1804

Sau TK, Rogach AL, Jäckel F, Klar TA, Feldmann J (2010) Properties and applications of colloidal nonspherical noble metal nanoparticles. Adv Mater 22(16):1805–1825

Sharma N, Pinnaka AK, Raje M, Fnu A, Bhattacharyya MS, Choudhury AR (2012) Exploitation of marine bacteria for production of gold nanoparticles. Microb Cell Factories 11(1):1–6

Sharon M, Mewada A, Swaminathan N, Sharon C (2017) Synthesis of biogenic gold nanoparticles and its applications as theranostic agent: a review. Nanomed Nanotechnol J 1(1):113

Shedbalkar U, Singh R, Wadhwani S, Gaidhani S, Chopade BA (2014) Microbial synthesis of gold nanoparticles: current status and future prospects. Adv Colloid Interf Sci 209:40–48

Shivaji SW, Arvind MD, Zygmunt S (2014) Biosynthesis, optimization, purification and characterization of gold nanoparticles. Afr J Microbiol Res 8(2):138–146

Shunmugam R, Balusamy SR, Kumar V, Menon S, Lakshmi T, Perumalsamy H (2021) Biosynthesis of gold nanoparticles using marine microbe (*Vibrio alginolyticus*) and its anticancer and antioxidant analysis. J King Saud Univ Sci 33(1):101260

Siddique S, Chow JC (2020) Gold nanoparticles for drug delivery and cancer therapy. Appl Sci 10(11):3824

Singaravelu G, Arockiamary JS, Kumar VG, Govindaraju K (2007) A novel extracellular synthesis of monodisperse gold nanoparticles using marine alga, *Sargassum wightii* Greville. Colloids Surf B: Biointerfaces 57(1):97–101

Singh PK, Kundu S (2014) Biosynthesis of gold nanoparticles using bacteria. Proc Natl Acad Sci Ind B: Biol Sci 84(2):331–336

Soisuwan S, Lirdprapamongko K, Warisnoicharoen W, Svasti J (2014) Seaweed fucoidan-stabilized gold nanoparticles and their antitumor activities. Pharma Nutr 2(3):81

Soltani NM, Shahidi BG, Khaleghi N (2015) Biosynthesis of gold nanoparticles using *Streptomyces fulvissimus* isolate. Nanomed J 2(2):153–159

Song J, Kim D, Lee D (2011) Size control in the synthesis of 1–6 nm gold nanoparticles via solvent-controlled nucleation. Langmuir 27(22):13854–13860
Srivastava SK, Constanti M (2012) Room temperature biogenic synthesis of multiple nanoparticles (Ag, Pd, Fe, Rh, Ni, Ru, Pt, Co, and Li) by *Pseudomonas aeruginosa* SM1. J Nanopart Res 14(4):1–10
Srivastava SK, Yamada R, Ogino C, Kondo A (2013) Biogenic synthesis and characterization of gold nanoparticles by *Escherichia coli* K12 and its heterogeneous catalysis in degradation of 4-nitrophenol. Nanoscale Res Lett 8(1):1–9
Srivastava S, Usmani Z, Atanasov AG, Singh VK, Singh NP, Abdel-Azeem AM, Prasad R, Gupta G, Sharma M, Bhargava A (2021) Biological nanofactories: using living forms for metal nanoparticle synthesis. Mini-Rev Med Chem 21(2):245–265
Suganya KU, Govindaraju K, Kumar VG, Dhas TS, Karthick V, Singaravelu G, Elanchezhiyan M (2015) Blue green alga mediated synthesis of gold nanoparticles and its antibacterial efficacy against Gram positive organisms. Mater Sci Eng C 47:351–356
Suresh AK, Pelletier DA, Wang W, Broich ML, Moon JW, Gu B, Allison DP, Joy DC, Phelps TJ, Doktycz MJ (2011) Biofabrication of discrete spherical gold nanoparticles using the metal-reducing bacterium *Shewanella oneidensis*. Acta Biomater 7(5):2148–2152
Tanwar S, Paidi SK, Prasad R, Pandey R, Barman I (2021) Advancing Raman spectroscopy from research to clinic: translational potential and challenges. Spectrochim Acta A Mol Biomol Spectrosc 260:119957. https://doi.org/10.1016/j.saa.2021.119957
Thakkar KN, Mhatre SS, Parikh RY (2010) Biological synthesis of metallic nanoparticles. Nanomedicine 6(2):257–262
Thakker JN, Dalwadi P, Dhandhukia PC (2013) Biosynthesis of gold nanoparticles using *Fusarium oxysporum* f. sp. cubense JT1, a plant pathogenic fungus. Int Scholar Res Notice 2013:515091
Thangadurai D, Sangeetha J, Prasad R (2020a) Functional bionanomaterials. Springer International Publishing. (ISBN 978-3-030-41464-1) https://www.springer.com/gp/book/9783030414634
Thangadurai D, Sangeetha J, Prasad R (2020b) Nanotechnology for food, agriculture, and environment. Springer International Publishing. (ISBN 978-3-030-31937-3) https://www.springer.com/gp/book/9783030319373
Tian EK, Wang Y, Ren R, Zheng W, Liao W (2021) Gold nanoparticle: recent progress on its antibacterial applications and mechanisms. J Nanomater 2021:1–8
Tikariha S, Singh S, Banerjee S, Vidyarthi AS (2012) Biosynthesis of gold nanoparticles, scope and application: a review. Int J Pharm Sci Res 3(6):1603
Tomar RS, Shrivastava V (2014) Synthesis of gold nanoparticles: a biological approach. Synthesis 3(2):5
Tran QH, Nguyen VQ, Le AT (2013) Silver nanoparticles: synthesis, properties, toxicology, application and perspectives. Adv Nat Sci Nanosci Nanotechnol 4(3):033001
Tyal-Abdullah Z, Al-Shawi AA, Aboud MN, Al Abdul Aziz B, QM Al-Furaiji H, Luaibi IN (2020) Synthesis and analytical characterization of gold nanoparticles using microwave-assisted extraction system and study their application in degradation. J Nanostruct 10(4):682–690
Verma HN, Singh P, Chavan RM (2014) Gold nanoparticle: synthesis and characterization. Vet World 7(2):72
Villaverde A (2010) Nanotechnology, bionanotechnology and microbial cell factories. Microb Cell Factories 9(1):1–4
Vines JB, Yoon JH, Ryu NE, Lim DJ, Park H (2019) Gold nanoparticles for photothermal cancer therapy. Front Chem 7:167
Wang C, Yu C (2013) Detection of chemical pollutants in water using gold nanoparticles as sensors: a review. Rev Anal Chem 32(1):1–14
Wang W, Wang J, Ding Y (2020) Gold nanoparticle-conjugated nanomedicine: design, construction, and structure–efficacy relationship studies. J Mater Chem B 8(22):4813–4830
Wnęk M, Górzny MŁ, Ward MB, Wälti C, Davies AG, Brydson R, Evans SD, Stockley PG (2012) Fabrication and characterization of gold nano-wires templated on virus-like arrays of tobacco mosaic virus coat proteins. Nanotechnology 24(2):025605

Xia H, Bai S, Hartmann J, Wang D (2010) Synthesis of monodisperse quasi-spherical gold nanoparticles in water via silver (I)-assisted citrate reduction. Langmuir 26(5):3585–3589

Yasmin A, Ramesh K, Rajeshkumar S (2014) Optimization and stabilization of gold nanoparticles by using herbal plant extract with microwave heating. Nano Converg 1(1):1–7

Yeh YC, Creran B, Rotello VM (2012) Gold nanoparticles: preparation, properties, and applications in bionanotechnology. Nanoscale 4(6):1871–1880

Yu X, Jiao Y, Chai Q (2016) Applications of gold nanoparticles in biosensors. Nano Life 6(2): 1642001

Zhang X (2015) Gold nanoparticles: recent advances in the biomedical applications. Cell Biochem Biophys 72(3):771–775

Zhang X, Yan S, Tyagi RD, Surampalli RY (2011) Synthesis of nanoparticles by microorganisms and their application in enhancing microbiological reaction rates. Chemosphere 82(4):489–494

Zhang XD, Wu D, Shen X, Chen J, Sun YM, Liu PX, Liang XJ (2012) Size-dependent radiosensitization of PEG-coated gold nanoparticles for cancer radiation therapy. Biomaterials 33(27):6408–6419

Zhang X, Qu Y, Shen W, Wang J, Li H, Zhang Z, Li S, Zhou J (2016) Biogenic synthesis of gold nanoparticles by yeast *Magnusiomyces ingens* LH-F1 for catalytic reduction of nitrophenols. Colloids Surf A Physicochem Eng Asp 497:280–285

Zhou W, Gao X, Liu D, Chen X (2015) Gold nanoparticles for in vitro diagnostics. Chem Rev 115(19):10575–10636

Zhou S, Huo D, Goines S, Yang TH, Lyu Z, Zhao M, Gilroy KD, Wu Y, Hood ZD, Xie M, Xia Y (2018) Enabling complete ligand exchange on the surface of gold nanocrystals through the deposition and then etching of silver. J Am Chem Soc 140(38):11898–11901

Ziegler C, Eychmuller A (2011) Seeded growth synthesis of uniform gold nanoparticles with diameters of 15–300 nm. J Phys Chem C 115(11):4502–4506

Biosynthesis, Characterization and Applications of Gold Nanoparticles

3

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Abstract

Nanotechnology is the study of matter at nanolevel. At nanolevel, the physical and chemical properties of the matter changed owing to various applications in various fields. Various metals and metal-oxides were used for the synthesis of nanoparticles (NPs). But among them, gold (Au) plays a precious role. Since the last decade, gold nanoparticles (AuNPs) have its unique features, including electrical, photothermal, and optical characteristics. Various methods were employed for the synthesis of gold nanoparticles, including physical, chemical and biological methods. Among them, biological methods of gold nanoparticle production are gaining popularity because of their ecofriendly methods, cheap, safe, etc. The current book chapter focuses on gold nanoparticles synthesis and their mechanism of formation by using microbes such as bacteria, fungus, actinomycetes, algae, and viruses. In addition to this, synthesized gold nanoparticle was subjected to characterization by using different techniques such as X-ray,

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Fourier transform infrared and UV–visible spectroscopy transmission electron microscopy, diffraction spectroscopy, scanning electron microscopy, atomic force microscopy, X-ray photoelectron spectroscopy, and electron dispersive X-ray. Finally, applications of gold nanoparticles were discussed.

Keywords

Gold nanoparticles · Characterization · Nanotechnology · Applications

3.1 Introduction

Nanotechnology involves principles of biology, physics, and chemistry for the production of nanoparticles (NPs) with specific purposes (Menon et al. 2017). NPs are characterized as having a size between 10 and 1000 nm. However, due to their comparable sizes to biomolecules and ease of penetrating, it is generally believed that materials smaller than 100 nm are beneficial for applications. Silver (Ag), gold (Au), platinum, palladium, and oxides like titanium oxide and zinc oxide possess special properties like electrical, mechanical, optical, chemical, and magnetic, which have been extensively used for NPs synthesis (Menon et al. 2017). Increased surface area to volume ratio, size, sphere, or rod shaped with special characteristics of nanomaterials with reduced size offers a wide range of biological research opportunities. Nanomaterials can interact with complicated biological systems in novel ways because of their dimensions, which are similar to those of biomolecules. Additionally, nanocarriers interact with proteins both inside and outside of the cell in such a way that cannot change their biological characteristics and activity (Gao et al. 2021). Such easy access to a living cell's inside offers tremendous benefits for basic and clinical research. In the treatment of disease, they aid in enhancing therapeutic efficacy and reducing drug toxicity (Pastorino et al. 2019; Ahmad et al. 2021). In addition to this, NPs have wider applications, including optoelectronics, display devices, catalysis, the fabrication of biological sensors, in the diagnostics involved in disease monitoring (cancer cells), drug discovery, the toxic metals detection, etc (Prasad et al. 2016).

3.2 Methods of Nanoparticles Production

Production of NPs by various methodologies has increased, but they were safe, environmentally safe processes that do not depend on using hazardous chemicals. Physical, chemical, and biological were three routes for NPs production fall under either the top-down or bottom-up categories. Size reduction by mechanical method used in the top-down strategy entails gradually disintegrating bulk materials into the nanolevel. Bottom-up approach is based on the assembly of nanoscale atoms or molecules into the molecular structure. Physical or chemical methods refer to

top-down, but the bottom-up strategy refers to chemical and biological routes of NPs production (Lombardo et al. 2020). High purity NPs of the desired size have been produced using physical and chemical methods, but these procedures are frequently expensive and are hazardous substances, which is the major drawbacks of physical methods. In the chemical synthesis, some toxic chemical species may end up being adsorbed onto the surface of NPs, causing toxicity when interact with human body.

To overcome these drawbacks, biological processes has paying their attention because they are quick, affordable, and environmentally beneficial. In comparison to chemical or physical processes, green synthesis techniques like biological ones offer a method for synthesizing NPs that is affordable, sustainable, and less abrasive (Prasad et al. 2016, 2018, Srivastava et al. 2021; Kisimba et al. 2023). Biological synthesis additionally provides control over size and form for necessary applications. Many species can create inorganic compounds either intracellularly or extracellularly, as is now widely known (Ghosh et al. 2021). Due to this, a wide variety of natural species, including algae, fungi, bacteria, viruses, and plants, are used for the biological synthesis of NPs. Green synthesis of NPs by algae is considered as "bio-nano factories" due to its unique structure, macroscopic size, and high metal uptake capacity (Aziz et al. 2014, 2015). With the aid of enzymes found in bacteria or plants, the hazardous compounds formed during the synthesis of NPs can be quickly broken down. For instance, the bio-reduction of NPs in fungi is mediated by nitrate reductase (Menon et al. 2017). In reality, respiration processes carried out by bacteria contribute to several metal oxides production (Kim et al. 2018). In anaerobic respiration, microbes transfer electrons from reduced organic to oxidized inorganic molecules, enabling the production of crystal/NPs and bioremediation processes. The ability of the genus *Shewanella* to oxidize organic acids as donors of electrons and reduce inorganic metals as electron acceptors has been well-documented (Harris et al. 2018).

Microorganisms generally have two different effects on the production of minerals. They can alter the solution's makeup to make it more or less supersaturated. Production of organic polymers by microbes is a second way they can affect mineral formation. The most effective environmentally safe green nanofactories for regulating the size of biological NPs are microbes. Plant-based NPs production yields polydisperse NPs due to the presence of phytochemicals (Ahmad et al. 2021; Prasad 2014). These were diverse benefits of microbes over plants in terms of producing NPs. Several microbes are thought to be viable candidates for NPs manufacturing (Priyadarshini et al. 2013). One of the reduced gold (Au) atoms that result from the reduction of an Au(III) ion binds to the cell surface and combines with other reduced Au to form gold nanoparticles (AuNPs). AuNPs acquire special properties due to alteration in localized energy levels and innovative unique features with quantum size effects, including small size, localized surface plasmon resonance, and electronic motion with spatial length scale (Bai et al. 2020). AuNPs synthesized from various microbes yield varied shapes with wider applications in different sectors, including clinical, diagnostics, and treatment of diseases.

3.3 Microbial Production of Nanoparticles

Microbial production of NPs has more benefits like easy to handle, ability to grow in in-expensive media, maintenance of safety levels, and potential to adsorb metal ions and reduces them into NPs by the microbial enzymes, due to these advantages microorganisms were used for NPs production (Jadoun et al. 2022; Prasad 2016, 2017, 2019a, b).

Microbes can produce either intracellular or extracellular NPs, depending on the environment. The intracellular mechanism involves particular ions being transported into the negatively charged cell wall, where they interact electrostatically with positive-charged metals to diffuse through the cell wall. The poisonous metals are then changed into nontoxic metal NPs by enzymes found in the cell walls of microorganisms. The extracellular method transforms the metallic ions into metallic NPs with the use of fungi or prokaryotic enzymes like nitrate reductase or hydroquinone, similarly AuNPs were made from *Rhodomonas capsulate*. The bacteria use metal binding, vacuole compartmentalization, and volatilization, or conversion, as detoxifying mechanisms (Menon et al. 2017; Koch et al. 2023).

3.4 Microbial Strains for the Production of AuNPs

Gold is one of the famous noble metals. It serves as a heat insulator, and some expensive CDs employ it as a reflective layer, coloring ingredient in cranberry glass, it results in a vivid red color. A multitude of types of gold have been utilized in medicine throughout civilization's history. Rheumatic illnesses like discoid lupus erythematosus, restorative dentistry and a number of inflammatory skin conditions like pemphigus, urticarial and psoriasis have all been treated with gold and gold compounds. Patients with facial nerve palsy and lagophthalmos are treated with gold eyelid implants. The properties of AuNPs are thought to differ from those of bulk materials, as is the case with other NPs. Due to their distinctive optical, electrical, and photothermal capabilities, AuNPs have gained prominence in recent years. They are also resistant to oxidation. Variations in AuNPs' phase and shape can change both their chemical and physical characteristics (Amina and Guo 2020).

Traditionally, physical and chemical processes have been used to create AuNPs. Using these approaches, AuNPs with sizes ranging from 1 to 100 nm and various forms have been produced. Despite the fact that these synthesis techniques have been thoroughly investigated, they have some disadvantages, including the employment of toxic chemicals, strict synthesis conditions, iii) an energy-dependent, costly process, and lower productivity. The mixed form of nanoparticles (NPs) produced by current synthetic techniques necessitates expensive and low-yield purifying by centrifugation. These processes also result in greater sludge and pose environmental risks since they use harmful solvents or additives (Ghosh et al. 2021).

Consequently, there is a growing demand to create sustainable, eco-friendly, nontoxic, and clean synthesis processes. The creation of low-cost, high-yield NPs production, enormous diversity, biological systems has been a focus for biological

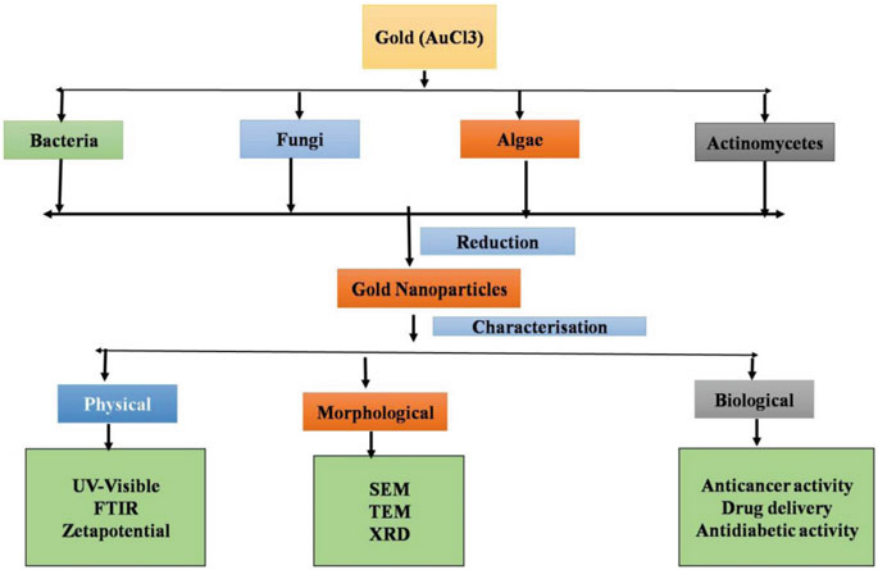

Fig. 3.1 Gold nanoparticle synthesis by using various microbes and their characterization

NP synthesis (Dikshit et al. 2021). Smaller particles can be produced on a massive scale through biosynthesis. It is significant to mention that biologically created NPs have improved morphological control and increased stability (Kaur et al. 2023). Biological systems with the ability to synthesize NPs include bacteria, fungus, actinomycetes, and plants (Fig. 3.1). Due to their innate potential, bacteria create NPs intracellular and/or extracellular (Pourali et al. 2017). Therefore, a thorough screening of microorganisms that provide extracellular NP biosynthesis is required (Khanna et al. 2023). Microorganisms can be used as potential biofactories to synthesize AuNPs, and this is a relatively new field of study with great potential.

3.4.1 Synthesis by Bacterial Strains

Microbes have drawn the most attention in the field of AuNPs production (Table 3.1). First report of AuNPs synthesis was reported by using *Bacillus subtilis* 168, with 5–25 nm NPs within the cell wall. At low concentration, 10–20 nm range spherical AuNPs were formed by *Rhodopseudomonas capsulata*, but at higher concentrations forms nanowires. There are six cyanobacteria that have been identified as producing AuNPs (Shedbalkar et al. 2014). Six cyanobacterial species include *Plectonema*, *Anabaena*, *Calothrix*, and *Leptolyngbya* involved in the synthesis of AuNPs (Pandey et al. 2022). AuNPs and Au core-Ag shell NPs were formed from single-cell protein *Spirulina platensis*. Microbes' amazing capacity to adapt to stressful environmental situations is what leads to the production of reduced metal ions by them (Kulkarni et al. 2015). The inhabitants of gold mines would be

Table 3.1 Microbial synthesis of gold nanoparticles and their applications

S. No.	Microorganisms	Size (nm)	Application	Reference
Bacteria				
1	*Paracoccus haeundaensis BC74171*	20.93 ± 3.46	Antioxidant activity and antiproliferative effect	Patil et al. (2019)
2	*Micrococcus yunnanensis*	53.8	Antibacterial, anticancer	Jafari et al. (2018)
3	*Mycobacterium* sp.	5–55	Anticancer	Camas et al. (2018)
4	*Pseudoalteromonas lipolytica*		Methylene and Congo red decolorization	Kulkarni et al. (2018)
5	*Bacillus subtilis*	20–25	Degradation of methylene blue	Srinath et al. (2018)
Actinomycetes				
6	*Streptomyces griseoruber*	5–50	Degradation of methylene blue	Ranjitha et al. (2018)
Fungus				
7	*Trichoderma harzianum*	32–44	Antibacterial activity	Tripathi et al. (2018)
8	*Morchella esculenta*	16.51	Antimicrobial activity and cytotoxic activity	Acay (2021)
9	*Cladosporium sp.*	5–10	Photodegradation, in vitro anticancer activity, and in vivo antitumor studies	Munawer et al. (2020)
10	*Penicillium janthinellum DJP06*	1–40	–	Pareek et al. (2020)
11	*Cladosporium oxysporum AJP03*	72–21	Degradation of rhodamine B	Bhargava et al. (2016)
12	*Rhizopus oryzae*	16–43	Hemocompatible activity	Kitching et al. (2016)
Algae				
13	*Spirulina platensis*	15.60–77.13	Antiviral activity	El-Sheekh et al. (2022)
14	*Sargassum cymosum*	7 and 20		Costa et al. (2020)
15	*Stephanopyxis turris*	10–30		Pytlik et al. (2017)
16	*Galaxaura elongata*	3.85–77	Antibacterial	Abdel-Raouf et al. (2017)
17	*Cystoseira baccata*	8.4	Anticancer	González-Ballesteros et al. (2017)
18	*Pleurotus ostreatus*	10–30	Anticancer and synergistic antimicrobial activity	El Domany et al. (2018)
19	*Saccharomyces cerevisiae*		Surface plasmon-enhanced applications	Qu et al. (2018)

(continued)

Table 3.1 (continued)

S. No.	Microorganisms	Size (nm)	Application	Reference
20	*Phaffia rhodozyma*	4–7	Antifungal activity	Rónavári et al. (2018)
21	*Magnusiomyces ingens*	20.3–28.3	Catalyst for nitrophenols reduction	Qu et al. (2018)
22	*Cystoseira baccata*	8.4	Anticancer activity	González-Ballesteros et al. (2017)
23	*Galaxaura elongata*	3.8–77.1	Antibacterial activity	Abdel-Raouf et al. (2017)

better equipped to withstand the poisonous effects of soluble gold and manufacture AuNPs (Srinath et al. 2018). The color of AuNPs varied with Acinetobacter sp. SW30 incubation due to varied concentrations of gold chloride and different cell densities, indicating change in size and shape. Fe(III) ions are reduced, and the magnetosome vesicles present in *Geobacter* sp., *Magneto spirillum magnetotacticum* undergo dehydration to create magnetite. Iron is stored in vesicles by an intracellular protein called ferritin, which keeps it in a soluble, nontoxic state. The generated NPs exhibit the qualities including great purity, few crystalline flaws, small size, mono-dispersive, and others. The extracellular manufacturing of silver (Ag) and gold (Au) NPs can benefit greatly from the use of thermophilic bacteria. The amount of nanomaterials is produced by these extracellular systems, which reduce the need for further processing of these metals (Jaiswal et al. 2022). Antibacterial drugs that work against $Gram^{+ve}$ or $Gram^{-ve}$ bacteria were synthesized by MDR (multi-drug resistant) microorganisms. It is well-known that $Gram^{-ve}$ bacteria have a very thin peptidoglycan contrasted to $Gram^{+ve}$ bacteria, has thick cell wall and exhibits better antibacterial resistance to drugs; the Gram-negative bacteria have a thin layer of cell wall that is vulnerable to NPs action. Therefore, there is a chance that the AuNPs will also be able to work against $Gram^{+ve}$ bacteria (Menon et al. 2017).

3.4.2 Synthesis by Fungal Strains

More fungi have recently been used for research purposes as it has been discovered that they may have a role in the biogenesis of AuNPs. They are commonly utilized because they secrete elevated quantities of enzymes that may be worked on in the lab and have several useful applications. Bacteria and algae, filamentous fungi offer distinct benefits due to their high metal tolerance and capacity for bioaccumulation. They also produce extracellular enzymes, whose manufacture at large scale is simple. Fungal active biomolecules regulate the shape and size distribution of the NPs. They took up the gold ions, which caused the intracellular formation of the AuNPs. When the ultrathin sections of Au-fungal cells were examined, it was discovered that AuNPs had accumulated in the cell vacuoles (Seku et al. 2023).

Because they are easier to cultivate both in the laboratory and on an industrial scale and release a lot of proteins, fungi seem to have more promise for the large-scale production of NPs (Table 3.1). In addition, fungi produce NPs with good monodispersity and specified dimensions. Numerous fungi, including *Fusarium oxysporum* and *Verticillium* sp., have been found to manufacture NPs either intracellular or extracellular (Kumari et al. 2023). Fungal extracts can be used to create gold nanoplates. *Pichia jadinii* and *Yarrowia lipolytica*, two yeasts that have previously been demonstrated to have a good potential for producing AuNPs, are currently being specifically explored for the purpose of engineering AuNPs (Punia et al. 2023).

3.4.3 Synthesis by Actinomycete

Actinomycetes are prokaryotes and are easily genetically manipulated to produce NPs of greater size and polydispersed distribution. The prokaryotes' characteristics resemble those of bacteria, but the actinomycetes' similarities to fungi are more striking (mycobacteria and coryneform). They are currently employed in nanotechnology because of their capacity to generate secondary metabolites that resemble antibiotics (Menon et al. 2017). Actinomycetes employ extracellular and intracellular routes for NPs synthesis. AuNPs were synthesized from *Nocardia farcinica*, *Streptomyces viridogens*, *Rhodococcus* species, *Streptomyces hygroscopicus*, and *Thermo actinomycete* species. The intracellular reduction of Au ions lowered AuNPs on the cell wall and membrane rather than in the cytoplasm. A combination of enzymes released from the cell wall and membrane initiated the reduction of AuNPs, and proteins involved in stabilization (Alsaiari et al. 2023).

3.4.4 Synthesis Using Strains of Algae

Algae are photoautotrophic, eukaryotic, aquatic, and oxygenic microorganism and can collect heavy metals. Researchers are working to develop more environmentally friendly methods for creating nanoparticles (Table 3.1). This is a benefit of using algae as a plentiful source of raw materials (Babu and Tirkey 2023). The fucoidans are the polysaccharide that marine brown algae cell walls secrete has shown to have several uses in a variety of sectors, including the anticoagulant, anti-inflammatory, antiviral, and even anticancer. They are also utilized as whitening or antiaging agents in the cosmetics industry. These fucoidans can be used to successfully synthesize AuNPs as an alternative to chemical processes as nanophytomedicine (Rathod and Arunkumar 2023). Due to its capacity to absorb heavy metals, brown algae have been utilized more than other species. Their intricate cell wall, which is abundant in mucilaginous polysaccharides, addresses the absorbable nature of heavy metals clearly. Additionally, it has functional groups, such as carboxyl groups, that are important for absorption.

3.5 Gold Nanoalloys

Clusters made of two or more metallic elements are known as nanoalloys. Compared with equivalent individual metal NPs, gold nanoalloys have distinctive and frequently improved electrical, optical, catalytic, and magnetic properties. Two metals can be combined naturally or artificially using various production techniques. When compared with monometallic particles, solitary bimetallic nanoparticles have superior physical stability and distinguishing characteristics. Due of their numerous intriguing applications, bimetallic NP synthesis is attracting a lot of attention (Ferrando 2022).

It was discovered that *Fusarium oxysporum* could produce 8–14 nm Au–Ag nanoalloy and that the fungus's NADH-dependent protein controlled the process (Salam et al. 2023). Spirulina platensis synthesizes Ag–Au alloy with 17–25 nm (Khanna et al. 2023). *Neurospora crassa* forms Au–Ag bimetallic alloy on the outer cell wall, when exposed to the ionic solutions of gold and silver (Mohammadi et al. 2023). Changes in the ionic concentration of the solution result in the formation of 3–90 nm of Au–Ag alloy (bimetallic NPs) (Mohammadi et al. 2023).

3.6 Gold Nanoconjugates

AuNPs are combined with a variety of biomolecules, including antibodies, proteins, peptides, DNA, and pharmaceuticals, to create gold nanoconjugates. The resulting conjugate displays the selectivity and specificity of NPs as well as their thermal, optical, imaging, and carrier properties. Smaller-sized AuNPs are desirable for immobilizing proteins and enzymes, and these nanoconjugates offer various benefits in biocatalysis, biosensing, and medicine. NPs have a great capacity for enzyme loading due to their high surface area to volume ratio (Oliveira et al. 2023).

3.7 Gold Nanoparticles Properties and Characterization

AuNPs display remarkable features that set them apart from metallic gold, indicating the enormous potential for use in medicine. These characteristics include: (1) outstanding optical and electrical properties, (2) facile surface functionalization, (3) excellent chemical and mechanochemical stability, (4) surface plasmon resonance effect, (5) distinct catalytic activity, and (6) biocompatibility. Additionally, the AuNPs have outstanding size dispersion properties, a controlled shape, and resistance to oxidation. Because of their greater surface area to volume ratio, AuNPs with diameters less than 10 nm display entirely distinct physiochemical/thermodynamic characteristics. The stability, optical, and electrical qualities are very crucial since they give AuNPs the rest of their other properties (Amina and Guo 2020).

3.7.1 Stability

Although AuNPs have great mechanical and chemical durability, nanostructure aggregation in a surfactant-free reaction is a frequent event that makes it challenging to study their properties and use them. AuNPs can be stabilized by chemical substances such as citrate, ascorbic acid, etc. In addition, the surface of AuNPs can be altered by thiol compounds, cysteine, or polyvinyl alcohol coating. It has been demonstrated that storing AuNPs in the dark at 4°C will increase their stability (Ielo et al. 2021).

3.7.2 Optical and Electronic Properties

Vibrant colors are produced by AuNPs through interactions with visible light. The surroundings, size, and physical characteristics of AuNPs have a significant impact on how they interact with light. These distinct optical-electronic characteristics have recently been used in medication administration, therapies, organic photovoltaics, sensory probes, electrical conductors, and catalysis. By altering the size, shape, surface chemistry, or aggregation state, AuNPs' optical and electrical properties can be tailored for use in applications, including drug delivery and targeted cancer imaging (Ielo et al. 2021).

3.7.3 Characterization

Numerous methods have been used to characterize gold nanoalloys and AuNPs produced by microbes. However, a variety of methodologies are required for characterization rather than just one methodology. For the primary sample, Ultraviolet–visible spectroscopy is employed for the detection of AuNPs being produced by microbial AuNPs synthesis. *Thermomonospora*, *Rhodopseudomonas capsulata*, *Sclerotium rolfsii*, and *extremophilic* yeasts are a few examples where a peak in the region of 500–550 nm clearly shows the existence of AuNPs (Noah 2019). Fourier Transform Infrared Spectroscopy analysis is used to find the functional groups involved in the reduction of Au ions. X-ray diffraction spectroscopy (XRD) is used to analyze the AuNPs' crystal structure, phase composition, and mean size. The atomic analysis, energy dispersive spectrum (EDS), and energy dispersive X-ray spectroscopy (EDX) can all be used to characterize the electronic state and chemical composition of materials. Characterization of AuNPs is produced by *Escherichia coli*, *Yarrowia lipolytica*, *Rhizopus oryzae*, and *Rhodopseudomonas capsulate* using EDS and EDX (Noah 2019).

Transmission electron microscopy (TEM) is used to map and image NPs in order to better understand their shape. Lattice fringes of AuNPs can be seen using high resonance transmission electron microscopy (HR-TEM) to confirm that its nature is crystalline. Scanning electron microscopy (SEM) is an imaging method that has been utilized to characterize AuNPs. Using HR-TEM, the particle size of *Spirulina*

platensis was identified as 5 nm with spherical shape (Lasita et al. 2022). According to TEM analysis, the size of *G. stearothermophilus* AuNPs were found to be 11, 12–14, and 5–8 nm sized particles (Molinaro et al. 2022), AUNPs of *P. denitrificans* were found to be 25–30 nm (Bharti et al. 2022). The majority of the AuNPs created by the *Enterobacteriaceae* family of bacteria were spherically shaped (Yassin and Subhi 2022), whereas triangles were produced by the *Bacillaceae* family (Donga and Chanda 2022) and spherical and blunt triangles by the *Pseudomonadaceae* family (Thipe et al. 2022). Using the FE-TEM (field enhanced transmission electron microscope), the *Planococcaceae* family member *Sphingomonas koreensis* created sphere-shaped AuNPs (Suresh et al. 2022). In addition to the techniques outlined above, resonance Raman scattering and cyclic voltammetry have also been utilized for the characterization of gold nanoconjugates. Gold nanoconjugates are also characterized using X-ray electron spectroscopy and thermogravimetric analysis (TGA).

3.8 Mechanism Gold Nanoparticles Synthesis by Microbes

A number of bacteria produce AuNPs by the reduction of Au^{3+} ions, but it is hypothesized that the microbial-secreted enzymes majorly involved the inbio-reduction of metal ions results in NPs synthesis. Hydrogenase, and nitrate reductase-mediated synthesis of AuNPs occurs. By understanding the metabolic processes that result in the bio mineralization of gold, a reasonable strategy for producing AuNPs can be created (34).

The synthesis of intracellular AuNPs was discovered to be influenced by physicochemical factors including temperature, pH, and substrate concentration (Banik et al. 2022). According to reports, these factors and the microorganisms' development circumstances can be changed to affect the morphology of AuNPs. By further adjusting these characteristics, monodispersity can be attained. AuNPs were stabilized by proteins and the amino acid residues (cysteine, tyrosine, and tryptophan). Proteins with free amino or cysteine groups can attach to the AuNPs and stabilize them. Tyrosine can occasionally connect to the surface of gold via amine groups and diminish silver ions at high pH, forming nanostructures with an Au core and an Ag shell. At basic pH, tryptophan has also been demonstrated to create metal NPs. By taking an electron from a transitory tryptophyl radical created by the conversion of a tryptophan residue contained in the peptide, a metal ion creates nanoparticles (NPs). Additionally, it was stated that certain proteins had an impact on the capping and stabilization of AuNPs (Banik et al. 2022).

Precipitation of AuNPs in *B. subtilis* 168 cells, while the cells were incubated with Au^{3+} ions, was described in the first mechanistic approach for the bacterial manufacture of AuNPs (Salam et al. 2023). *Shewanella* reduces Au^{3+} ions in the presence of hydrogen gas yielding 10–20 nm AuNPs in anaerobic conditions (Singh et al. 2022). *Desulfovibrio desulfuricans* and *E. coli* reduce Au^{3+} ions and accumulate AuNPs by serving (H2) gas as electron donor and periplasmic hydrogenases involved in bioreduction (Varia et al. 2014). *Plectonema boryanum* UTEX 485, cubic AuNPs precipitate at temperatures between 25 and 100°C for up to a

month and 200°C for a single day (Nitnavare et al. 2022). This may be caused by how cyanobacteria and aqueous gold chloride interact, which at first encourages the precipitation of NPs of amorphous gold.

In *Trichothecium* sp., different growth conditions like static and shaking were used to regulate the synthesis of AuNPs. AuNPs were synthesized extracellularly and intracellularly under shaking and static conditions, respectively (Kar 2022). Additionally, mushrooms produce proteins and reduce agents that aid in the stability of NPs produced extracellularly. By regulating the activities and cellular growth circumstances in yeast strains, AuNPs can be synthesized under controlled conditions. The bioreduction of Au^{3+} ions to produce AuNPs is thought to be carried out by species-specific NADH reliant reductases in *Fusarium oxysporum* and *Rhodopseudomonas capsulata* (Noah 2019). The precise mechanism underlying the Au^{3+} ion reduction dependent on NADH is unknown. An innovative fungal enzyme-based invitro technique for nanomaterial production has now become available for the first time. Electrostatic interactions between the cell wall of *Verticillium* with lysine residues in enzymes Au^{3+} ions were trapped on the surface of fungal mycelia surface. As a result, the bioreduction of Au^{3+} ions by enzymes caused metal atoms to aggregate and the creation of AuNPs (Banik et al. 2022).

The proteins and enzymes on the cell surface trap and reduce Au+ ions to create nuclei, which then go through crystal development to form aggregates (size 12,870 nm) of AuNPs at normal pH (2–3.5). Reduction and binding of positive amino and sulfhydryl groups and negative carboxylic groups in proteins mediate the binding of gold ions. A persistent extracellular glycosylated laccase derivative was discovered to be necessary for the formation of extracellular AuNPs in growth media. Enzymes have been demonstrated to be crucial for the stability of NPs and the reduction of metal ions in actinomycete *Thermomonospora*, enabling the effective generation of monodispersed AuNPs (Banik et al. 2022).

3.9 Applications of Gold Nanoparticles Produced by Microbes

There are just two papers that indicate AuNPs made by microorganisms that can be employed in medical applications. The AuNPs that *Candida albicans* generate have their potential for detecting whether liver cancer has been researched (116). It has been used to explore the cytotoxic effects of AuNPs produced by *Penicillium brevicompactum* against mouse mayo blast carcinoma C2C12 cells (107).

Nearly every human life is now affected by cancer, and scientists are striving to treat it with gold and silver nanoparticles. The anticancer nanoparticles have been standardized to combat different types of human cancer such as cancerous cells in the prostate, colon, lungs, heart, and breast (Cheng et al. 2021). NPs has the capability for adsorptive behavior and electron transport used in biosensors (Mostafavi et al. 2022). Different kinds of harmful metals from the environment have been detected using nanoparticles (Mitra et al. 2022). Copper necessary for physiological functions but at higher levels induces Wilson's disorder (Garza et al. 2022).

The usage of AuNPs at the cathodes, along with the quantized charging effect and no external power source, has recently been discovered to be a tremendous assistance in catalyzing the production of hydrogen via microbial fuel cells (MFCS) (Chen et al. 2022).

Trichoderma sp. was used to create spherical AuNPs with strong antibacterial activity (Soliman et al. 2022). The experiment for the manufacture of AuNPs with the fungus *Penicillium oxalicum* had shown that at pH levels of 8 and 12, the average particle size determined by TEM and DLS analyses was close to 6 and 4 nm. It was observed that TEM data showed smaller particle sizes than DLS analyses, which may be caused by the NPs tendency to aggregate. They discovered that pH levels between 8 and 12 produced the greatest outcomes, and they used the DLS analysis to confirm particle size and distribution.

The TEM study had shown that the morphologies of the nanoparticles produced by the algal (Galaxaura elongata)-mediated process included spherical (predominantly), rod, triangular or truncated triangular, and even hexagonal (Heinemann and Dias 2022). Although the FTIR results supported the formation of a coat that protects the particle from agglomeration is facilitated by the presence of carbonyl stretch and N-H stretch, which have a stronger capacity to connect with the metal nanoparticle. The zeta potential also verified the particles' stability and surface charge. The sample was a Prasiola crisp, a freshwater epilithic green alga, with dimensions of 5–25 nm and a spherical shape as determined by TEM examination (Menon et al. 2017).

When compared with the TEM investigation, which showed that the *Sargassum swartzii* yields AuNPs in the range of 20–60 nm, DLS measurements showed that the particle size is significantly greater (Costa et al. 2020). The brown alga *Stoechospermum marginatum* formed AuNPs (Murugesan et al. 2017). The minimal size of the NPs in *Thermomonospora* sp. is 8 nm. TEM analysis showed the *Botrytis cinerea's* generated AuNPs size and form (Chowdhury et al. 2022). *Yarrowia lipolytica*, a member of the *Dipodascaceae* family, was used in the manufacture of AuNPs (Kolhe et al. 2022). *Candida guilliermondii* produced spherical particles with sizes between 50 and 70 nm with hexagonal and triangular shapes (Umamaheswari and Abirami 2023). Additionally, the Dipodascaceae family member *Magnusiomyces ingens LH-F1* created nanoparticles with geometries like spheres, triangles, and hexagons that ranged in size from 9.8 to 80.1 nm (Skrotska et al. 2022).

AuNPs has wider applications in various fields as antibacterial agents, antiproliferative agents, dye degradation, etc. The applications of AuNPs were listed in Table 3.1.

Paracoccus haeundaensis BC74171 AuNPs *were with* 20.93 ± 3.46 nm *possess* antioxidant activity and antiproliferative activity (Patil et al. 2019). *Micrococcus yunnanensis* AuNPs were with 53.8 nm possess antibacterial and anticancer (Jafari et al. 2018). Similarly, anticancer activity of AuNPs was reported by Camas et al. (2018) by using *Mycobacterium* sp., González-Ballesteros et al. (2017) by using *Cystoseira baccata*, El Domany et al. (2018) by using *Pleurotus ostreatus*, González-Ballesteros et al. (2017) by using *Cystoseira baccata*, Abdel-Raouf et al. (2017) by using *Galaxaura elongate*, and Munawer et al. (2020) by using

Cladosporium sp. Antibacterial activity of AuNPs was reported by Tripathi et al. (2018) by using *Trichoderma harzianum*, Acay (2021), Abdel-Raouf et al. (2017) by using *Galaxaura elongate*, and Acay (2021) by using *Morchella esculenta*. Dye degradation activity of AuNPs was reported by Kulkarni et al. (2018) by using *Pseudoalteromonas lipolytica*, Srinath et al. (2018) by using *Bacillus subtilis*, and Ranjitha et al. (2018) by using *Streptomyces griseoruber*.

3.10 Future Prospects

Microbes were abundant in the environment; hence, various microorganisms were screened for the production of AuNPs. *Glidobacteria*, *beta epsilon*, and *zeta proteobacteria* members have were not reported to synthesize NPs; therefore, groups should be investigated for AuNP production. Monodispersed AuNPs with required size was trustworthy objective for future research for AuNPs produced by microbes. The clarification of the mechanism of AuNPs produced by microbes is one of the difficult problems in nanotechnology. Additionally, a proteomic technique has to be applied to investigate the precise process of AuNP formation. It is necessary to conduct a differential proteome study of the AuNPs production process. The synthesis of proteins and biomolecules that mediate the creation and characterization of AuNPs should also be the subject of research. Studies should concentrate on AuNP stability and methods to stop AuNP aggregation. In addition to their function in synthesis, these proteins are frequently claimed to stabilize the NPs. It is necessary to find newer stabilizing agents for NPs.

3.11 Conclusion

Microbes are abundant in the environment, making it crucial to screen each prospective one. It is also vital to take into account the compounds that play a role in how these microbes produce nanoparticles. Consequently, these bimolecular molecules can be characterized physiochemically and via purification. NPs aggregation is another crucial element that needs to be closely monitored because the outcomes of aggregated particles can vary. As a result, it is possible to incorporate novel stabilizing agents into the synthesis to stabilize these nanoparticles. The developing field of bio-nanotechnology has opened up numerous avenues for the development of unique products that can benefit people. As a result, additional study has been conducted to explain how these particles are created and how they may be utilized to cure rare disorders, including all the various cancers. Hence limiting the use of nonbiodegradable plastics and reducing the infiltration of bacteria and dangerous microbes. Additionally, they can function as nano-sensors to help identify harmful metals or food spoilage. These are only a few potential future uses for green synthesis to produce nanoparticles.

References

Abdel-Raouf N, Al-Enazi NM, Ibraheem IB (2017) Green biosynthesis of gold nanoparticles using Galaxaura elongata and characterization of their antibacterial activity. Arab J Chem 10:S3029–S3039

Acay H (2021) Utilization of Morchella esculenta-mediated green synthesis golden nanoparticles in biomedicine applications. Prep Biochem Biotechnol 51(2):127–136

Ahmad R, Srivastava S, Ghosh S, Khare SK (2021) Phytochemical delivery through nanocarriers: a review. Colloids Surf B: Biointerfaces 197:111389

Alsaiari NS, Alzahrani FM, Amari A, Osman H, Harharah HN, Elboughdiri N, Tahoon MA (2023) Plant and microbial approaches as green methods for the synthesis of nanomaterials: synthesis, applications, and future perspectives. Molecules 1:463

Amina SJ, Guo B (2020) A review on the synthesis and functionalization of gold nanoparticles as a drug delivery vehicle. Int J Nanomedicine 15:9823–9857

Aziz N, Fatma T, Varma A, Prasad R (2014) Biogenic synthesis of silver nanoparticles using Scenedesmus abundans and evaluation of their antibacterial activity. J Nanoparticles 2014:689419. https://doi.org/10.1155/2014/689419

Aziz N, Faraz M, Pandey R, Sakir M, Fatma T, Varma A, Barman I, Prasad R (2015) Facile algae-derived route to biogenic silver nanoparticles: synthesis, antibacterial and photocatalytic properties. Langmuir 31:11605–11612. https://doi.org/10.1021/acs.langmuir.5b03081

Babu PJ, Tirkey A (2023) Green synthesis of gold nanoparticles and their biomedical and healthcare applications. In: Nanotechnology and human health. Elsevier, Amsterdam, pp 191–229

Bai X, Wang Y, Song Z, Feng Y, Chen Y, Zhang D, Feng L (2020) The basic properties of gold nanoparticles and their applications in tumor diagnosis and treatment. Int J Mol Sci 21(7):2480

Banik A, Vadivel M, Mondal M, Sakthivel N (2022) Molecular mechanisms that mediate microbial synthesis of metal nanoparticles. In: Microbial metabolism of metals and metalloids. Springer International Publishing, Cham, pp 135–166

Bhargava A, Jain N, Khan MA, Pareek V, Dilip RV, Panwar J (2016) Utilizing metal tolerance potential of soil fungus for efficient synthesis of gold nanoparticles with superior catalytic activity for degradation of rhodamine B. J Environ Manag 183:22–32

Bharti B, Kumar R, Kumar H, Li H, Zha X, Ouyang F (2022) Advanced applications and current status of green nanotechnology in the environmental industry. In: Green functionalized nanomaterials for environmental applications. Elsevier, Amsterdam, pp 303–340

Camas M, Sazak Camas A, Kyeremeh K (2018) Extracellular synthesis and characterization of gold nanoparticles using Mycobacterium sp. BRS2A-AR2 isolated from the aerial roots of the Ghanaian mangrove plant, Rhizophora racemosa. Indian J Microbiol 58:214–221

Chen QY, Lu RC, Zhu YC, Wang YH (2022) Metal recovery and electricity generation from wastewater treatment: the state of the art. Processes 11(1):88

Cheng Z, Li M, Dey R, Chen Y (2021) Nanomaterials for cancer therapy: current progress and perspectives. J Hematol Oncol 14(1):1–27

Chowdhury NK, Choudhury R, Gogoi B, Chang CM, Pandey RP (2022) Microbial synthesis of gold nanoparticles and their application. Curr Drug Targets 23(7):752–760

Costa LH, Hemmer JV, Wanderlind EH, Gerlach OM, Santos AL, Tamanaha MS, Bella-Cruz A, Corrêa R, Bazani HA, Radetski CM, Almerindo GI (2020) Green synthesis of gold nanoparticles obtained from algae sargassum cymosum: optimization, characterization and stability. Bio Nanoscience 10:1049–1062

Dikshit PK, Kumar J, Das AK, Sadhu S, Sharma S, Singh S, Gupta PK, Kim BS (2021) Green synthesis of metallic nanoparticles: applications and limitations. Catalysts 11(8):902

Donga S, Chanda S (2022) Recent trends in green synthesis of gold nanoparticles (AuNPs) and their biological efficacies: a mini review. Nanotechnol Sci Technol 1:1

El Domany EB, Essam TM, Ahmed AE, Farghali AA (2018) Biosynthesis physico-chemical optimization of gold nanoparticles as anti-cancer and synergetic antimicrobial activity using *Pleurotus ostreatus* fungus. J Appl Pharmaceut Sci 8(5):119–128

El-Sheekh MM, Shabaan MT, Hassan L, Morsi HH (2022) Antiviral activity of algae biosynthesized silver and gold nanoparticles against Herps Simplex (HSV-1) virus in vitro using cell-line culture technique. Int J Environ Health Res 32(3):616–627

Ferrando R (2022) Global optimization of gold-based nanoalloys: AuCo, AuCu, and AuRh. In: Frontiers of nanoscience, vol 21. Elsevier, London, pp 71–91

Gao C, Wang Y, Ye Z, Lin Z, Ma X, He Q (2021) Biomedical micro-/nanomotors: from overcoming biological barriers to in vivo imaging. Adv Mater 33(6):2000512

Garza NM, Swaminathan AB, Maremanda KP, Zulkifli M, Gohil VM (2022) Mitochondrial copper in human genetic disorders. Trends Endocrinol Metab 34:21

Ghosh S, Ahmad R, Zeyaullah M, Khare SK (2021) Microbial nano-factories: synthesis and biomedical applications. Front Chem 9:626834

González-Ballesteros N, Prado-López S, Rodríguez-González JB, Lastra M, Rodríguez-Argüelles M (2017) Green synthesis of gold nanoparticles using brown algae Cystoseira baccata: its activity in colon cancer cells. Colloids Surf B: Biointerfaces 153:190–198

Harris HW, Sánchez-Andrea I, McLean JS, Salas EC, Tran W, El-Naggar MY, Nealson KH (2018) Redox sensing within the genus Shewanella. Front Microbiol 8:2568

Heinemann MG, Dias D (2022) Biogenic synthesis of metallic nanoparticles from algae. In: Bioprospecting algae for nanosized materials. Springer, Berlin, pp 71–91

Ielo I, Rando G, Giacobello F, Sfameni S, Castellano A, Galletta M, Drommi D, Rosace G, Plutino MR (2021) Synthesis, chemical–physical characterization, and biomedical applications of functional gold nanoparticles: a review. Molecules 26(19):5823

Jadoun S, Chauhan NP, Zarrintaj P, Barani M, Varma RS, Chinnam S, Rahdar A (2022) Synthesis of nanoparticles using microorganisms and their applications: a review. Environ Chem Lett 20(5):3153–3197

Jafari M, Rokhbakhsh-Zamin F, Shakibaie M, Moshafi MH, Ameri A, Rahimi HR, Forootanfar H (2018) Cytotoxic and antibacterial activities of biologically synthesized gold nanoparticles assisted by Micrococcus yunnanensis strain J2. Biocatal Agric Biotechnol 15:245–253

Jaiswal S, Roy N, Dhwaj A, Verma D, Prabhakar A (2022) A review on the various mechanisms of green synthesis of metal nanoparticles for biomedical applications. Curr Green Chem 9(2): 62–73

Kar S (2022) Green synthesis of gold nanoparticles for bio-applications. J Sustain Sci Transform Res Rev Lett 1(2):59–62

Kaur A, Gupta H, Dhiman S (2023) Biogenic metallic nanoparticles: synthesis and applications using medicinal plants. Handbook of green and sustainable nanotechnology. Springer, Cham

Khanna K, Kohli SK, Bakshi P, Sharma P, Kour J, Bhardwaj T, Sharma N, Dogra N, Ohri P, Sirhindi G, Bhardwaj R (2023) Green biosynthesis of nanoparticles: mechanistic aspects and applications. In: Environmental applications of microbial nanotechnology. Elsevier, Amsterdam, pp 99–126

Kim TY, Kim MG, Lee JH, Hur HG (2018) Biosynthesis of nanomaterials by Shewanella species for application in lithium ion batteries. Front Microbiol 9:2817

Kisimba K, Krishnan A, Faya M, Byanga K, Kasumbwe K, Vijayakumar K, Prasad R (2023) Synthesis of metallic nanoparticles based on green chemistry and their medical biochemical applications: synthesis of metallic nanoparticles. J Renew Mater 11(6):2575–2591. https://doi.org/10.32604/jrm.2023.026159

Kitching M, Choudhary P, Inguva S, Guo Y, Ramani M, Das SK, Marsili E (2016) Fungal surface protein mediated one-pot synthesis of stable and hemocompatible gold nanoparticles. Enzym Microb Technol 95:76–84

Koch N, Sonowal S, Prasad R (2023) Elucidate the smart tailored biogenic nanoparticles and their applications in remediation. Biotechnol Genet Eng Rev. https://doi.org/10.1080/02648725.2023.2219942

Kolhe N, Damle E, Pradhan A, Zinjarde S (2022) A comprehensive assessment of Yarrowia lipolytica and its interactions with metals: current updates and future prospective. Biotechnol Adv 59:107967

Kulkarni RR, Shaiwale NS, Deobagkar DN, Deobagkar DD (2015) Synthesis and extracellular accumulation of silver nanoparticles by employing radiation-resistant *Deinococcus radiodurans*, their characterization, and determination of bioactivity. Int J Nanomedicine 10: 963

Kulkarni R, Harip S, Kumar AR, Deobagkar D, Zinjarde S (2018) Peptide stabilized gold and silver nanoparticles derived from the mangrove isolate Pseudoalteromonas lipolytica mediate dye decolorization. Colloids Surf A Physicochem Eng Asp 555:180–190

Kumari KA, Mangatayaru KG, Reddy GB (2023) Fungal and yeast-mediated biosynthesis of metal nanoparticles: characterization and bio applications. In: Fungal cell factories for sustainable nanomaterials productions and agricultural applications. Elsevier, Amsterdam, pp 309–336

Lasita AL, Pabrekar S, Wagh NS, Lakkakula J (2022) Metallic biomaterials in biomedical applications. In: Functional biomaterials: drug delivery and biomedical applications. Springer, Singapore, pp 341–370

Lombardo D, Calandra P, Pasqua L, Magazu S (2020) Self-assembly of organic nanomaterials and biomaterials: the bottom-up approach for functional nanostructures formation and advanced applications. Materials 13:1048. https://doi.org/10.3390/ma13051048

Menon S, Rajeshkumar S, Kumar V (2017) A review on biogenic synthesis of gold nanoparticles, characterization, and its applications. Resour Eff Technol 3(4):516–527

Mitra S, Chakraborty AJ, Tareq AM, Emran TB, Nainu F, Khusro A, Idris AM, Khandaker MU, Osman H, Alhumaydhi FA, Simal-Gandara J (2022) Impact of heavy metals on the environment and human health: novel therapeutic insights to counter the toxicity. J King Saud Univ Sci 34: 101865

Mohammadi P, Ali AA, Ghadam P (2023) Mycogenic nanoparticles and their applications as antimicrobial and antibiofilm agents in postharvest stage. In: Fungal cell factories for sustainable nanomaterials productions and agricultural applications. Elsevier, Amsterdam, pp 635–655

Molinaro C, Bénéfice M, Gorlas A, Da Cunha V, Robert HM, Catchpole R, Gallais L, Forterre P, Baffou G (2022) Life at high temperature observed in vitro upon laser heating of gold nanoparticles. Nat Commun 13(1):5342

Mostafavi E, Medina-Cruz D, Truong LB, Kaushik A, Iravani S (2022) Selenium-based nanomaterials for biosensing applications: progress and prospects. Mater Adv 3:7742

Munawer U, Raghavendra VB, Ningaraju S, Krishna KL, Ghosh AR, Melappa G, Pugazhendhi A (2020) Biofabrication of gold nanoparticles mediated by the endophytic Cladosporium species: photodegradation, in vitro anticancer activity and in vivo antitumor studies. Int J Pharm 588: 119729

Murugesan S, Bhuvaneswari SU, Sivamurugan V (2017) Green synthesis, characterization of silver nanoparticles of a marine red alga Spyridia fusiformis and their antibacterial activity. Int J Pharm Sci 9(5):192–197

Nitnavare R, Bhattacharya J, Thongmee S, Ghosh S (2022) Utilizing photosynthetic microbes in nanobiotechnology: applications and perspectives. Sci Total Environ 1:156457

Noah N (2019) Green synthesis: characterization and application of silver and gold nanoparticles. In: Green synthesis, characterization and applications of nanoparticles. Elsevier, Amsterdam, pp 111–135

Oliveira BB, Ferreira D, Fernandes AR, Baptista PV (2023) Engineering gold nanoparticles for molecular diagnostics and biosensing. Wiley Interdiscipl Rev Nanomed Nanobiotechnol 15(1): e1836

Pandey S, Rai LC, Dubey SK (2022) Cyanobacteria: miniature factories for green synthesis of metallic nanomaterials: a review. BioMetals 35(4):653–674

Pareek V, Bhargava A, Panwar J (2020) Biomimetic approach for multifarious synthesis of nanoparticles using metal tolerant fungi: a mechanistic perspective. Mater Sci Eng B 262: 114771

Pastorino F, Brignole C, Di Paolo D, Perri P, Curnis F, Corti A, Ponzoni M (2019) Overcoming biological barriers in neuroblastoma therapy: the vascular targeting approach with liposomal drug nanocarriers. Small 15(10):1804591

Patil MP, Kang MJ, Niyonizigiye I, Singh A, Kim JO, Seo YB, Kim GD (2019) Extracellular synthesis of gold nanoparticles using the marine bacterium Paracoccus haeundaensis BC74171T and evaluation of their antioxidant activity and antiproliferative effect on normal and cancer cell lines. Colloids Surf B: Biointerfaces 183:110455

Pourali P, Badiee SH, Manafi S, Noorani T, Rezaei A, Yahyaei B (2017) Biosynthesis of gold nanoparticles by two bacterial and fungal strains, Bacillus cereus and *Fusarium oxysporum*, and assessment and comparison of their nanotoxicity in vitro by direct and indirect assays. Electron J Biotechnol 29:86–93

Prasad R (2014) Synthesis of silver nanoparticles in photosynthetic plants. J Nanoparticles 2014:963961. https://doi.org/10.1155/2014/963961

Prasad R (2016) Advances and applications through fungal nanobiotechnology. Springer, International Publishing Switzerland. (ISBN: 978-3-319-42989-2)

Prasad R (2017) Fungal nanotechnology: applications in agriculture, industry, and medicine. Springer Nature Singapore Pte Ltd. (ISBN 978-3-319-68423-9)

Prasad R (2019a) Microbial nanobionics: basic research and applications. Springer International Publishing. (ISBN 978-3-030-16534-5) https://www.springer.com/gp/book/9783030165338

Prasad R (2019b) Microbial nanobionics: state of art. Springer International Publishing. (ISBN 978-3-030-16383-9) https://www.springer.com/gp/book/9783030163822

Prasad R, Pandey R, Barman I (2016) Engineering tailored nanoparticles with microbes: quo vadis. WIREs Nanomed Nanobiotechnol 8:316–330. https://doi.org/10.1002/wnan.1363

Prasad R, Jha A, Prasad K (2018) Exploring the realms of nature for nanosynthesis. Springer International Publishing. (ISBN 978-3-319-99570-0) https://www.springer.com/978-3-319-99570-0

Priyadarshini S, Gopinath V, Priyadharsshini NM, Mubarak Ali D, Velusamy P (2013) Synthesis of anisotropic silver nanoparticles using novel strain, Bacillus flexus and its biomedical application. Colloids Surf B: Biointerfaces 102:232–237

Punia A, Singh RP, Singh V, Chauhan NS (2023) Environment sustainability with microbial nanotechnology. In: Environmental applications of microbial nanotechnology. Elsevier, Amsterdam, pp 289–314

Pytlik N, Kaden J, Finger M, Naumann J, Wanke S, Machill S, Brunner E (2017) Biological synthesis of gold nanoparticles by the diatom Stephanopyxis turris and in vivo SERS analyses. Algal Res 28:9–15

Qu Y, You S, Zhang X, Pei X, Shen W, Li Z, Li S, Zhang Z (2018) Biosynthesis of gold nanoparticles using cell-free extracts of *Magnusiomyces ingens LH-F1* for nitrophenols reduction. Bioprocess Biosyst Eng 41:359–367

Rathod P, Arunkumar K (2023) Nanoparticles synthesized by compounds of marine macroalgae for drug delivery. In: Nanophytomedicine. CRC Press, Boca Raton, FL, pp 115–130

Rónavári A, Igaz N, Gopisetty MK, Szerencsés B, Kovács D, Papp C, Vágvölgyi C, Boros IM, Kónya Z, Kiricsi M, Pfeiffer I (2018) Biosynthesized silver and gold nanoparticles are potent antimycotics against opportunistic pathogenic yeasts and dermatophytes. Int J Nanomedicine 13:695

Salam S, Khaliq N, Hussain N, Baqar Z, Iqbal HM, Bilal M (2023) Microbially synthesized nanoparticles: application in health-care management. In: Microbial biomolecules. Academic Press, London, pp 53–76

Seku K, Hussaini SS, Reddy MR, Reddy GB, Kumar KK (2023) Fungal-mediated synthesis of gold nanoparticles and their biological applications. In: Fungal cell factories for sustainable nanomaterials productions and agricultural applications. Elsevier, Amsterdam, pp 23–58

Shedbalkar U, Singh R, Wadhwani S, Gaidhani S, Chopade BA (2014) Microbial synthesis of gold nanoparticles: current status and future prospects. Adv Colloid Interf Sci 209:40–48

Singh S, Rajesh P, Ravindra Y (2022) Study and evaluation of the microorganisms for the formation of metal nanoparticles and their application. J Posit School Psychol 6:4425–4433

Skrotska O, Laziuka Y, Kharchenko Y (2022) Silver and gold nanoparticles: practical application, biosynthesis using yeast bioactivity. Biotechnologies 28:18

Soliman MK, Salem SS, Abu-Elghait M, Azab MS (2022) Biosynthesis of silver and gold nanoparticles and their efficacy towards antibacterial, antibiofilm, cytotoxicity, and antioxidant activities. Appl Biochem Biotechnol 195:1–26

Srinath BS, Namratha K, Byrappa K (2018) Eco-friendly synthesis of gold nanoparticles by Bacillus subtilis and their environmental applications. Adv Sci Lett 24(8):5942–5946

Srivastava S, Usmani Z, Atanasov AG, Singh VK, Singh NP, Abdel-Azeem AM, Prasad R, Gupta G, Sharma M, Bhargava A (2021) Biological nanofactories: using living forms for metal nanoparticle synthesis. Mini-Rev Med Chem 21(2):245–265

Suresh M, Balu S, Jose SC, Jeevanandam J (2022) Phytosynthesized metal nanomaterials as an effective mosquitocidal agent. In: Emerging nanomaterials for advanced technologies. Springer, Berlin, pp 369–396

Thipe VC, Karikachery AR, Cakilkaya P, Farooq U, Genedy HH, Kaeokhamloed N, Phan DH, Rezwan R, Tezcan G, Roger E, Katti KV (2022) Green nanotechnology—an innovative pathway towards biocompatible and medically relevant gold nanoparticles. J Drug Deliv Sci Technol 70:103256

Tripathi RM, Shrivastav BR, Shrivastav A (2018) Antibacterial and catalytic activity of biogenic gold nanoparticles synthesised by Trichoderma harzianum. IET Nanobiotechnol 12(4):509–513

Umamaheswari K, Abirami M (2023) Assessment of antifungal action mechanism of green synthesized gold nanoparticles (AuNPs) using Allium sativum on Candida species. Mater Lett 333:133616

Varia J, Zegeye A, Roy S, Yahaya S, Bull S (2014) Shewanella putrefaciens for the remediation of Au3+, Co2+ and Fe3+ metal ions from aqueous systems. Biochem Eng J 85:101–109

Yassin HA, Subhi BF (2022) Studying the effect of Gold Nanoparticles on some bacterial species isolated from surgical wound infections. J Pharmaceut Negat Results 13(4):798–803

Fungal-Based Nanoparticles

4

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Abstract

Nanotechnology research represents a cutting-edge technology due to its diverse applications. One of the difficult problems in nanotechnology is the production of nanoparticles with high monodispersity, particularly composition, and size. Due to their lower toxicity, biosynthesis of nanoparticles is significant in this context. Nanoparticles can be created using both physical and chemical processes; however, the employment of dangerous chemicals and high temperatures throughout the process raises questions. Therefore, it is essential to create environmentally benign methods for the manufacturing of nanoparticles. It has been stated that the production of nanoparticles by fungus, bacteria, actinomycetes, lichen, and viruses is environment friendly. Furthermore, the fungal system has proven to be a successful method for synthesizing nanoparticles since fungi have unique characteristics, such as a high capacity for wall binding, ease of growth, and ease

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of managing biomass. Nanoparticles produced via mycosynthesis have a wide range of uses, including disease detection and control, wound healing, food preservation, textile fibres, and many more. We have covered fungus as a crucial tool for creating nanoparticles in this chapter. Additionally, techniques and mechanisms for nanoparticle production, as well as possible applications, have been examined.

4.1 Introduction

The most advanced field of science and technology, known as nanotechnology, is employed to address the issue of material size at the nanoscale. The quantitative and qualitative characteristics of the nano-sized components vary greatly from its macroscopic enormous reserves (Mansoori 2005). When we talk about nanotechnology, we usually mean a technique or process that allows us to create and use microscopic systems and structures that can control their size and shape. Nanoparticles differ significantly from their macroscopic counterparts due to their tiny size. The production of nanoparticles from a range of materials is used in the production of important goods such as sophisticated materials, energy storage technologies, electrical and optical displays, and pharmaceuticals that save lives (Osherov et al. 2023). There are many different physical and chemical techniques for synthesizing nanoparticles, but recently, "green chemistry" or "nanobiology synthesis" has captured the attention of the scientific community. In this process, living cells like bacteria, fungi, actinomycetes, and plants are used to synthesize metal nanoparticles, as shown in Fig. 4.1 (Chou and Ren 2000; Geethalakshmi and Sarada 2010; Guilger-Casagrande and de Lima 2019; Lee et al. 2020; Prasad 2014; Prasad et al. 2016; Srivastava et al. 2021; Kisimba et al. 2023; Eftekhari et al. 2023; Koch et al. 2023).

Due to their tolerance for metal accumulation, high binding affinity, and dominance of intracellular metal ion absorption when compared to other microbes, fungal mycoflora and the large-scale biosynthesis of nanoparticles from these microbes have received attention in this area at the present time (Zhang et al. 2011; Chung et al. 2016; Thakkar et al. 2010; Dhillon et al. 2012; Ranjani et al. 2021; Prasad 2016, 2017, 2019a, b). Fungi have been preferred among biological agents for the creation of a range of nanoparticles. Mycosynthesis is the term for the fungi-based nanoparticle synthesis process that is the subject of myconanotechnology (Ingle et al. 2008, 2009; Rai et al. 2009a, b; Yadav et al. 2015). For the creation of nanoparticles, filamentous fungi have advantages over other biological agents (such as bacteria) (Gade et al. 2010a, b). These primarily include a high tolerance for heavy metals, ease of mass fungal growing, extracellular nanoparticle production that lowers the cost of down streaming, etc. Because fungus may produce nanoparticles through extracellular and intercellular modes of action, biosynthesis of nanoparticles by fungi is a relatively simple and logical process. For the synthesis of nanoparticles from fungal microbes, the mycelia are first grown in a suitable broth medium for long enough incubation periods. After the incubation period is complete, the mycelia are washed with sterile distilled water to remove the medium from the

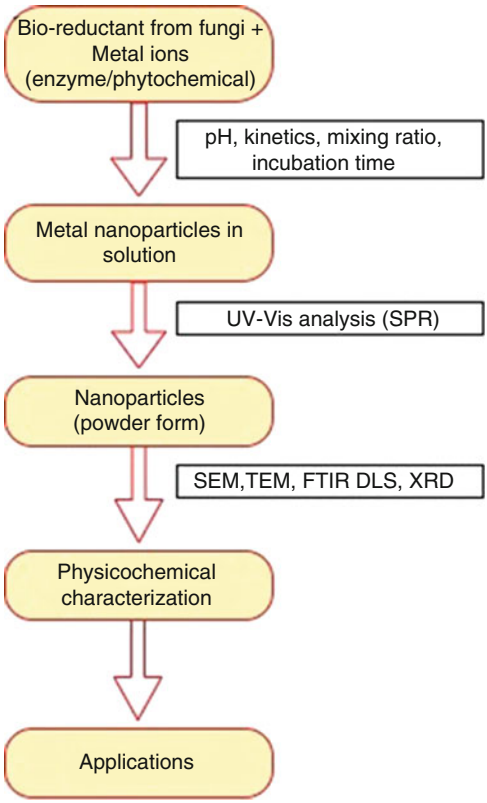

Fig. 4.1 Generalized flow chart for the biosynthesis of metallic nanoparticles

fungal met, and they are then transferred to the deionized water flask and incubated for 24, 48, or 72 h. Following this, the biomass filter will be used once more with Whatman filter paper, cell-free culture filtrate (CFCF) will be collected, combined with an adequate amount of aqueous metal solution, and incubated until the visual colour has improved. Different metals exhibit colour changes in the CFCF during the biosynthesis of nanoparticles, with white yellow to yellow indicating the production of manganese and zinc nanoparticles, pale yellow to pinkish indicating the formation of gold nanoparticles, and pale yellow to brownish indicating the formation of silver nanoparticles (Narayanan and Sakthivel 2010; Waghmare et al. 2011; Jeevan et al. 2012; Punjabi et al. 2015; Mohd Yusof et al. 2019). Different methods of nanoparticle synthesis have been showcased in Fig. 4.2.

4.2 Microbial Synthesis of Nanoparticles

Microorganisms, particularly fungi, are used in the green production of nanoparticles, which possesses unique chemical, electrical, magnetic, mechanical, and electromagnetic capabilities. The properties of the material, such as increasing

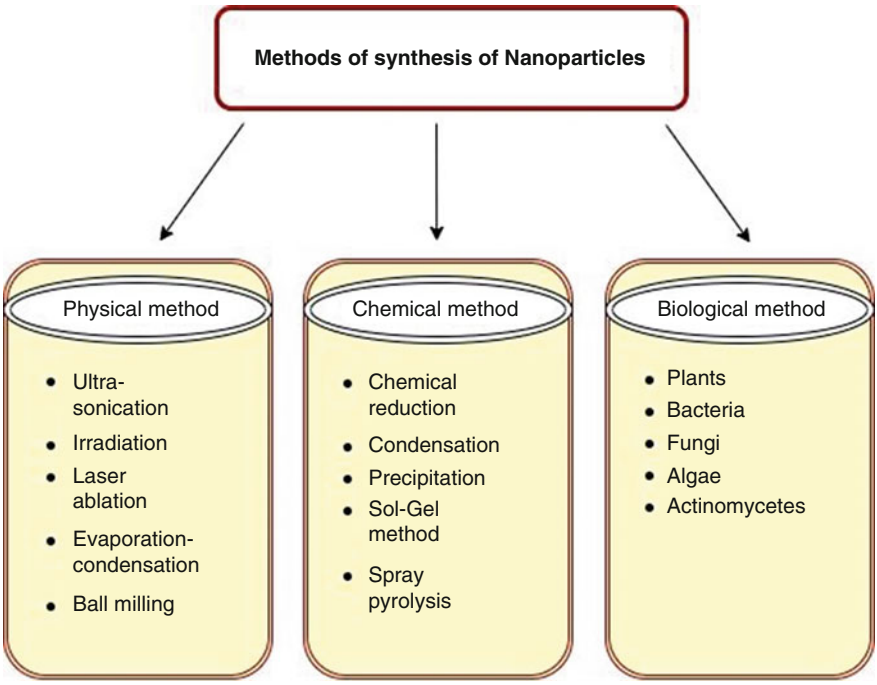

Fig. 4.2 Different methods of nanoparticles synthesis

large surface area, surface density, reducing imperfection, and spatial conformation, which are variable from their original form size material, are influenced by the fact that the nanoparticles are produced by fungi due to the reduction of metal ion dimensions. As a result of having a lower melting point and transition temperature than their bulk form, fungi-produced nanoparticles exhibit significant thermal characteristics (Khandel and Shahi 2016). Due to the interaction of the electron clouds on the surface of the nanoparticles with electromagnetic radiation, these particles also displayed a variety of optical properties that helped to make them suitable sensors depending on their shape, size, and surrounding medium. These optical properties also varied in the visible region for these particles. The magnetic properties of nanoparticles are among their other noteworthy characteristics. These characteristics are vital in the medical sciences, particularly in the many diagnostic approaches (Akbarzadeh et al. 2012). Other biosynthesized iron-based nanoparticles, such as Feridex, are frequently employed as magnetic memory storage devices, magnetic refrigeration, and other applications (Bulte et al. 1999), as well as to track the migration of stem cell inserts into the wound site. Additionally, nanoparticles have surface plasmon characteristics that are valuable for researching adsorption and chemosorption, among other physical and chemical traits of molecules (Ramesh et al. 2014). Microorganisms including bacteria, fungus, yeast, and algae are frequently chosen for use in the synthesis of nanoparticles due to their

ease of cultivation, rapid rate of development, and capacity to thrive under normal pH, temperature, and pressure settings. Diverse biological agents and various metal solutions have different reactions when it comes to the production of nanoparticles. Numerous microorganisms manufacture various inorganic compounds either extracellularly or intracellularly, and the mechanisms vary from one organism to another both intracellularly and extracellularly (Fariq et al. 2017; Hulkoti and Taranath 2014). Metal ions are first trapped on the surface of the cell, and then, in the presence of enzymes produced by microorganisms, they are reduced to nanoparticles. Two forms of microbial nanoparticle production can be distinguished:

4.2.1 Biosorption

It entails the binding of metal cations that are present in aqueous environments to the organism's cell wall. Stable nanoparticles are created as a result of interactions with the cell wall or peptides (Pantidos and Horsfall 2014). The probable processes for the biosorption of metals onto microbial species include physical mechanisms including physisorption, precipitation, ion exchange, and complexation. Glycoprotein, lipopolysaccharide, and other extrapolysaccharide compounds are typically secreted by microorganisms. These molecules typically have anionic functional groups that have the ability to draw cations from polluted or aqueous solutions. Peptidoglycan, liposaccharides, teichoic acids, and phospholipids, specifically, are components of bacteria whose cell walls are responsible for positive metal binding to negative charges in the cell wall. Chitin was found to be the primary component of the fungal cell wall, and it is involved in the complexation of heavy metals, which leads to the creation of nanoparticles (Wang et al. 2018). Few studies have described the biosynthesis of copper nanoparticles via a biosorptive method from dead *Rhodotorula mucilaginosa* biomass. The spherical form of the produced nanoparticles made them accessible to simultaneous pollution removal and nanoparticle production. It has also been reported on another work that used *Clostridium pasteurianum* to produce metallic molybdenum nanoparticles (Salvadori et al. 2014; Nordmeier et al. 2018).

4.2.2 Bioreduction

Utilizing inert bacteria and their enzymes that can be carefully removed from polluted environments, bioreduction involves chemically reducing metal ions to a biologically stable state (Jamkhande et al. 2019). Different substances present in microbial cells, such as amines, amides, carbonyl groups, pigments, proteins, alkaloids, and other reducing agents, may cause the formation of nanoparticles (Asmathunisha and Kathiresan 2013). Microbes like bacteria, fungus, and algae typically release chemicals with high capacity to oxidise or decrease metal ions to produce zero valent or magnetic nanoparticles. These creatures are manageable and open to genetic manipulation for making inorganic nanomaterials, either within or

outside of cells. In the case of intracellular synthesis, accumulating nanoparticles are polydispersed and have certain diameters depending on where the reductive cell components are located. Extracellular generation of nanoparticles has a wide variety of applications since intracellular nanoparticle synthesis necessitates additional processing procedures (Gahlawat and Choudhury 2019; Patil and Kim 2018). A variety of intricate biochemical processes, including complexolysis, alkylation, acidolysis, redoxolysis, etc., are combined during microbial-aided synthesis. The algae's phytochemicals are useful for immobilizing and stabilizing nanoparticles. In the generation of metal nanoparticles by yeast, encapsulation by the plasma membrane plays a significant function in the process. Yeast cells function as an efficient bio-system for producing metal nanoparticles inside of them while simultaneously cleaning up the surroundings because of their improved catalytic activity. Algal cells are used to create nanoparticles quickly because they have more amino acids and negative charges than yeast, which promote faster crystal formation and nucleation. Algal cells may be used to easily interrupt nanoparticle manufacturing and scale it up economically. They have thus attracted a lot of attention for the production of nanoparticles (Sathiyanarayanan et al. 2017; Gautam et al. 2019). Some of the difficulties associated with biological technique of synthesis of nanoparticles include lack of shape and size control, poor production quantity and rate, process scale up, and explanation of production mechanism (Raouf and Nasiri 2015; Chen et al. 2014).

4.3 Fungal-Mediated Nanoparticles Synthesis

Numerous applications for fungi-produced nanoparticles are found in the medical, chemical, electrical, agricultural, and astrophysical fields (Khandel and Shahi 2016). Using fungus to biosynthesize gold nanoparticles is a creative technique to guarantee a safe, economical, and ecologically responsible nanotechnology process (Sanghi and Verma 2009). Ahar mine in North West Iran's *Penicillium chrysogenum* strain of fungi was also capable of converting aqueous gold ions to nanoparticles, and the presence of nanoparticles was confirmed by XRD, UV-visible spectrum, and electron microscope transmission (Sheikhloo and Salouti 2011). The *Aspergillus niger*-produced gold nanoparticles were biosynthesized, tested for insecticidal activity against *Anopheles stephensi*, *Culex quinquefasciatus*, and *Aedes aegypti* larvae, and measured by probit analysis at six different concentrations over a period of 24, 48, and 72 h. It has been noted that the creation of gold nanoparticles produced by fungi can be quick and environmentally benign, and that this development can be superior to present methods of mosquito control (Soni and Prakash 2011). The *Fusarium oxysproum* isolate from a wilt-infected banana plant also led to the formation of nanoparticles of auric chloride solution with particles as small as 22 nm and encapsulated by protein (Thakker et al. 2013). In the case of a lower molar concentration of 0.3–0.5 mm of gold chloride solution, stable gold nanoparticles of varying sizes and shapes were generated between 7–13 nm and 15–18 nm. *Aspergillus fumigatus*, an endophytic fungus isolated from the *Cannabis*

sativa plant, produced silver nanoparticles, which were verified by surface resonance Plasmon analysis using the UV-visible spectrum (Patil 2015). *Escherichia coli*, *Klebsiella pneumoniae*, *Enterococcus* sp., and *Staphylococcus albus* were all successfully eradicated by endophytic fungi-produced nanoparticles (Bala and Arya 2013). Agar well diffusion method was used to detect the antibacterial activity of synthesized nanoparticles against human pathogenic bacteria, including Methicillin-resistant *Staphylococcus aureus*, *S. boydii*, *A. baumannii*, *S. sonnei*, and *S. typhimurium*. Fungal strain *Trichoderma viride* was also observed for silver nanoparticle synthesis ranging in size from 1 to 50 nm (Elgorban et al. 2016). The NADPH-dependent enzyme nitrate reductase is crucial for the production of silver nanoparticles (Anil Kumar et al. 2007). Silver nanoparticles are created when nitrate reductase lowers Ag+ ions in $AgNO_3$, as shown by XRD, TEM, and UV-visible absorption. With several uses in conductive film, lubrication, nanofluids, catalysis, and having shown nano-scale antibacterial activity, copper nanoparticles produced by fungus are far more affordable than silver and non-toxic than silver nanoparticles (Din and Rehan 2016). In a study, it has been demonstrated that the fungal strain *Stereum hirsutum*, when cultured under different pH settings, is capable of generating the synthesis of copper nano-parts. The white rot *S. hirstum* was discovered to have potential for the synthesis of copper nanoparticles after confirmation of the size of the nanoparticles produced by the fungal strain was observed using UV-visible spectroscopy, electron microscopy (TEM), X-ray diffraction analysis (XRD), and Fourier transforms (Cuevas et al. 2015). Fungal strain *Aspergillus fumigates* was identified for better biosynthesis of copper nanoparticles. Fungal species isolated from Egyptian soil were observed for copper nanoparticle synthesis. The process that generated the maximum production of nanoparticles was submerged incubation at 30 °C for 60 h with mycelium in contact with a 1 mM copper nitrate solution that had been pH-adjusted to 6 (Ghareib et al. 2018). Hexachloroplatinic acid solution (H_2PtCl_6) is incubated with *Fusarium oxysporum* under atmospheric conditions, which reduces the precursor and aids in the formation of platinum nanoparticles (Syed and Ahmad 2012). When the strain of Streptomyces was placed in hexahydrate chloroplatinic acid, it was able to synthesize platinum nanoparticles. The sediment sample was taken from the coastal area of Chennai, India. The fungus *Alternaria alternata* produced nano-platinum, which was characterized using a variety of spectroscopic techniques (Sarkar and Acharya 2017). Iron nanoparticles are currently widely employed in a variety of applications, including the treatment of water, food processing, the textile industry, and as possible antibacterial agents (Lowy 1998; Hawkey 2008; Tran et al. 2010). The fungus *Alternaria alternata* was used to biosynthesize the iron nanoparticles by reducing the aqueous Fe^{3+} ions in a dark process. The synthesized nanoparticles have a cubic structure and a size arrangement of 9 nm (Mohamed et al. 2015). The *Pleurotus* sp.-produced iron nanoparticles were further supported by FTIR, SEM, and UV-spectra investigation (Mazumdar and Haloi 2011). In a different investigation, the fungus *Apsergillus* sp. was recovered from a Hyderabad soil sample. A variety of $FeSO_4 \cdot 5H_2O$ concentrations were used in the fungus culture medium to develop the isolated fungus strain. After growing *Aspergillus* sp. in 1 mM ferrous

sulphate for 48 h, the medium was centrifuged to remove the fungus pellet, which was then collected and examined by TEM (Pavani et al. 2012). By employing *Aspergillus japonicas* to hydrolyze the salt solution to suitable conditions, which released ferric and ferrous ions and underwent protein-mediated co-precipitation and nucleation, iron oxide nanoparticles were synthesized (Bhargava et al. 2014). With crystal sizes between 8 and 9 nm, magnetic iron and magnetite nanoparticles have been created using the fungus *Aspergillus niger*. The magnetic properties of the synthesized nanoparticles have also been observed, and for Fe and Fe_3O_4 nanoparticles, respectively, they exhibit superparamagnetic and ferromagnetic-like behaviours (Abdeen et al. 2013). Due to their significantly larger heat capacity, thermal conductivity, low thermal expansion coefficient, and high melting temperature, zinc oxides also have significant technical significance. Microorganisms have produced zinc nanoparticles that are widely employed in the fields of catalysis, photodetectors, LEDs, sensors, medicine, and cosmetics (Purkait et al. 2015). In order to create the zinc, magnesium, and titanium nanoparticles, soil-isolated fungus known as *Aspergillus flavus*, *Aspergillus terreus*, *Aspergillus tubingensis*, *Aspergillus niger*, *Rhizoctonia bataticola*, *Aspergillus fumigates*, and *Aspergillus oryzae* were used (Raliya and Tarafdar 2014). Silver and zinc nanoparticles were produced using the fungus *Candida* diverse strain JA1 that was isolated from milk processing facility waste water and characterized using a variety of analytical techniques, including UV-visible spectrophotometer, X-ray diffraction pattern analysis (XRD), and FE-Scanning electron microscope (SEM) with EDX-analysis (EDXA) (Chauhan et al. 2011). Fungal nanoparticle production is favoured over other microbial synthesis due to the strong resistance of fungal mycelial mesh to greater flow and agitation in bioreactors.

4.4 Mechanism of Myco-Synthesis of Nanoparticles

These nanoparticles have used in several fields, and the microorganisms that were employed to create them are biocompatible and less toxic. Due to all of these characteristics, they are beneficial for the development of drug delivery systems and carrier materials for sensors in diagnostic equipment (Ahmad et al. 2003a, b, 2015). Microorganisms such as bacteria, fungi, yeast, and actinomycetes have been shown to be beneficial for the production of nanoparticles and their use in different sectors. The rate of intracellular synthesis of nanoparticles, as well as their size and structure, may be controlled and prolonged by regulating and changing the parameters pH, temperature, substrate concentration, and exposure time to the substrate (Gericke and Pinches 2006). Although fungi may create nanoparticles both extracellularly and intracellularly, the precise mechanism is not fully known. During intracellular production, heavy metal attachment to the fungal cell wall by proteins or enzymes present on it through electrostatic interactions is one of the putative processes. Enzymes found in the cell wall also decrease the metal ions. As a result, metal ions group together and create nanoparticles. Extracellular synthesis presupposed interactions between metal ions and enzymes, namely, reductase, with

the creation of nanoparticles in solution as a result. Extracellular synthesis presupposed interactions between metal ions and enzymes, namely, reductase, with the creation of nanoparticles in solution as a result (Kashyap et al. 2013). In contrast to intracellular synthesis, which requires the use of analytical tools and time-consuming processing methods, extracellular synthesis of nanoparticles has the advantage of not requiring the lysis of fungal cells or downstream processing for the recovery and purification of nanoparticles (Gade et al. 2008).

4.4.1 Extracellular Mechanism

In their in-depth analysis of the process of myconanosynthesis, fungi experience stress and respond as a cellular defence at three separate levels when exposed to metal/metal oxide solution (Jha and Prasad 2016). Bioreduction, which results in the formation of nanoparticles on the cell wall surfaces, is started by ion stress. It has been noted in earlier research that fungi develop enzymes and metabolites to avoid metal toxicity and transform it into a product that is less toxic, like nanoparticles (Kashyap et al. 2013). Due to the abundance of cytosolic and membrane-bound enzymes such as cellulase, nitrate reductase, oxidoreductase, and oxidase (Durán et al. 2005), fusarium is being extensively investigated for the creation of nanoparticles (Jha and Prasad 2016). These enzymes are praised for their adaptability since they provide a switch-on and switch-off mode in response to pH changes, with reductase catalysing a reaction at higher pH and oxidase at lower pH (Jha and Prasad 2010). Most people are aware of nitrate reductase's function in extracellular production (Ahmad et al. 2003a, b; Durán et al. 2005; Ingle et al. 2008; Li et al. 2011). As a result, the silver ion (Ag+) is converted to neutral silver by the actions of both anthraquinone and NADPH (Ag^0). Another research found that hydroxyquinoline, an electron shuttle, is responsible for the transfer of electrons from Ag^+ ions to Ag^0 once -NADPH is reduced to -NADP (Anil Kumar et al. 2007). In reaction to metallic stress, the lower fungus *Aspergillus* and *Penicillium* species generate a large number of hydroxy/methoxy derivatives of benzoquinones and toluquinones (Jha and Prasad 2016). According to the theory put out by Jha and Prasad (2010), these metabolites swiftly go through a redox process to produce nanoparticles. In other words, the reduction of NADPH to NADH, which releases electrons to cause the conversion, occurs when the enzyme (reductase) attaches to the silver ion as a substrate. The unspoken reality is that proteins are essentially what enzymes are. Researchers have proposed that polypeptides/proteins play an important function as an encapsulating agent and are involved in the bioreduction of metal ions to their corresponding nanoparticles (Das et al. 2009; Mukherjee et al. 2008; Jain et al. 2011; Gade et al. 2008). Unexpectedly, the processes that have been suggested so far are mostly for silver and gold nanoparticles. Metal oxide mechanism has been proposed by a few researchers (Bansal et al. 2004; Durán and Seabra 2012; Jha and Prasad 2016).

4.4.2 Intracellular Mechanism

Beginning with the chelation of metal ions across the fungal cell surface, intracellular production begins. The presence of positively charged groups in enzymes and proteins near the cell wall may have an electrostatic interaction with the metal ions, causing this (Rai et al. 2009a, b; Kashyap et al. 2013). Extracellular mucilaginous materials have excellent hazardous metal-binding capacities (Jha and Prasad 2016). These metal ions are delivered inside cells by transporters or channels (proteins). This causes metabolic mayhem inside the cell, and to get around it, the cell releases the required nanoparticles. There is a chance that nanoparticle diffusion is caused by a concentration gradient only when the rate at which the substrate enters the cell is in balance with the product generated. If not, nanoparticles could combine and damage cells as a result of an excessive buildup of particles inside.

4.5 Characterization of Fungal-Mediated Nanoparticles

Nanoparticles are exposed to numerous characterization procedures in order to determine their size, shape, distribution, surface morphology, and surface area. Any nanoparticle's characterization process starts with the visual evaluation of colour shift. It is possible to see a colour change from yellow to red during the production of gold nanoparticles. Additionally, the colour changes from a deep red to a purple hue as the particle size increases. Colour change is seen as a result of variations in the nanoparticles' Surface Plasmon Resonance (SPR) (Zhang et al. 2016). The transition from yellow to brown can be used to visually validate the production of silver nanoparticles. All nanoparticles exhibit a variety of colour tints due to size diversity, much as the gold nanoparticle. Metallic nanoparticles have displayed remarkable optical characteristics due to Surface Plasmon Resonance (SPR), which may be seen by UV-vis spectroscopy. Due to radiation's interaction with metals, which encourages the transfer of electrons from their ground state to higher energy states, a particular SPR band is produced. Up to a certain point, this aids in the deduction of nanoparticles (2–100 nm). For example, the absorption spectrum of AgNPs is between 400 and 450 nm, while that of AuNPs is between 500 and 550 nm. The ZnO-NPs' wavelength range is 350–390 nm (Aboelfetoh et al. 2017; Shukla and Iravani 2017). The emergence of reddish brown colour from green colour suggests the creation of copper nanoparticles when absorbance is measured for copper nanoparticles in the region of 550–700 nm. Similar dark brown colour indicates that magnesium nitrate has been converted to magnesium nanoparticles (Khani et al. 2018; Sharma et al. 2017a, b).

Sample preparation is necessary for SEM analysis, which uses an electron microscope. Initially, samples of carbon were dropped onto the grip and dried for 5 min under a mercury lamp to create thin films of carbon coating on copper grids (Menon et al. 2017). The specimen's surface is in contact with the electron beam. As a result of the detection of secondary electrons, back-scattering electrons, and distinctive X-rays, a 3D picture of the material is produced at various magnifications.

The appearance, structure, and elemental content of the zinc oxide nanoparticles produced by *Pseudomonas putida* culture were identified using a Field Emission Scanning Electron Microscope (FE-SEM) in conjunction with Energy Dispersive Spectroscopy (EDX). Silver nanoparticles made from endophytic fungus *Penicillium citrinum* were analyzed by EDX, which suggested the presence of phosphate, ferrous, and oxygen elements. These elements may have been present because their extract contains bioactive substances (Jayabalan et al. 2019; Danagoudar et al. 2020; Liu et al. 2012).

Another effective method for determining the size, shape, morphology, and aggregation of nanoparticles is transmission electron microscopy (TEM). The main task in the TEM examination of nanoparticles is the correct reparation of a dry sample with the proper thickness. TEM images in two dimensions are created from the electrons that passed through the material. Sub-nanometer resolution of TEM in polymeric nanoparticles can offer information on the inner-particle structures of the nanocarriers and polymeric walls of nanocapsules (Crucho and Barros 2017). TEM micrographs of the silver nanoparticles produced by a fungus showed a spherical shape with a size of 2–4 nm (Balaji et al. 2009). Cryo-TEM, which examines the sample in its frozen-hydrated form, can avoid some of the drawbacks of TEM analysis, including low specimen thickness and structural damage to materials (Stewart 2017). ZnO NPs made from *Periconium* sp. appeared quasi-spherical, polydispersed, and less agglomerated in SEM and TEM pictures (Ganesan et al. 2020).

A non-destructive characterization method for metallic nanoparticles is X-ray diffraction (XRD). Data about material structure, composition, and molecular interactions may be found by analysing XRD data. In addition to controlling sample phase and phase content, it also determines particle size (Reddy et al. 2016). Characteristic X-ray spectra are produced when electrons have enough energy to cause the inner shell electrons of target materials to dislocate. The synthesis and characterization of intracellular gold nanoparticles from *Aspergillus fumigatus* were also reported. The peak location at 37.8 revealed the existence of gold nanoparticles, uneven shape, and crystalline nature of the particles (Bathrinarayanan et al. 2013).

One of the extensively used methods for determining the size of nanoparticles is dynamic light scattering (DLS), also known as photon correlation spectroscopy (PCS). In DLS analysis, a colloidal solution is illuminated by monochromatic laser light, which scatters into a photon detector. The hydrodynamic particle size is determined by studying the intensity of scattered light as a function of time. Other benefits of DLS for colloidal suspensions include selectivity, sensitivity, ease of use, and shorter measurement times (Kumari et al. 2019).

Atomic Force Microscopy (AFM), in which a cantilever scans the material and enables imaging of nanoparticles, is an illustration of Scanning Probe Microscopy (SPM). A probe can be attached to a cantilever in an AFM experiment to quantify the attractive and repulsive forces acting on the sample surface. A laser-photodiode system is then used to monitor the cantilever's deflection by detecting the variation in photodetector output voltage. Tapping mode and contact mode AFM are the two most often utilized AFM imaging modalities. From AFM topography imaging, it is

possible to determine the nanocrystals' growth process. AFM was used to measure the height and roughness of cobalt oxide nanoparticles, and the average roughness was determined to be 3.16 nm (Crucho and Barros 2017; Vijayanandan and Balakrishnan 2018). AFM analysis may also be used to determine the nanoparticles' size, aggregation, and form. From an AFM picture, it was determined that silver nanoparticles isolated from the filamentous fungus *Penicillium decumbens* were spherical in form, well disseminated, and aggregated (Majeed et al. 2016a, b).

Using Brunauer–Emmett–Teller (BET) analysis, the surface area of nanoparticles is examined. Nanoparticle surface area is crucial in environmental applications. A higher surface area of nanoparticles is needed to absorb the contaminants in the case of heavy metals and colours. BET surface area was found to be 86.95 m^2/g in a study involving the adsorption of Ni(II) ions by supermagnetic iron oxide nanoparticles covered with green extract. The region was large enough and mesoporous, which made it easier for Ni(II) ions to bind to nanoparticles (Christopher et al. 2017; Nithya et al. 2018). In order to properly transport medication molecules to crops, nanoparticles can also be utilized in agricultural areas as carrier molecules. Greater surface area can improve medication collection and delivery to crops. The surface area to volume ratio of smaller nanoparticles was found to be greater, contributing to the faster dissolving rate needed to transport target molecules to the microorganisms for pollution cleanup. The surface area of nanoparticles controls their aggregation state, which affects how stable they are under particular physiological parameters for the repair process.

Infrared spectroscopy may be used to characterize a variety of nanoparticles, including metallic nanoparticles, carbon nanoparticles, and polymeric nanomaterials. Fourier Transform Infra-Red Spectroscopy (FTIR) can be used to identify the potential biomolecules responsible for capping nanoparticles (Menon et al. 2017). The Attenuated total reflectance (ATR) method was used to prepare the samples for the FTIR analysis of the silver nanoparticle sample from *Gelidium corneum*. The results of the investigation showed that the oxidation of azo compounds and aldehyde groups was a key factor in the reduction of silver nitrate to silver nanoparticles (Oztürk et al. 2019). FTIR may also be used to investigate metallic nanoparticles deposited onto activated carbon. Flavonoids, triterpenoids, and protein needed for the reduction and capping processes were found in *Phomopsis liquidambaris* silver nanoparticles (Saravanan et al. 2016; Seetharaman et al. 2018).

In recent years, magnetic nanoparticles have become a potentially useful material for a variety of applications. It consists of an exterior active-group shell and a magnetic core made up of metal ions. Magnetic nanoparticles that have been functionalized raise more issues with magnetization, surface effect, and magneto-mechanical effect. The capacity to be manoeuvred by an external magnetic field is one of the main properties of magnetic nanoparticles. These characteristics facilitate increased oil recovery by facilitating the removal of adsorbent nanoparticles from the remediated solutions under magnetic fields. Magnetic nanoparticles with high saturation magnetization values and low residual magnetization and coercivity values were shown to be more effective for treating water. Therefore, identifying such

features is crucial for an effective rehabilitation approach (Neeraj et al. 2016). Vibrating Sample Magnetometers can be used to examine the magnetic characteristics of nanomaterials (VSM). By generating vibration and supplying a magnetic field to the embedded coil in the apparatus, induced current proportional to the magnetic property of the sample is produced. By passing the induced current to the instrument, a hysteresis loop is produced, which is used to detect the magnetic characteristics of nanoparticles. Superparamagnetism was noticed for the magnetic iron nanoparticles that were isolated from *Bacillus cereus*, and this was supported by the fact that there was no magnetization in the presence of an external magnetic field (Fatemi et al. 2018). Using an inductively coupled plasma mass spectrometer (ICP-MS), nanoparticles may be analyzed qualitatively and quantitatively (Oztürk et al. 2019). The hydrodynamic diameter, zeta potential measurements, and particle size distribution may all be determined using zeta sizer analysis. The presence of fungal filtrate accelerated the production of nanoparticles during the synthesis of Ag nanoparticles from *Fusarium oxysporum*. Zeta potential measurements are also used to characterize the magnetite nanoparticles. The avoidance of nanoparticle aggregation and dispersion is achieved by three main factors of attraction, including gravitational force, magnetic force, and Vanderwaal's force. Gold nanoparticles made from *Fusarium solani* were subjected to zeta potential tests, which revealed a change from negative to positive values. The positive values suggest poorer NP stability because of increased aggregation and decreased interparticle attraction (Srivastava et al. 2019; Clarance et al. 2019).

4.6 Factors Affecting the Synthesis of Nanoparticles by Fungi

Temperature, metal ion concentration, pH, extract concentration, raw material concentration, incubation period, and reaction mixture are only a few of the environmental parameters that affect the synthesis of nanoparticles as well as the development of fungus. As a result, the optimization condition is crucial for excellent growth and increases product yields. The physical and chemical parameters, which primarily include temperature, pH, the presence of particular enzymes, the type of biomass, exposure time to substrate, and substrate concentration, are what have the biggest effects on the synthesis of nanoparticles, including their size, shape, and monodispersity.

4.6.1 pH

A significant component that has a significant impact on the production of metal nanoparticles is pH. In a study by Gericke and Pinches (Gericke and Pinches 2006), they showed how changes in pH may cause nanoparticles' shapes to alter. They also discovered that *V. luteoablum* produces spherical nanoparticles of size (about 10.0 nm) at pH 3, but when pH is increased to 5, hexagonal, triangular, and rod-shaped nanoparticles are produced instead. Further increases in pH (Goswami

et al. 2010; Gade et al. 2010a, b; Hebeish et al. 2010) led to the discovery of nanoparticles with erratic and ill-defined forms. Similar research was done by Sanghi and Verma, who looked at how pH affected the production of nanoparticles made by *Coriolus versicolor*. The acquired data also indicated that metal ions' reduction was highly sensitive to pH (Davis and Ogden 1997; Sanghi and Verma 2009).

4.6.2 Temperature

A crucial physical factor that affects the formation of metallic nanoparticles is temperature. According to a study, temperature change regulates the transport of ions and the activity of microbial biomass. It is also possible to argue that temperature has a significant impact on fungal development and environmental metal absorption (Dhillon et al. 2012). Temperature has a direct impact on nanoparticle production (Gericke and Pinches 2006). After 1 h of exposure to a gold metal ion solution, they discovered that a variety of nanoparticles with spherical forms developed at low temperatures. The quantity of smaller nanoparticles will decrease as incubation time is extended up to 24 h, while the giant particles exhibit clearly defined forms of larger sizes. The segregation of smaller nanoparticles at high temperatures is to blame for this. The form and size of the nanoparticles produced after 1 and 24 h of exposure to the metal ion solution are same at temperatures up to 50 °C. The size of nanoparticles can be regulated by running the reaction mixture at low temperature, but it would allow nanoparticles to grow at a slower rate, according to further research on the impact of temperature on the biogenesis of metal nanoparticles (Punjabi et al. 2015).

4.6.3 Concentration of Metal Ions

The formation of metal nanoparticles is also influenced by the concentration of metal ions. According to earlier findings, the presence of the fungus *Penicillium fellutanum* in large concentrations would prevent the creation of nanoparticles. According to research, the size, shape, and monodispersity of the nanoparticles deviate from the desired nano size at high concentrations of silver ions (Kathiresan et al. 2009). Similar to chemical processes, the pace of reaction is determined by the reactant concentration, which also has an impact on the size and form of the produced particles. *Verticillium luteoalbum* was reportedly used to create gold nanoparticles (Gericke and Pinches 2006). The obtained findings also indicated that the size of the gold nanoparticles was somewhat narrow and consistent size ranges (>20 nm) when the concentration of $AuCl_4^-$ was less than 500 mg/L. While the size of the produced nanoparticles increased along with the rise in $AuCl_4^-$ concentration, the concentration was not linear. Additionally, it was discovered that smaller particles might aggregate at high metal ion concentrations (Davis and Ogden 1997).

4.6.4 Exposure Time to Substrate

It was also investigated how the creation of nanoparticles at various time intervals affected the process. It has been discovered that as the incubation time grows, so do the form and size of the nanoparticles in the reaction mixture. Additionally, it has been discovered that as incubation duration rises, so does nanoparticle creation. The bulk of nanoparticles are produced after an hour of incubation with a metal-containing solution (Gade et al. 2010a, b). The clump formation or segregation of smaller-size nanoparticles is what causes the synthesis of larger-size nanoparticles to occur when incubation time is extended up to 24 h. Additionally, it has been shown that the synthetic nanoparticles exhibit a change in their real form and size as the passage of time rises up to 2–4 days (Darroudi et al. 2011).

4.6.5 Type of Enzyme Used

The kind of enzymes released by the microorganisms has a significant impact on the employment of various types of enzymes for the bioreduction of metal ions into metal nanoparticles. The primary benefit of employing these enzymes for biosynthesis is that it allows for the intracellular manufacture of nanoparticles using fungal mycelia in vitro without the requirement for harvesting or optimizing processes. It has been discovered that fungi's released enzymes are also employed to create numerous metallic nanoparticles with varying chemical compositions, forms, and sizes. In a research, it was discovered that the creation of silver nanoparticles occurs when the reaction mixture contains the *Fusarium oxysporum* strain rather than when *Fusarium moniliforme*. The in-depth analysis of these two fungi's metabolites and the results of their protein assays revealed that the particular reductase enzyme (NADH-dependent reductase) was exclusively generated by the fungus *F. oxysporum* and not by the other strain, *F. moniliforme*. The findings further show that the production of metal nanoparticles by *F. oxysporum* is caused by the presence of certain nitrate reductase enzymes in the cytoplasm or cell membrane of this organism (Shakibaie et al. 2010). In another research, it was found in a different investigation that *F. oxysporum* also produces silica (Si) nanoparticles. The silicates were bioleached by the fungus *F. oxysporum* into the zircon sand's silicic acid, which was subsequently converted into silica nanoparticles (Bansal et al. 2005; Kashyap et al. 2013).

4.7 Applications of Fungal-Mediated Nanoparticles

There are several applications for biosynthesized fungal nanoparticles in pharmaceutical research, medicine, and technology. There are several microbially created nanoparticles that have been shown to have unique anti-bacterial, anti-fungal, anti-viral, anti-inflammatory, anti-tumour, insecticide, and antioxidant effects. Present-day applications for nanoparticles produced by fungus and other microorganisms

include fruit preservation, labelling and sensing, antibacterial agents, textiles, and the pharmaceutical industry (Durán et al. 2011; Gudadhe et al. 2014).

4.7.1 Antibacterial Activity

Researchers have previously reported on the antibacterial investigation of fungi-produced nanoparticles against microbes (Sandhu et al. 2019). *Escherichia coli* and *Staphylococcus aureus* were shown to be resistant to the antibacterial effects of silver nanoparticles made from encapsulated biomass beads of the fungus *Phoma exigua* (Shende et al. 2016). Strong antibacterial action against many human pathogenic bacteria has also been found in gold nanoparticles synthesized utilizing endophytic fungus (Priyadarshini et al. 2014). In addition to being exploited for the creation of silver nanoparticles, the endophytic fungus *Talaromyces purpureogenus*, which was isolated from *Pinus densiflora* S., also shown notable antibacterial, anticancer, and cell wound healing activities (Hu et al. 2019). When isolated from *Bertholletia excelsa* (Brazil-nut) seeds, the endophytic fungus *Trichoderma* spp. was able to green synthesize silver nanoparticles and detect their antibacterial effectiveness against many Gram-negative bacteria (Ramos et al. 2020).

4.7.2 Anticancer Activity

The dose-dependent cytotoxicity of the biosynthesized *Agaricus bisporus* silver nanoparticles against MCF7 breast cancer cells was examined. Their size ranges from 8 to 20 nm. Similar to this, *Penicillium brevicompactum*-produced silver nanoparticles demonstrated anticancer efficacy against the MCF-7 breast cancer cell line (Majeed et al. 2016a, b). By using ITS sequences to identify it, the endophytic fungus *Botryosphaeria rhodina* was able to produce silver nanoparticles and exhibit a variety of lethal effects on the cancer cell line (Akther et al. 2019). By inducing apoptosis in the cancer cell line, gold nanoparticles produced by *Fusarium solani* from *Chonemorpha fragrans* also showed efficacy against human breast and cervical cancer cell lines (Clarance et al. 2020).

4.7.3 Antiviral Activity

Viral infections pose a serious challenge on a worldwide scale as a result of their resistance to certain antiviral medications. Due to their potential antiviral effect against viral particles and bacterio-phage, the nanoparticles bio-synthesized by fungus interact strongly (Galdiero et al. 2011). A colloidal solution of these nanoparticles suppressed the development of the virus in the *E. coli* host strain. The fungus *Aspergillus niger* produced silver nanoparticles in the 3–10 mm range that were reported to have excellent antiviral activity (Panchangam and Upputuri

2019). It was also noted that the nanoparticle from *Scedosporium* fungi has antibacterial and anticancer properties. The ability of silver nanoparticles to control viral infection by inhibiting the interaction of the virus with the cell depends on their zeta potential and size, according to research on the antiviral activity of silver nanoparticles against simplex virus types 1 and 2 and human para-influenza virus type 3 (Gaikwad et al. 2013).

4.7.4 Insecticidal Activity

Due to their ability to decompose dangerous pesticides like chlorpyrifos at various pH levels, fungi-produced nanoparticles also play a significant role in agriculture. One example of this is the ability of sliver nanoparticles formed from *Penicillium pinophilum* to prevent or kill harmful insects. Both *Culex quinquefasciatus* and *Anopheles stephensi* larvae were shown to be vulnerable to gold nanoparticles and silver nanoparticles produced by the entomogenous fungus *Chrysosporium tropicum* (Soni and Prakash 2012). *Culex quinquefasciatus* larvae were also reported to be more susceptible to silver nanoparticles. Using a concentration range of 25–250 ppm against I, II, III, and IV instar larvae and pupae of *Culex quinquefasciatus*, the larvicidal activity of silver nanoparticles generated from *Penicillium verucosum* against filarial causative organism *Culex quinquefasciatus* was discovered (Kamalakannan et al. 2014).

4.7.5 Antifungal Activity

The durability or antifungal activity of fungus nanoparticles produced biologically may be enhanced against pathogenic fungi (Gaba et al. 2023; Dhiman et al. 2022, 2023). The pathogenic fungus *Candida albicans* and *Candida glabrata* were both susceptible to the antifungal action of *Penicillium fallutanum*'s silver nanoparticles. In order to create the nanoparticles, Roy et al. used the extracellular filtrate of the *Aspergillus foetidus* MTCC8876 fungal species. This species was tested using the agar well diffusion method against other *Aspergillus* species, including *Aspergillus niger*, *Aspergillus flavus*, *Aspergillus foetidus*, *Aspergillus oryzae*, *Aspergillus parasiticus* and *Fusarium oxysporum* (Roy et al. 2013). *Fusarium verticillioides*, *Fusarium moniliforme*, *Penicillium brevicompactum*, *Helminthosporium oryzae*, and *Pyricularia grisea* are just a few of the tested fungal colonies that have experienced a significant decline as a result of *Trichoderma longibrachiatum*'s extracellular synthesis of silver nanoparticles (Elamawi et al. 2018). *Arthroderma fulvum* was found to have the ability to synthesize silver nanoparticles that had better antifungal activity against ten fungal pathogens, including *Candida* spp., *Aspergillus* spp., and *Fusarium* spp. 17 fungi were isolated from the soil sample collected from the Nahu Park China (Xue et al. 2016).

4.7.6 Agricultural Applications

Nanotechnology is a young, rapidly developing field of study with significant implications for agriculture. Numerous fungal genera, including species of *Fusarium*, *Phoma*, *Aspergillus*, *Phytopthora*, *Phyllostica*, and others, are frequent plant diseases that can all be controlled by nanoparticles (Rai and Ingle 2012). A strategy for the gradual and continuous release of chemical fertilizers into chitosan nanoparticles was also developed (Corradini et al. 2010). This idea is useful for regulating the release of chemical fertilizers into the soil and preventing excessive environmental discharge of chemical fertilizers. According to research, silver nanoparticles have a higher antibacterial activity than bulk silver molecules because they have a larger surface area and a higher percentage of surface atoms. According to another research, applying nanoformulations in the form of biopesticides to the leaf surfaces of developing crops enhances the efficiency of plant development by deterring the assault of any viral infections (Liu et al. 2013). In a different study, Goswami et al. discovered that liquid formulations known as nanoemulsions of silver, aluminium oxides (Al_2O_3), zinc oxides (ZnO), and titanium di oxides (TiO_2) were used to treat a variety of plant diseases, including grasseries and weevils in *Bombyx mori*, which are brought on by the attack of the pathogens *Sitophilus oryzae* and *Baculo* (BmNPV) (Goswami et al. 2010). The obtained data further show that about 70% of the insects died after being exposed to these nanoemulsions for 7 days in rice fields. Similar to Mukherjee et al., these nanomaterials were employed to create well-defined silver nanoparticles with sizes between 13 and 18 nm that were synthesized using *T. asperellum*. These nanomaterials were then used to create bionanoemulsions to inhibit the growth of several plant diseases (Mukherjee et al. 2008). Recent study has identified the necessity for the creation of intelligent delivery systems for the gradual release of biopesticides and biofertilizers. In order to address these issues, a new class of nanopesticides was created in which the well-known pesticide validamycin is coated with porous hollow silica nanoparticles (PHSNs), which can also be used as an intelligent delivery system for the delivery of pesticides that are water soluble. These PHSNs are an effective carrier in agriculture for the regulated delivery of pesticides and also the biofertilizers whose extended release is necessary for the growing crops due to their controlled release behaviour (Liu et al. 2013; Bhattacharyya et al. 2016).

4.8 Toxicity of Myco-Nanoparticles

Because they possess different combinations of properties from standard materials, nanoparticles are special kinds of materials (Camargo et al. 2009). NPs have a wide range of uses, including in environmental applications, industrial, medicinal, and biological domains, as well as in human health appliances (Hamzeh and Sunahara 2013). Among all nanoparticles, AgNPs are the most frequently utilized in pharmacology, engineering, energy, magnetic fields, medicine, medical devices, biotechnology, electronics, and engineering (Yu et al. 2013). They are also used extensively

in environmental cleanup. Their extremely potent antibacterial properties have found uses in a variety of industrial fields, such as textiles, food, consumer goods, and medicine (Naidu et al. 2015). Nanoparticles are in great demand across a variety of industries due to their distinctive physical, chemical, and biological (e.g. antibacterial, anticancer, and antiparasitic) capabilities that set them apart from similar bulk materials. However, the widespread and elevated usage of nanoparticles might enhance their toxicity, endangering both the environment and living things (Akter et al. 2018). The cytotoxicity of nanoparticles from Fusarium species, primarily AgNPs, and their underlying molecular processes have been shown in several investigations using various model cell lines to date (Salaheldin et al. 2016; Pourali et al. 2018; Mohamed et al. 2019; Clarance et al. 2020). Proteins and other organic molecules serve as the caps on biological nanoparticles (Akhtar et al. 2013; Karatoprak et al. 2017; Siddiqi et al. 2018). Corona is the definition of this capping. The biological response is strongly impacted by this nanoparticle corona (Barbalinardo et al. 2018). The corona may be classified into two types: hard corona and soft corona, depending on the surface affinity and exchange rate. The hard corona proteins are stiff for the incursion into the biological system, whereas the soft corona proteins are 'vehicles' for the silver ions (Ritz et al. 2015). The nanoparticle-protein corona is formed in large part by the functional groups of the corona (Nguyen and Lee 2017). The cytotoxic characteristics of the nanoparticle corona are also controlled by these functional groups and protein charges (Nguyen and Lee 2017; Barbalinardo et al. 2018). As demonstrated by AgNPs (Abbaszadegan et al. 2015), the surface charge of nanoparticles is crucial to their bactericidal action against both Gram-positive and Gram-negative bacteria. Transmission electron microscopy (TEM) has demonstrated that AgNPs may enter cellular structures such as endosomes, lysosomes, and mitochondria. According to several studies, it is the proteins present in the corona of the nanoparticles—not the particles themselves—that interact with the cells (Walczyk et al. 2010; Monopoli et al. 2012). The corona's development and content therefore have significant effects on toxicity (Lee et al. 2014) and internalization (Lesniak et al. 2012). To summarize, the corona structure is influenced by particle size (Yilma et al. 2013), shape (Yin et al. 2013), surface qualities (Braydich-Stolle et al. 2005), biological fluid properties, and composition, which have a negative impact on human health and the environment (Lesniak et al. 2012; Navya and Daima 2016).

According to a study, *F. oxysporum*-produced AgNPs generated notable vacuolation in the human breast cancer cell line (MCF-7), indicating strong cytotoxic action (Salaheldin et al. 2016). When these mycogenic AgNPs were tested on mice for 21 days, the renal corpuscle and collecting tubule both enlarged, and there was haemorrhage in the interstitial space between the tubules. The scientists draw the conclusion that AgNPs may enter and move about inside of cells, and that the size of the AgNPs fluctuates depending on how hazardous it is to the cell and its organelles. As a result, it was considered that all nanoparticles were poisonous and that the only ones that may harm human health were likely to be free nanoparticles that could enter tiny organelles like the mitochondria (Al-Sharqi 2020). Applications and properties of different myco-synthesized nanoparticles are shown in Table 4.1.

Table 4.1 Applications and properties of different nanoparticles synthesized using fungi

Fungi	Confinement	NPs	Size (nm)	Shape	Application	References
Penicillium crustosum	Extracellular	AuNPs	10	Aggregates	Antifungal	Roy et al. (2013)
Rhizopus stolonifer	Extracellular	AuNPs	25–30	Irregular	Bioreducer	Binupriya et al. (2010)
Cylindrocladium floridanum	Outer surface of the cell wall	AuNPs	18–35	Spherical	Toxic organic pollutant reducer	Narayanan and Sakthivel (2010)
Fusarium oxysporum	Extracellular	AuNPs	50–150	Spherical and hexagonal	Antibacterial	Naimi-Shamel et al. (2019)
Arthroderma fulvum	Intracellular	AgNPs	20–56	Spherical	Antifungal	Xue et al. (2016)
Aspergillus niger	Extracellular	AgNPs	1–20	Spherical	Antimicrobial	
Fusarium semitectum	Extracellular	AgNPs	10–50	Spherical and ellipsoid	Antibacterial	Shelar and Chavan (2014)
Duddingtonia flagrans	Extracellular	AgNPs	30–409	Spherical	Antimicrobial, antiviral	Costa Silva et al. (2017)
Sclerotinia sclerotiorum	Extracellular	AgNPs	10–15	Spherical	Antibacterial	Saxena et al. (2016)
Fusarium oxysporum	Extracellular	AgNPs	24	Spherical	Antibacterial	Hamedi et al. (2017)
Penicillium oxalicum	Extracellular	AgNPs	10–40	Spherical	Antimicrobial	Rose et al. (2019)
Trichoderma longibrachiatum	Extracellular	AgNPs	24–43	Spherical	Antifungal	Elamawi et al. (2018)
Beauveria bassiana	Extracellular	AgNPs	10–50	Triangular, circular, hexagonal	Antimicrobial	Tyagi et al. (2019)
Hypocrea lixii	Extracellular	CuNPs	24.5	Spherical	Bioremediation of wastewater	Salvadori et al. (2014)
Stereum hirsutum	Extracellular	CuNPs	10–25	Spherical	Antimicrobial	Mohd Yusof et al. (2019)
Trichoderma asperellum	Extracellular	CuNPs	10–190	Spherical	Anticancer	Hu et al. (2019)

Fusarium oxysporum	Extracellular	PtNPs	25	Aggregates	Antioxidant and antimicrobial	Gupta and Chundawat (2019)
Fusarium oxysporum	Extracellular	PtNPs	70–180	Spherical, triangular	Bio-reduction	Govender et al. (2009)
Alternaria alternata	Extracellular	FeNPs	9 ± 3	Cubic	Antibacterial	Mohamed et al. (2015)

4.9 Conclusion and Future Directions

One of the newest areas, nanotechnology, has many practical uses for issues related to the environment and the economy. Typically, top-down and bottom-up strategies are used to create nanoparticles. Except for biosynthesis of nanoparticle production, all top-down and certain bottom-up processes are harmful. Different microorganisms can produce nanoparticles, which offer a number of benefits over traditional processes. The two processes used to create nanoparticles are extracellular and intracellular syntheses. The reduction process is caused by biomolecules that are already present or that are released by the organisms. Metal ion reduction to nanoparticles relies heavily on reductase enzymes like nitrate reductase. Metal nanoparticle biosynthesis is regarded as a secure and sustainable process. For a better knowledge of nanoparticle synthesis, different metal nanoparticle creation from bacteria, fungus, algae, and yeast has been focused on. Mycosynthesis in particular, as well as other forms of microbial synthesis are less expensive and more environmentally friendly than physical and chemical techniques of nanoparticle synthesis. Myconanotechnology, also known as mycosynthesis of nanoparticles, is therefore now a significant topic in bionanotechnology. The implicated fungi might be thought of as innovative biomills for the creation of nanoparticles because of their efficiency in both intracellular and extracellular nanoparticle synthesis. However, a number of things need to be addressed, including the rate of synthesis, monodispersity, and downstream processing. There needs to be further investigation into the potential processes involved in the creation of nanoparticles employing various fungi. Additionally, there is a pressing need to research the large-scale manufacturing of nanoparticles for industrial uses.

References

Abbaszadegan A, Ghahramani Y, Gholami A, Hemmateenejad B, Dorostkar S, Nabavizadeh M, Sharghi H (2015) The effect of charge at the surface of silver nanoparticles on antimicrobial activity against gram-positive and gram-negative bacteria: a preliminary study. J Nanomater 16(1):53–53

Abdeen S, Isaac RR, Geo S, Sornalekshmi S, Rose A, Praseetha PK (2013) Evaluation of antimicrobial activity of biosynthesized iron and silver nanoparticles using the fungi Fusarium oxysporum and Actinomycetes sp. on human pathogens. Nano Biomed Eng 5(1):39

Aboelfetoh EF, El-Shenody RA, Ghobara MM (2017) Eco-friendly synthesis of silver nanoparticles using green algae (Caulerpa serrulata): reaction optimization, catalytic and antibacterial activities. Environ Monit Assess 189(7):349. https://doi.org/10.1007/s10661-017-6033-0

Ahmad A, Mukherjee P, Senapati S, Mandal D, Khan MI, Kumar R, Sastry M (2003a) Extracellular biosynthesis of silver nanoparticles using the fungus Fusarium oxysporum. Colloids Surf B: Biointerfaces 28(4):313–318

Ahmad A, Senapati S, Khan MI, Kumar R, Sastry M (2003b) Extracellular biosynthesis of monodisperse gold nanoparticles by a novel extremophilic actinomycete, Thermomonospora sp. Langmuir 19(8):3550–3553

Ahmad A, Jagdale T, Khan V, Patil S, Parsricha S, Ravi V (2015) Adv Mater 19:3295–3297

Akbarzadeh A, Samiei M, Davaran S (2012) Magnetic nanoparticles: preparation, physical properties, and applications in biomedicine. Nanoscale Res Lett 7(1):144

Akhtar MS, Panwar J, Yun YS (2013) Biogenic synthesis of metallic nanoparticles by plant extracts. ACS Sustain Chem Eng 1(6):591–602

Akter M, Sikder MT, Rahman MM, Ullah AA, Hossain KFB, Banik S, Hosokawa T, Saito T, Kurasaki M (2018) A systematic review on silver nanoparticles-induced cytotoxicity: physico-chemical properties and perspectives. J Adv Res 9:1–16

Akther T, Mathipi V, Kumar NS, Davoodbasha M, Srinivasan H (2019) Fungal-mediated synthesis of pharmaceutically active silver nanoparticles and anticancer property against A549 cells through apoptosis. Environ Sci Pollut Res 26:13649–13657

Al-Sharqi SAH (2020) Histological and biometric study of the effects of Fusarium graminarum silver nanoparticles on the kidney in male albino mice. Med Leg Update 20:1028–1035

Anil Kumar S, Abyaneh MK, Gosavi SW, Kulkarni SK, Pasricha R, Ahmad A, Khan MI (2007) Nitrate reductase-mediated synthesis of silver nanoparticles from AgNO 3. Biotechnol Lett 29: 439–445

Asmathunisha N, Kathiresan K (2013) A review on biosynthesis of nanoparticles by marine organisms. Colloids Surf B Biointerfaces 103:283–287. https://doi.org/10.1016/j.colsurfb.2012.10.030

Bala M, Arya V (2013) Biological synthesis of silver nanoparticles from aqueous extract of endophytic fungus Aspergillus Fumigatus and its antibacterial action. Int J Nanomater Biostruct 3(2):37–41

Balaji K, Mohammed Fayaz A, Kalaichelvan PT, Venkatesan R (2009) Fungal based synthesis of silver nanoparticles and effect of temperature on the size of particles. Colloids Surf B Biointerfaces 74(1):123–126. https://doi.org/10.1016/j.colsurfb.2009.07.002

Bansal V, Rautaray D, Ahmad A, Sastry M (2004) Biosynthesis of zirconia nanoparticles using the fungus Fusarium oxysporum. J Mater Chem 14(22):3303–3305

Bansal A, Yang H, Li C, Cho K, Benicewicz BC, Kumar SK, Schadler LS (2005) Quantitative equivalence between polymer nanocomposites and thin polymer films. Nat Mater 4(9):693–698

Barbalinardo M, Caicci F, Cavallini M, Gentili D (2018) Protein corona mediated uptake and cytotoxicity of silver nanoparticles in mouse embryonic fibroblast. Small 14(34):1801219

Bathrinarayanan VP, Thangavelu D, Muthukumarasamy VK, Munusamy C, Gurunathan B (2013) Biological synthesis and characterization of intracellular gold nanoparticles using biomass of Aspergillus fumigatus. Bull Mater Sci 36(7):1201–1205. https://doi.org/10.1007/s12034-013-0599-0

Bhattacharyya A, Duraisamy P, Govindarajan M, Buhroo AA, Prasad R (2016) Nano-biofungicides: emerging trend in insect pest control. In: Prasad R (ed) Advances and applications through fungal nanobiotechnology. Springer International Publishing Switzerland, pp 307–319

Bhargava A, Jain N, Barathi LM, Akhtar MS, Yun YS, Panwar J (2014) Synthesis, characterization and mechanistic insights of mycogenic iron oxide nanoparticles. In: Nanotechnology for sustainable development. Springer International Publishing, Cham, pp 337–348

Binupriya AR, Sathishkumar M, Yun SI (2010) Biocrystallization of silver and gold ions by inactive cell filtrate of Rhizopus stolonifer. Colloids Surf B: Biointerfaces 79(2):531–534

Braydich-Stolle L, Hussain S, Schlager JJ, Hofmann MC (2005) In vitro cytotoxicity of nanoparticles in mammalian germline stem cells. Toxicol Sci 88(2):412–419

Bulte JWM, Zhang SC, Van Gelderen P, Herynek V, Jordan EK, Duncan ID, Frank JA (1999) Neurotransplantation of magnetically labeled oligodendrocyte progenitors: magnetic resonance tracking of cell migration and myelination. Proc Natl Acad Sci 96(26):15256–15261

Camargo PHC, Satyanarayana KG, Wypych F (2009) Nanocomposites: synthesis, structure, properties and new application opportunities. Mater Res 12:1–39

Chauhan A, Zubair S, Tufail S, Sherwani A, Sajid M, Raman SC, Azam A, Owais M (2011) Fungus-mediated biological synthesis of gold nanoparticles: potential in detection of liver cancer. Int J Nanomedicine 6:2305–2319

Chen G, Yi B, Zeng G, Niu Q, Yan M, Chen A, Du J, Huang J, Zhang Q (2014) Facile green extracellular biosynthesis of CdS quantum dots by white rot fungus Phanerochaete

chrysosporium. Colloids Surf B Biointerfaces 117:199–205. https://doi.org/10.1016/j.colsurfb.2014.02.027
Chou KS, Ren CY (2000) Synthesis of nanosized silver particles by chemical reduction method. Mater Chem Phys 64(3):241–246
Christopher FC, Anbalagan S, Kumar PS, Pannerselvam SR, Vaidyanathan VK (2017) Surface adsorption of poisonous Pb(II) ions from water using chitosan functionalised magnetic nanoparticles. IET Nanobiotechnol 11(4):433–442. https://doi.org/10.1049/iet-nbt.2016.0166
Chung IM, Park I, Seung-Hyun K, Thiruvengadam M, Rajakumar G (2016) Plant-mediated synthesis of silver nanoparticles: their characteristic properties and therapeutic applications. Nanoscale Res Lett 11(1):1–14
Clarance P, Luvankar B, Sales J, Khusro A, Agastian P, Tack J-C, Al-Shwaiman HA, Al Khulaifi MM, Elgorban AM, Syed A, Kim HJ (2019) Green synthesis and characterization of Gold Nanoparticles using endophytic fungi Fusarium solani and its in-vitro anticancer and biomedical applications. Saudi. J Biol Sci 27(2):706–712. https://doi.org/10.1016/j.sjbs.2019.12.026
Clarance P, Luvankar B, Sales J, Khusro A, Agastian P, Tack JC, Al Khulaifi MM, Al-Shwaiman HA, Elgorban AM, Syed A, Kim HJ (2020) Green synthesis and characterization of gold nanoparticles using endophytic fungi Fusarium solani and its in-vitro anticancer and biomedical applications. Saudi J Biol Sci 27(2):706–712
Corradini E, De Moura MR, Mattoso LHC (2010) A preliminary study of the incorporation of NPK fertilizer into chitosan nanoparticles. Express Polym Lett 4(8):509
Costa Silva LP, Oliveira JP, Keijok WJ, da Silva AR, Aguiar AR, Guimarães MC, Ferraz CM, Araújo JV, Tobias FL, Braga FR (2017) Extracellular biosynthesis of silver nanoparticles using the cell-free filtrate of nematophagous fungus Duddingtonia flagrans. Int J Nanomedicine 31:6373–6381
Crucho CIC, Barros MT (2017) Polymeric nanoparticles: a study on the preparation variables and characterization methods. Mater Sci Eng C 80:771–784. https://doi.org/10.1016/j.msec.2017.06.004
Cuevas R, Durán N, Diez MC, Tortella GR, Rubilar O (2015) Extracellular biosynthesis of copper and copper oxide nanoparticles by Stereum hirsutum, a native white-rot fungus from chilean forests. J Nanomater 16(1):1–7
Danagoudar A, Pratap GK, Shantaram M, Ghosh K, Kanade Santosh R, Joshi Chandrashekhar G (2020) Characterization, cytotoxic and antioxidant potential of silver nanoparticles biosynthesised using endophytic fungi (Penicillium citrinum CGJ-C1). Mater Today 25:101385. https://doi.org/10.1016/j.mtcomm.2020.101385
Darroudi M, Ahmad MB, Zamiri R, Zak AK, Abdullah AH, Ibrahim NA (2011) Time-dependent effect in green synthesis of silver nanoparticles. Int J Nanomedicine 6:677–681
Das SK, Das AR, Guha AK (2009) Gold nanoparticles: microbial synthesis and application in water hygiene management. Langmuir 25(14):8192–8199
Davis MW, Ogden WC (1997) Free resources and advanced alignment for cross-language text retrieval. TREC 1997:385–395
Dhillon GS, Brar SK, Kaur S, Verma M (2012) Green approach for nanoparticle biosynthesis by fungi: current trends and applications. Crit Rev Biotechnol 32(1):49–73
Dhiman S, Varma A, Prasad R, Goel A (2022) Mechanistic insight of the antifungal potential of green synthesized zinc oxide nanoparticles against *Alternaria brassicae*. J Nanomater 2022:7138843, 13. https://doi.org/10.1155/2022/7138843
Dhiman S, Varma A, Rao M, Prasad R, Goel A (2023) Deciphering the fertilizing and disease suppression potential of phytofabricated zinc oxide nanoparticles on *Brassica juncea*. Environ Res. https://doi.org/10.1016/j.envres.2023.116276
Din IM, Rehan R (2016) Synthesis, characterization, and applications of copper 2 nanoparticles. Anal Lett 50(1):50–62
Durán N, Seabra AB (2012) Metallic oxide nanoparticles: state of the art in biogenic syntheses and their mechanisms. Appl Microbiol Biotechnol 95:275–288

Durán N, Marcato PD, Alves OL, De Souza GI, Esposito E (2005) Mechanistic aspects of biosynthesis of silver nanoparticles by several Fusarium oxysporum strains. J Nanobiotechnol 3:1–7

Durán N, Marcato PD, Durán M, Yadav A, Gade A, Rai M (2011) Mechanistic aspects in the biogenic synthesis of extracellular metal nanoparticles by peptides, bacteria, fungi, and plants. Appl Microbiol Biotechnol 90:1609–1624

Eftekhari A, Khalilov R, Kavetskyy T, Keskin C, Prasad R, Rosic GL (2023) Biological/chemical-based metallic nanoparticles synthesis, characterization, and environmental applications. Front Chem 11:1191659. https://doi.org/10.3389/fchem.2023.1191659

Elamawi RM, Al-Harbi RE, Hendi AA (2018) Biosynthesis and characterization of silver nanoparticles using Trichoderma longibrachiatum and their effect on phytopathogenic fungi. Egypt J Biol Pest Contr 28(1):1–11

Elgorban AM, Al-Rahmah AN, Sayed SR, Hirad A, Mostafa AAF, Bahkali AH (2016) Antimicrobial activity and green synthesis of silver nanoparticles using Trichoderma viride. Biotechnol Biotechnol Equip 30(2):299–304

Fariq A, Khan T, Yasmin A (2017) Microbial synthesis of nanoparticles and their potential applications in biomedicine. J Appl Biomed 15(4):241–248. https://doi.org/10.1016/j.jab.2017.03.004

Fatemi M, Mollania N, Momeni-Moghaddam M, Sadeghifar F (2018) Extracellular biosynthesis of magnetic iron oxide nanoparticles by Bacillus cereus strain HMH1: characterization and in vitro cytotoxicity analysis on MCF-7 and 3T3 cell lines. J Biotechnol 270:1–11. https://doi.org/10.1016/j.jbiotec.2018.01.021

Gaba S, Prasad L, Varma A, Rai AK, Prasad R, Goel A (2023) Leveraging of mycogenic copper oxide nanostructures for disease management of Alternaria blight of *Brassica juncea*. Green Processing and Synthesis 12:20230015. https://doi.org/10.1515/gps-2023-0015

Gade AK, Bonde PP, Ingle AP, Marcato PD, Duran N, Rai MK (2008) Exploitation of Aspergillus niger for synthesis of silver nanoparticles. J Biobased Mater Bioenergy 2(3):243–247

Gade A, Gaikwad S, Tiwari V, Yadav A, Ingle A, Rai M (2010a) Biofabrication of silver nanoparticles by Opuntia ficus-indica: in vitro antibacterial activity and study of the mechanism involved in the synthesis. Curr Nanosci 6(4):370–375

Gade A, Ingle A, Whiteley C, Rai M (2010b) Mycogenic metal nanoparticles: progress and applications. Biotechnol Lett 32:593–600

Gahlawat G, Choudhury AR (2019) A review on the biosynthesis of metal and metal salt nanoparticles by microbes. RSC Adv 9:12944–12967. https://doi.org/10.1039/c8ra10483b

Gaikwad SC, Ingle A, Gade A, Galidiero S (2013) Antiviral activity of mycosynthesized silver nanoparticles against herpes simplex virus and human parainfluenza virus type 3. Int J Nanomedicine 8:4303–4314

Galdiero S, Falanga A, Vitiello M, Cantisani M, Marra V, Galdiero M (2011) Silver nanoparticles as potential antiviral agents. Molecules 16(10):8894–8918

Ganesan V, Hariram M, Vivekanandhan S, Muthuramkumar S (2020) Periconium sp. (endophytic fungi) extract mediated sol-gel synthesis of ZnO nanoparticles for antimicrobial and antioxidant applications. Mater Sci Semicond Process 105:104739. https://doi.org/10.1016/j.mssp.2019.104739

Gautam PK, Singh A, Misra K, Sahoo AK, Samanta SK (2019) Synthesis and applications of biogenic nanomaterials in drinking and wastewater treatment. J Environ Manag 231:734–748. https://doi.org/10.1016/j.jenvman.2018.10.104

Geethalakshmi R, Sarada DVL (2010) Synthesis of plant-mediated silver nanoparticles using Trianthema decandra extract and evaluation of their anti microbial activities. Int J Eng Sci Technol 2(5):970–975

Gericke M, Pinches A (2006) Biological synthesis of metal nanoparticles. Hydrometallurgy 83(1–4):132–140

Ghareib M, Tahon MA, Abdallah WE, Tallima A (2018) Green biosynthesis of copper oxide nanoparticles using fungi isolated from Egyptian soil. Int J Res Pharmaceut Nano Sci 7(4):119–128

Goswami A, Roy I, Sengupta S, Debnath N (2010) Novel applications of solid and liquid formulations of nanoparticles against insect pests and pathogens. Thin Solid Films 519(3): 1252–1257

Govender Y, Riddin T, Gericke M, Whiteley CG (2009) Bioreduction of platinum salts into nanoparticles: a mechanistic perspective. Biotechnol Lett 31:95–100

Gupta K, Chundawat TS (2019) Bio-inspired synthesis of platinum nanoparticles from fungus Fusarium oxysporum: its characteristics, potential antimicrobial, antioxidant and photocatalytic activities. Mater Res Express 6(10):1050d6

Gudadhe JA, Yadav A, Gade A, Marcato PD, Durán N, Rai M (2014) Preparation of an agar-silver nanoparticles (A-AgNp) film for increasing the shelf-life of fruits. IET Nanobiotechnol 8(4): 190–195

Guilger-Casagrande M, de Lima R (2019) Synthesis of silver nanoparticles mediated by fungi: a review. Front Bioeng Biotechnol 7:287

Hamedi S, Ghaseminezhad M, Shokrollahzadeh S, Shojaosadati SA (2017) Controlled biosynthesis of silver nanoparticles using nitrate reductase enzyme induction of filamentous fungus and their antibacterial evaluation. Artif Cells Nanomed Biotechnol 45(8):1588–1596

Hamzeh M, Sunahara GI (2013) In vitro cytotoxicity and genotoxicity studies of titanium dioxide (TiO2) nanoparticles in Chinese hamster lung fibroblast cells. Toxicol in Vitro 27(2):864–873

Hawkey PM (2008) The growing burden of antimicrobial resistance. J Antimicrob Chemother 62: 125

Hebeish AA, El-Rafie MH, Abdel-Mohdy FA, Abdel-Halim ES, Emam HE (2010) Carboxymethyl cellulose for green synthesis and stabilization of silver nanoparticles. Carbohydr Polym 82(3): 933–941

Hu X, Saravanakumar K, Jin T, Wang MH (2019) Mycosynthesis, characterization, anticancer and antibacterial activity of silver nanoparticles from endophytic fungus Talaromyces purpureogenus. Int J Nanomedicine 14:3427–3438

Hulkoti NI, Taranath T (2014) Biosynthesis of nanoparticles using microbesda review. Colloids Surf B Biointerfaces 121:474–483. https://doi.org/10.1016/j.colsurfb.2014.05.027

Ingle A, Gade A, Pierrat S, Sonnichsen C, Rai M (2008) Mycosynthesis of silver nanoparticles using the fungus Fusarium acuminatum and its activity against some human pathogenic bacteria. Curr Nanosci 4(2):141–144

Ingle A, Rai M, Gade A, Bawaskar M (2009) Fusarium solani: a novel biological agent for the extracellular synthesis of silver nanoparticles. J Nanopart Res 11:2079–2085

Jain N, Bhargava A, Majumdar S, Tarafdar JC, Panwar J (2011) Extracellular biosynthesis and characterization of silver nanoparticles using Aspergillus flavus NJP08: a mechanism perspective. Nanoscale 3(2):635–641

Jamkhande PG, Ghule NW, Bamer AH, Kalaskar MG (2019) Metal nanoparticles synthesis: an overview on methods of preparation, advantages and disadvantages, and applications. J Drug Deliv Sci Technol 53:101174. https://doi.org/10.1016/j.jddst.2019.101174

Jayabalan J, Mani G, Krishnan N, Pernabas J, Devadoss JM, Jang HT (2019) Green biogenic synthesis of zinc oxide nanoparticles using Pseudomonas putida culture and its in vitro antibacterial and anti-biofilm activity. Biocatal Agric Biotechnol 21:101327. https://doi.org/10.1016/j.bcab.2019.101327

Jeevan P, Ramya K, Rena AE (2012) Extracellular biosynthesis of silver nanoparticles by culture supernatant of Pseudomonas aeruginosa. Indian J Biotechnol 11:72–76

Jha AK, Prasad K (2010) Understanding biosynthesis of metallic/oxide nanoparticles: a biochemical perspective. Biocompatible nanomaterials synthesis, characterization and applications. NOVA Science Publishers Inc., Hauppauge, NY

Jha AK, Prasad K (2016) Understanding mechanism of fungus mediated nanosynthesis: a molecular approach. In: Advances and applications through fungal nanobiotechnology. Springer, Cham, pp 1–23

Kamalakannan S, Gobinath C, Ananth S (2014) Synthesis and characterization of fungus mediated silver nanoparticle for toxicity on filarial vector, Culex quinquefasciatus. Int J Pharmaceut Sci Rev Res 24(2):124–132

Karatoprak GŞ, Aydin G, Altinsoy B, Altinkaynak C, Koşar M, Ocsoy I (2017) The Effect of Pelargonium endlicherianum Fenzl. root extracts on formation of nanoparticles and their antimicrobial activities. Enzym Microb Technol 97:21–26

Kashyap PL, Kumar S, Srivastava AK, Sharma AK (2013) Myconanotechnology in agriculture: a perspective. World J Microbiol Biotechnol 29:191–207

Kathiresan K, Manivannan S, Nabeel MA, Dhivya B (2009) Studies on silver nanoparticles synthesized by a marine fungus, Penicillium fellutanum isolated from coastal mangrove sediment. Colloids Surf B: Biointerfaces 71(1):133–137

Khandel P, Shahi SK (2016) Microbes mediated synthesis of metal nanoparticles: current status and future prospects. Int J Nanomater Biostruct 6(1):1–24

Khani R, Roostaei B, Bagherzade G, Moudi M (2018) Green synthesis of copper nanoparticles by fruit extract of Ziziphus spina-christi (L.) Willd.: application for adsorption of triphenylmethane dye and antibacterial assay. J Mol Liq 255:541–549. https://doi.org/10.1016/j.molliq.2018.02.010

Kisimba K, Krishnan A, Faya M, Byanga K, Kasumbwe K, Vijayakumar K, Prasad R (2023) Synthesis of metallic nanoparticles based on green chemistry and their medical biochemical applications: synthesis of metallic nanoparticles. J Renew Mater 11(6):2575–2591. https://doi.org/10.32604/jrm.2023.026159

Koch N, Sonowal S, Prasad R (2023) Elucidate the smart tailored biogenic nanoparticles and their applications in remediation. Biotechnol Genet Eng Rev. https://doi.org/10.1080/02648725.2023.2219942

Kumari Y, Kaur G, Kumar R, Singh SK, Gulati M, Khursheed R, Clarisse A, Gowthamarajan K, Karri VVSNR, Mahalingam R, Ghosh D, Awasthi A, Kumar R, Yadav AK, Kapoor B, Singh PK, Dua K, Porwal O (2019) Gold nanoparticles: new routes across old boundaries. Adv Colloid Interf Sci 274:102037. https://doi.org/10.1016/j.cis.2019.102037

Lee YK, Choi EJ, Webster TJ, Kim SH, Khang D (2014) Effect of the protein corona on nanoparticles for modulating cytotoxicity and immunotoxicity. Int J Nanomedicine 10:97

Lee KX, Shameli K, Yew YP, Teow SY, Jahangirian H, Rafiee-Moghaddam R, Webster TJ (2020) Recent developments in the facile bio-synthesis of gold nanoparticles (AuNPs) and their biomedical applications. Int J Nanomedicine 15:275–300

Lesniak A, Fenaroli F, Monopoli MP, Åberg C, Dawson KA, Salvati A (2012) Effects of the presence or absence of a protein corona on silica nanoparticle uptake and impact on cells. ACS Nano 6(7):5845–5857

Li G, He D, Qian Y, Guan B, Gao S, Cui Y, Yokoyama K, Wang L (2011) Fungus-mediated green synthesis of silver nanoparticles using Aspergillus terreus. Int J Mol Sci 13(1):466–476

Liu J, Yu S, Yin Y, Chao J (2012) Methods for separation, identification, characterization and quantification of silver nanoparticles. TrAC Trends Anal Chem 33:95–106. https://doi.org/10.1016/j.trac.2011.10.010

Liu M, Johnston MB, Snaith HJ (2013) Efficient planar heterojunction perovskite solar cells by vapour deposition. Nature 501(7467):395–398

Lowy F (1998) Staphylococcus aureus infections. N Engl J Med 339:520–532

Majeed S, Abdullah MSB, Nanda A, Ansari MT (2016a) In vitro study of the antibacterial and anticancer activities of silver nanoparticles synthesized from Penicillium brevicompactum (MTCC-1999). J Taibah Univ Sci 10(4):614–620

Majeed S, Abdullah MS, Dash GK, Ansari MT, Nanda A (2016b) Biochemical synthesis of silver nanoparticles using filamentous fungi Penicillium decumbens (MTCC-2494) and its efficacy against A-549 lung cancer cell line. Chin J Nat Med 14(8):615–620. https://doi.org/10.1016/s1875-5364(16)30072-3

Mansoori GA (2005) Principles of nanotechnology: molecular-based study of condensed matter in small systems. World Scientific, Singapore

Mazumdar H, Haloi N (2011) A study on biosynthesis of Iron nanoparticles by Pleurotus sp. J Microbiol Biotechnol Res 1(3):39–49

Menon S et al (2017) A review on biogenic synthesis of gold nanoparticles, characterization, and its applications. Resour Eff Technol 3(4):516–527. https://doi.org/10.1016/j.reffit.2017.08.002
Mohamed YM, Azzam AM, Amin BH, Safwat NA (2015) Mycosynthesis of iron nanoparticles by Alternaria alternata and its antibacterial activity. Afr J Biotechnol 14(14):1234–1241
Mohamed AA, Fouda A, Abdel-Rahman MA, Hassan SED, El-Gamal MS, Salem SS, Shaheen TI (2019) Fungal strain impacts the shape, bioactivity and multifunctional properties of green synthesized zinc oxide nanoparticles. Biocatal Agric Biotechnol 19:101103
Mohd Yusof H, Mohamad R, Zaidan UH, Abdul R (2019) Microbial synthesis of zinc oxide nanoparticles and their potential application as an antimicrobial agent and a feed supplement in animal industry: a review. J Anim Sci Biotechnol 10:57
Monopoli MP, Åberg C, Salvati A, Dawson KA (2012) Biomolecular coronas provide the biological identity of nanosized materials. Nat Nanotechnol 7:779–786
Mukherjee P, Roy M, Mandal BP, Dey GK, Mukherjee PK, Ghatak J, Tyagi AK, Kale SP (2008) Green synthesis of highly stabilized nanocrystalline silver particles by a non-pathogenic and agriculturally important fungus T. asperellum. Nanotechnology 19(7):075103
Naidu KSB, Adam JK, Govender P (2015) Biomedical applications and toxicity of nanosilver: a review. Med Technol SA 29(2):13–19
Naimi-Shamel N, Pourali P, Dolatabadi S (2019) Green synthesis of gold nanoparticles using Fusarium oxysporum and antibacterial activity of its tetracycline conjugant. J Mycol Med 29 (1):7–13
Narayanan KB, Sakthivel N (2010) Biological Synthesis of metal nanoparticles by microbes. Adv Colloid Interf Sci 156(1–2):1–13
Navya PN, Daima HK (2016) Rational engineering of physicochemical properties of nanomaterials for biomedical applications with nanotoxicological perspectives. Nano Converg 3:1–14
Neeraj G, Krishnan S, Senthil Kumar P, Shriaishvarya KR, Vinoth Kumar V (2016) Performance study on sequestration of copper ions from contaminated water using newly synthesized high effective chitosan coated magnetic nanoparticles. J Mol Liq 214:335–346. https://doi.org/10.1016/j.molliq.2015.11.051
Nguyen VH, Lee BJ (2017) Protein corona: a new approach for nanomedicine design. Int J Nanomedicine 12:3137–3151
Nithya K, Sathish A, Senthil Kumar P, Ramachandran T (2018) Fast kinetics and high adsorption capacity of green extract capped superparamagnetic iron oxide nanoparticles for the adsorption of Ni(II) ions. J Ind Eng Chem 59:230–241. https://doi.org/10.1016/j.jiec.2017.10.028
Nordmeier A, Merwin A, Roeper DF, Chidambaram D (2018) Microbial synthesis of metallic molybdenum nanoparticles. Chemosphere 203:521–525. https://doi.org/10.1016/j.chemosphere.2018.02.079
Osherov A, Prasad R, Chrzanowski W, New EJ, Brazaca L, Sadik O, Haynes CL, Maine E (2023) Responsible nanotechnology for a sustainable future. One Earth 6(7):763–766. https://doi.org/10.1016/j.oneear.2023.06.010
Oztürk BY, Gürsu BY, Dag I (2019) Antibiofilm and antimicrobial activities of green synthesized silver nanoparticles using marine red algae Gelidium corneum. Process Biochem 89:208–219. https://doi.org/10.1016/j.procbio.2019.10.027
Panchangam RL, Upputuri RTP (2019) In vitro biological activities of silver nanoparticles synthesized from Scedosporium sp. isolated from soil. Brazilian Journal of Pharmaceutical. Science 55:e00254
Pantidos N, Horsfall LE (2014) Biological synthesis of metallic nanoparticles by bacteria, fungi and plants. J Nanomed Nanotechnol 5(5):233. https://doi.org/10.4172/2157-7439.1000233
Patil DR (2015) Synthesis and characterization of silver nanoparticles using fungi and its antimicrobial activity. Int J Res Stud Biosci 3:146–152
Patil MP, Kim GD (2018) Marine microorganisms for synthesis of metallic nanoparticles and their biomedical applications. Colloids Surf B Biointerfaces 172:487–495. https://doi.org/10.1016/j.colsurfb.2018.09.007

Pavani KV, Sunil Kumar N, Sangameswaran BB (2012) Synthesis of lead nanoparticles by Aspergillus species. Pol J Microbiol 61(1):61–63
Pourali P, Yahyaei B, Afsharnezhad S (2018) Bio-synthesis of gold nanoparticles by Fusarium oxysporum and assessment of their conjugation possibility with two types of β-lactam antibiotics without any additional linkers. Microbiology 87:229–237
Prasad R (2014) Synthesis of silver nanoparticles in photosynthetic plants. J Nanoparticles 2014:963961. https://doi.org/10.1155/2014/963961
Prasad R (2016) Advances and applications through fungal nanobiotechnology. Springer, International Publishing Switzerland. (ISBN: 978-3-319-42989-2)
Prasad R (2017) Fungal nanotechnology: applications in agriculture, industry, and medicine. Springer Nature Singapore Pte Ltd. (ISBN 978-3-319-68423-9)
Prasad R (2019a) Microbial nanobionics: basic research and applications. Springer International Publishing. (ISBN 978-3-030-16534-5) https://www.springer.com/gp/book/9783030165338
Prasad R (2019b) Microbial nanobionics: state of art. Springer International Publishing. (ISBN 978-3-030-16383-9) https://www.springer.com/gp/book/9783030163822
Prasad R, Pandey R, Barman I (2016) Engineering tailored nanoparticles with microbes: quo vadis. WIREs Nanomed Nanobiotechnol 8:316–330. https://doi.org/10.1002/wnan.1363
Priyadarshini E, Pradhan N, Sukla LB, Panda PK (2014) Controlled synthesis of gold nanoparticles using Aspergillus terreus IF0 and its antibacterial potential against Gram negative pathogenic bacteria. J Nanotechnol 2014:1–9
Punjabi K, Choudhary P, Samant L, Mukherjee S, Vaidya S, Chowdhary A (2015) Biosynthesis of nanoparticles: a review. Int J Pharm Sci Rev Res 30(1):219–226
Purkait PK, Roy J, Maitra S, Choudhuri MG (2015) Green synthesis of zinc oxide nanoparticles - a review. Sci Voyage 1(2):32–46
Rai M, Ingle A (2012) Role of nanotechnology in agriculture with special reference to management of insect pests. Appl Microbiol Biotechnol 94:287–293
Rai M, Yadav A, Gade A (2009a) Silver nanoparticles as a new generation of antimicrobials. Biotechnol Adv 27(1):76–83
Rai MR, Alka Yadav AY, Bridge P, Aniket Gade AG (2009b) Myconanotechnology: a new and emerging science. In: Applied mycology. CABI, Wallingford, pp 258–267
Raliya R, Tarafdar JC (2014) Biosynthesis and characterization of zinc, magnesium and titanium nanoparticles: an eco-friendly approach. Int Nano Lett 93:3–10
Ramesh V, Ahmed John S, Koperuncholan M (2014) Impact of cement industries dust on selective green plants: a case study in Ariyalur industrial zone. Int J Pharmaceut Chem Biol Sci 4(1): 152–158
Ramos MM, Morais ES, Sena IS, Lima AL, de Oliveira FR, de Freitas CM, Fernandes CP, de Carvalho JC, Ferreira IM (2020) Silver nanoparticle from whole cells of the fungi Trichoderma spp. isolated from Brazilian Amazon. Biotechnol Lett 42:833–843
Ranjani S, Shariq Ahmed M, Adnan M, Senthil Kumar N, Ruckmani K, Hemalatha S (2021) Synthesis, characterization and applications of endophytic fungal nanoparticles. Inorg Nano-Metal Chem 51(2):280–287. https://doi.org/10.1080/24701556.2020.1784231
Raouf HM, Nasiri SM (2015) Recent achievements in the microbial synthesis of semiconductor metal sulfide nanoparticles. Mater Sci Semicond Process 40:293–301. https://doi.org/10.1016/j.mssp.2015.06.003
Reddy AVB, Yusop Z, Jaafar J, Reddy YVM, Aris AB, Majid ZA, Talib J, Madhavi G (2016) Recent progress on Fe-based nanoparticles: synthesis, properties, characterization and environmental applications. J Environ Chem Eng 4(3):3537–3553. https://doi.org/10.1016/j.jece.2016.07.035
Ritz S, Schöttler S, Kotman N, Baier G, Musyanovych A, Kuharev J, Landfester K, Schild H, Jahn O, Tenzer S, Mailänder V (2015) Protein corona of nanoparticles: distinct proteins regulate the cellular uptake. Biomacromolecules 16(4):1311–1321
Rose GK, Soni R, Rishi P, Soni SK (2019) Optimization of the biological synthesis of silver nanoparticles using Penicillium oxalicum GRS-1 and their antimicrobial effects against common food-borne pathogens. Green Process Synth 8(1):144–156

Roy S, Mukherjee T, Chakraborty S, Das TK (2013) Biosynthesis, characterisation & antifungal activity of silver nanoparticles synthesized by the fungus Aspergillus foetidus MTCC8876. Digest J Nanomater Biostruct 8(1):197–205

Salaheldin TA, Husseiny SM, Al-Enizi AM, Elzatahry A, Cowley AH (2016) Evaluation of the cytotoxic behavior of fungal extracellular synthesized Ag nanoparticles using confocal laser scanning microscope. Int J Mol Sci 17(3):329

Salvadori MR, Ando RA, Oller do Nascimento CA, Correa B (2014) Intracellular biosynthesis and removal of copper nanoparticles by dead biomass of yeast isolated from the wastewater of a mine in the Brazilian amazonia. PLoS One 9(1):e87968. https://doi.org/10.1371/journal.pone.008796

Sandhu RS, Aharwal RP, Kumar S (2019) Green synthesis: a novel approach for nanoparticles synthesis. Int J Pharm Sci Res 10(8):3550–3562

Sanghi R, Verma P (2009) Biomimetic synthesis and characterization of protein capped silver nanoparticles. Bioresour Technol 100(1):501–504

Saravanan A, Kumar PS, Karthiga Devi G, Arumugam T (2016) Synthesis and characterization of metallic nanoparticles impregnated onto activated carbon using leaf extract of Mukia maderasapatna: evaluation of antimicrobial activities. Microb Pathog 97:198–203. https://doi.org/10.1016/j.micpath.2016.06.019

Sarkar J, Acharya K (2017) Alternaria alternata culture filtrate mediated bioreduction of chloroplatinate to platinum nanoparticles. Inorg Nano-Metal Chem 47(3):365–369

Sathiyanarayanan G, Dineshkumar K, Yang YH (2017) Microbial exopolysaccharide-mediated synthesis and stabilization of metal nanoparticles. Crit Rev Microbiol 43:731–752. https://doi.org/10.1080/1040841x.2017.1306689

Saxena J, Sharma PK, Sharma MM, Singh A (2016) Process optimization for green synthesis of silver nanoparticles by Sclerotinia sclerotiorum MTCC 8785 and evaluation of its antibacterial properties. Springerplus 5(1):1–10

Seetharaman PK, Chandrasekaran R, Gnanasekar S, Chandrakasan G, Gupta M, Manikandan DB, Sivaperumal S (2018) Antimicrobial and larvicidal activity of eco-friendly silver nanoparticles synthesized from endophytic fungi Phomopsis liquidambaris. Biocatal Agric Biotechnol 16:22–30

Shakibaie M, Forootanfar H, Mollazadeh-Moghaddam K, Bagherzadeh Z, Nafissi-Varcheh N, Shahverdi AR, Faramarzi MA (2010) Green synthesis of gold nanoparticles by the marine microalga Tetraselmis suecica. Biotechnol Appl Biochem 57(2):71–75

Sharma G, Kumar A, Chauhan C, Okram A, Sharma S, Pathania D, Kalia S (2017a) Pectin-crosslinked -guar gum/SPION nanocomposite hydrogel for adsorption of m-cresol and p chlorophenol. Sustain Chem Pharm 6:96–106

Sharma G, Soni R, Jasuja ND (2017b) Phytoassisted synthesis of magnesium oxide nanoparticles with Swertia chirayaita. J Taibah Univ Sci 11(3):471–477

Sheikhloo Z, Salouti M (2011) Intracellular biosynthesis of gold nanoparticles by the fungus Penicillium chrysogenum. Int J Nanosci Nanotechnol 7(2):102–105

Shelar GB, Chavan AM (2014) Fusarium semitectum mediated extracellular synthesis of silver nanoparticles and their antibacterial activity. Int J Biomed Adv Res 5(07):20–24

Shende S, Gade A, Rai M (2016) Large-scale synthesis and antibacterial activity of fungal-derived silver nanoparticles. Environ Chem Lett 15:427–434

Shukla AK, Iravani S (2017) Metallic nanoparticles: green synthesis and spectroscopic characterization. Environ Chem Lett 15(2):223–231. https://doi.org/10.1007/s10311-017-0618-2

Siddiqi KS, Husen A, Rao RA (2018) A review on biosynthesis of silver nanoparticles and their biocidal properties. J Nanobiotechnol 16(1):1–28

Soni N, Prakash S (2011) Factors affecting the geometry of silver nanoparticles synthesis in Chrysosporium tropicum and Fusarium oxusporum. Am J Nanotechnol 2(1):112–121

Soni N, Prakash S (2012) Entomopathogenic fungus generated Nanoparticles for enhancement of efficacy in Culex quinquefasciatus and Anopheles stephensi. Asian Pac J Trop Dis 2(1):S356–S361

Srivastava S, Bhargava A, Pathak N, Srivastava P (2019) Production, characterization and antibacterial activity of silver nanoparticles produced by Fusarium oxysporum and monitoring of protein-ligand interaction through in-silico approaches. Microb Pathog 129:136–145. https://doi.org/10.1016/j.micpath.2019.02.013

Srivastava S, Usmani Z, Atanasov AG, Singh VK, Singh NP, Abdel-Azeem AM, Prasad R, Gupta G, Sharma M, Bhargava A (2021) Biological nanofactories: using living forms for metal nanoparticle synthesis. Mini-Rev Med Chem 21(2):245–265

Stewart PL (2017) Cryo-electron microscopy and cryo-electron tomography of nanoparticles. Wiley Interdiscip Rev Nanomed Nanobiotechnol 9(2):e1417

Syed A, Ahmad A (2012) Extracellular biosynthesis of platinum nanoparticles using the fungus Fusarium oxysporum. Colloids Surf B: Biointerfaces 1(97):27–31

Thakkar KN, Mhatre SS, Parikh RY (2010) Biological synthesis of metallic nanoparticles. Nanomedicine 6(2):257–262

Thakker JN, Dalwadi P, Dhandhukia PC (2013) Biosynthesis of gold nanoparticles using Fusarium oxysporum f. sp. cubense JT1, a plant pathogenic fungus. Int Scholar Res Notice 2013:515091

Tran N, Mir A, Mallik D, Sinha A, Nayar S, Webster TJ (2010) Bactericidal effect of iron oxide nanoparticles on Staphylococcus aureus. Int J Nanomedicine 5:277–283

Tyagi S, Tyagi PK, Gola D, Chauhan N, Bharti RK (2019) Extracellular synthesis of silver nanoparticles using entomopathogenic fungus: characterization and antibacterial potential. SN Applied Sciences 1, pp. 1–9

Vijayanandan AS, Balakrishnan RM (2018) Biosynthesis of cobalt oxide nanoparticles using endophytic fungus Aspergillus nidulans. J Environ Manag 218:442–450. https://doi.org/10.1016/j.jenvman.2018.04.032

Waghmare SS, Deshmukh AM, Kulkarni SW, Oswaldo LA (2011) Biosynthesis and characterization of manganese and zinc nanoparticles. Univers J Environ Res Technol 1(1):64–69

Walczyk D, Bombelli FB, Monopoli MP, Lynch I, Dawson KA (2010) What the cell "sees" in bionanoscience. J Am Chem Soc 132(16):5761–5768

Wang L, Liu X, Lee D-J, Tay J-H, Zhang Y, Wan C-L, Chen X-F (2018) Recent advances on biosorption by aerobic granular sludge. J Hazard Mater 357:253–270. https://doi.org/10.1016/j.jhazmat.2018.06.010

Xue B, He D, Gao S, Wang D, Yokoyama K, Wang L (2016) Biosynthesis of silver nanoparticles by the fungus Arthroderma fulvum and its antifungal activity against genera of Candida, Aspergillus and Fusarium. Int J Nanomedicine 11:1899

Yadav A, Kon K, Kratosova G, Duran N, Ingle AP, Rai M (2015) Fungi as an efficient mycosystem for the synthesis of metal nanoparticles: progress and key aspects of research. Biotechnol Lett 37:2099–2120

Yilma AN, Singh SR, Dixit S, Dennis VA (2013) Anti-inflammatory effects of silver-polyvinyl pyrrolidone (Ag-PVP) nanoparticles in mouse macrophages infected with live Chlamydia trachomatis. Int J Nanomedicine 8:2421–2432

Yin N, Liu Q, Liu J, He B, Cui L, Li Z, Yun Z, Qu G, Liu S, Zhou Q, Jiang G (2013) Silver nanoparticle exposure attenuates the viability of rat cerebellum granule cells through apoptosis coupled to oxidative stress. Small 9(9–10):1831–1841

Yu SJ, Yin YG, Liu JF (2013) Silver nanoparticles in the environment. Environ Sci Process Impacts 15(1):78–92

Zhang X, Yan S, Tyagi RD, Surampalli RY (2011) Synthesis of nanoparticles by microorganisms and their application in enhancing microbiological reaction rates. Chemosphere 82(4):489–494

Zhang X, Qu Y, Shen W, Wang J, Li H, Zhang Z, Li S, Zhou J (2016) Biogenic synthesis of gold nanoparticles by yeast Magnusiomyces ingens LH-F1 for catalytic reduction of nitrophenols. Colloids Surf A Physicochem Eng Asp 497:280–285. https://doi.org/10.1016/j.colsurfa.2016.02.033

Synthesis and Applications of Fungal-Mediated Nanoparticles

5

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Abstract

Vast research has been carried out for past 20 years to find ways to synthesize nanoparticles through fungi or fungal extracts. There is a demand to create eco-friendly techniques for the synthesis of nanoparticles. Employing fungal strains for nanoparticle biosynthesis is technologically attractive, reasonable and commercially feasible. Amongst other organisms, fungi make an appropriate option for the production of metallic nanoparticles because they secrete a large amount of proteins, thus increasing productivity, and their easy usage in the laboratory. Fungal nanobiotechnology has been utilized in agricultural, medical and industrial sectors for goods and services improvement and delivery to mankind. Agriculturally, it has found applications in plant disease management and production of environmentally friendly, nontoxic insecticides, fungicides to enhance agricultural production in general. Medically, diagnosis and treatment of diseases, particularly of microbial origin, has been improved with fungal nanoparticles through more efficient drug delivery systems with major advantage to pharmaceutical industries.

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5.1 Introduction

The nanoscience is the study of unique properties of the materials between 1 and 100 nm. Nanotechnology is an important field of research since last century. The prefix "nano" is referred to a Greek prefix meaning "dwarf" or very small and depicts 1000 millionth of a meter (10^{-9} m). The nanostructured materials are nanomaterials with single dimension in nanoscale range (<100 nm) and are made up of a single or multiple materials. Hence, nanostructured materials are composed of inter linked parts in the nanoscale range (Jeevanandam et al. 2018). The nanoparticles and nanostructured materials can be made up of simple materials (e.g. carbon, metal and polymer) (Barhoum et al. 2021). The material researchers extensively studied how to exploit nanoparticles and nanostructured materials in the field of biomedical and healthcare sectors in the last 50 years (Gaur et al. 2021). Nanotechnologies show significant potential in the medical field, including in imaging techniques and diagnostic tools, tissue-engineered constructs, drug delivery systems, pharmaceutical therapeutics and implants (Filipponi and Nicolau 2006), and also have advanced treatments for many diseases, including cardiovascular, cancer, psychiatric and neuro-degenerative diseases, diabetes, infections of bacteria and viruses (Lombardo et al. 2019).

The concept of nanotechnology has been introduced by the American physicist and Nobel Prize winner Richard Feynman in 1959. In the annual meeting of the American Physical Society, Feynman presented a lecture on "There's Plenty of Room at the Bottom" at California Institute of Technology. In this lecture, he made hypothesis "Why can't we write the whole 24 volumes of Encyclopedia Britannica on the head of a pin?" and explained a vision of using machines for constructing the smaller machines and down to molecular level (Feynman 1960).

The United States National Nanotechnology Initiative (NNI) defines nanotechnology as the research and development efforts at atomic or molecular level to produce structures and systems that are appropriate in diverse aspects (Balzani 2005; Drexler and Peterson 1989). The history of nanotechnology lies in the fourth and fifth centuries BC, when traditional medical practitioners in India and China succeeded in making the gold colloids for therapeutic uses (Paul and Chugh 2011). In the middle-ages in Europe, Paracelsus applied colloidal gold for the treatment of mental disorders and syphilis (Dykman and Khlebtsov 2012). The nanotechnology is a branch of science that combines distinct fields, such as engineering, chemistry, physics, biology, medicine etc., with an ultimate aim of making things at atom scale. One nanometre (1 billionth of a metre) is a diameter of hydrogen atom.

5.2 History of Nanotechnology

The nanotechnology showed rapid development owing to its auspicious potential. The study of nanoparticles is not new, the concept of a "nanometre" was first proposed by Nobel Laureate Richard Zsigmondy in 1925 in chemistry. He coined the term nanometre clearly for characterizing and to measure the particles size like

gold colloids by a microscope. The nanomaterials history began instantly after the big bang, when nanoparticles and nanostructures were produced in the early meteorites. Later on, nature created many other nanoparticles as well as nanostructures. In the recent years, nanomaterials research attracted amazing interest from the scientists and engineers throughout the world. Before the era of nanotechnology, people were unknowingly coming across with different nanosized objects and using the nano level processes. Dyeing hair in black was common in the ancient Egypt, and for a long time, it was believed to be on the basis of plant products like henna (Tolochko 2009). On the other hand, research on the hair samples from the ancient Egyptian burial sites shows that hair has dyed with paste from lime, lead oxide and water (Walter et al. 2006). In the process of dyeing, galenite nanoparticles were formed. The ancient Egyptians were capable to create the dyeing paste react with sulphur (part of hair keratin) and make small lead sulphide nanoparticles, which provides even and steady dyeing. Perhaps the most well-known example for the ancient use of nanotechnology is the Lycurgus cup (ancient roman cup), which possesses the unusual optical properties as it changes its colour on the basis of the location of light source. In the natural light, the cup is green; however, when it is illuminated with a candle, it become red. The recent study showed that the cup contains 50–100 nm Au and Ag nanoparticles (Barber and Freestone 1990), which are responsible for the unusual colouring of the cup with effects of the plasmon excitation of electrons (Atwater 2007). In 1940s, silica nanoparticles were manufactured and sold in the United States of America and Germany as substitutes to carbon black for rubber reinforcement (Kumar and Kumbhat 2010). Moungi Bawendi of MIT invented a process for synthesis of nanocrystals (quantum dots) under controlled conditions in 1992 (Bawendi et al. 1992) paving the method for applications ranging from computing to biology to high-efficiency photovoltaics and lighting.

5.3 Nanoparticle Synthesis

Synthesis of nanoparticle using biological systems is rapid, viable and eco-friendly. The microbes such as bacteria, yeast, fungi and algae are preferably used for the synthesis of nanoparticles owing to rapid growth rate, simpler cultivation and their capacity to grow at atmospheric pH, temperature and pressure situations. Nanoparticles synthesis by bacteria, fungi, actinobacteria, microalgae and yeast has been investigated by several researchers for the production of most wanted NPs (Salem and Fouda 2021; Fariq et al. 2017; Castro et al. 2014; Jang et al. 2015; Singh et al. 2016a; Saravanan et al. 2018; Buszewski et al. 2018; Sanaeimehr et al. 2018). Microorganisms have the natural capability to grow in various habitats and are fast growing and simple to maintain. The use of microbes for the nanoparticle synthesis is unique and also has a scope for the improvement. Outbreak of COVID-19 introduced a huge challenge to the medical field. It is known that microbes, which include bacteria, actinomycetes, cyanobacteria, yeast and fungi, create inorganic nanoparticles like gold, calcium, silver (Ag), iron, silicon, lead and

gypsum. Due to their intrinsic potential, they make nanoparticles, which are intra or extracellularly in nature (Asmathunisha and Kathiresan 2013). The nanotechnology has immense potential to deliberately find solutions and to cope with such pandemic situations, as the NPs (Nanoparticles) can be deployed for diagnosis as well as treatment of the COVID-19 disease (Chan 2020).

5.4 Fungal-Mediated Synthesis of Nanoparticles

In general, fungi are eukaryotic microorganisms, which are the predominant decomposers. Over 1.5 million fungal species are believed to thrive and survive in diverse habitats on the earth; however, only 70,000 species were well taxonomically identified. Moreover, fungi are reported to make proteins in large quantities, they are essential in the large-scale production of nanoparticles. Few of the fungi, which are widely used for nanoparticles synthesis, include *Trichoderma viride* (Fayaz et al. 2010), *Trichoderma reesei* (Vahabi et al. 2011), *Phytophthora infestans* (Thirumurugan et al. 2009), *Aspergillus niger* (Jaidev and Narasimha 2010), *Aspergillus clavatus* (Verma et al. 2011), *Fusarium oxysporum* (Duran et al. 2005), *Verticillium* sp. (Mukherjee et al. 2001; Bharde et al. 2006), *Aspergillus flavus* (Jain et al. 2011), *Pleurotus sajor-caju* (Nithya and Ragunathan 2009) and *Penicillium* sp. (Hemath et al. 2010). The first scientific articles concerned with mycosynthesis of nanoparticles started in 2001 (Mukherjee et al. 2001). Various fungi can be grown easily because they require simple nutrients and ease of manipulation with produced biomass (Yadav et al. 2015). Fungi can also withstand a wider range of growth conditions when compared with other microorganisms and plants. Moreover, fungi can produce large quantities of proteins and they play a key role in the production of nanoparticles. In their normal environment, they generally gather their food from the decomposing organic matter. Furthermore, the synthesis of nanoparticles using fungi is cost-effective and does not require any definite conditions such as high pressure, temperature and energy (Singh et al. 2016b; Prasad 2016, 2017, 2019a, b). Synthesis of nanoparticles by fungi is more efficient and cost-effective than bacteria, as fungi have a higher affinity to accumulate metals. Furthermore, the biomass treatment and downstream processing of nanoparticles are easy in the fungal-based synthesis of nanoparticles. Thus, fungi have been extensively studied for different nanoparticles synthesis like silver, gold, etc. The fungi involved in the synthesis different metal nanoparticles are presented in Table 5.1. When compared with bacteria, fungi secrete a higher amount of bioactive materials, which made them more suitable for the large-scale production (Narayanan and Sakthivel 2010). The fungal cell components, such as cell wall, cell membrane, enzymes, proteins and other intracellular components, play a crucial role in nanoparticle synthesis. Many fungal strains are used as promising resources for the fabrication of nanoparticles, for example, *Fusarium*, *Verticillium, Aspergillus* and *Penicillium*. Several fungal species are potential candidates for the intra and extracellular production of metal nanoparticles. Fungi have high cell wall binding ability with metal ions and have a high potential to tolerate metal concentrations. Therefore,

Table 5.1 List of metal nanoparticles synthesized by fungi

S. No	Name of the fungi	Mode of synthesis	Nanoparticles	References
1.	*Aspergillus flavus*	Intracellular	Ag	Vala et al. (2014)
2.	*Penicillium citrinum*	Extracellular	Ag	Honary et al. (2013)
3.	*Fusarium oxysporum*, *Verticillium* sp.	Extracellular	Magnetite	Bharde et al. (2006)
4.	*Colletotrichum* sp.	Extracellular	Au	Shankar et al. (2003)
5.	*Penicillium fellutanum*	Extracellular	Ag	Kathiresan et al. (2009)
6.	*Agaricus bisporus*	Extracellular	Ag	Zhang et al. (2008)
7.	*Neurospora oryzae*	Intracellular/ extracellular	Ag	Saha et al. (2010)
8.	*Trichoderma harzianum*	Extracellular	Cu, Ag	Gajbhiye et al. (2009)
9.	*Aspergillus fumigatus*	Extracellular	ZnO	Raliya and Tarafdar (2013)
10.	*Volvariella volvacea*	Extracellular	Au-Ag	Thakkar et al. (2010)

fungi can yield a high number of nanoparticles when compared with bacterial cells (Singh et al. 2016). Filamentous fungi are used as a potential source for the synthesis of nanoparticles. The fungal mycelium has large surface area that secretes a high amount of proteins, which can participate directly in the production of nanoparticles (Mohanpuria et al. 2008; Aziz et al. 2016, 2019). The nanoparticles production by filamentous fungi is considered better because of their capacity to secrete enzymes, proteins and metabolites, simple scaling up and downstream handling, economic feasibility, increased surface area due to presence of mycelia (Fouda et al. 2018; Spagnoletti et al. 2019; Koch et al. 2023). The filamentous fungi show metal uptake capacities and can be easily cultured in huge quantity using solid substrate fermentation. Most of the fungal proteins hydrolyze the metal ions. Therefore, fungi are isolated easily and cultured. Fungi are the excellent protein secretors, resulting in a higher yield of nanoparticles, when compared with bacteria and other microorganisms (Mughal et al. 2021; Guilger-Casagrande and Lima 2019). Synthesis of nanoparticle by fungi is favoured over other microbial synthesis methods because of the resistance of fungal mycelial mesh to higher flow and agitation in the bioreactors (Saravanan et al. 2020). Chitin was the key ingredient in cell wall of the fungi, which is involved in heavy metal complexation, resulting in nanoparticles synthesis (Wang et al. 2018). The fungal-mediated nanoparticles are effectively used in wide range of scientific domains, which include medicines, agriculture, pharmaceuticals and electronics (Singhal et al. 2017; Rai and Prasad 2023). Thus, some of the evaluations focussed on the use of mycogenic nanoparticles against mycotoxin management, plant diseases, post-harvest antibiotics and plant pests, as well as animal pathogens. Moreover, fungal nanomaterials are more potential and

promise for the enhanced diagnostics, precision agriculture, biosensors, and targeted smart delivery systems. For instance, soil mycobiota influence the mobilization of zinc from ZnO (Zinc oxide) nanoparticles in soils and as a result zinc mobility and bioavailability. The common soil fungus, *Aspergillus niger*, was chosen as a test organism to evaluate the fungal interactions with ZnO nanoparticles. The *Aspergillus niger* strain has a significant effect on the stability of particulate forms of ZnO due to the acidification of its environment (Šebesta et al. 2020). Macrofungi-derived nanoparticles synthesized using mushroom species like *Agaricus bisporus*, *Lentinus* spp., *Pleurotus* spp. and *Ganoderma* spp. are widely recognized as they have strong nutritional, immune modulatory, antifungal, antibacterial, antiviral, antioxidant and anticancer activities (Bhardwaj et al. 2020). Biogenic synthesis on the basis of fungi has numerous benefits in terms of efficiency and generation of different metabolites under optimal conditions. Moreover, because fungi naturally produce a wide variety of antimicrobial compounds, using them as a capping agent of nanoparticles might result in a synergistic antimicrobial impact with metal nanoparticles against pathogenic microbes (Chauhan et al. 2022; Aziz et al. 2016).

5.5 Mechanism of Fungal-Mediated Biogenic Synthesis of Nanoparticles

Synthesis of nanoparticles by microorganisms has a great potential and enormous benefits to human, because they reduce the use of toxic chemicals and minimize the cost of production involved in synthesis. Amongst the biological agents, fungi have been used preferably for the production of various nanoparticles. Nanoparticles synthesis by fungi is called as mycosynthesis (Ingle et al. 2008, 2009; Rai et al. 2009; Yadav et al. 2015). The fungi are able to produce nanoparticles by both extracellular and intracellular ways (Khandel and Shahi 2018; Molnár et al. 2018). Extracellular microbial enzymes act as a reducing agent and play a key role in the production of metallic nanoparticles (Subbaiya et al. 2017). The intracellular synthesis is appropriate for the formation of composite films. However, in extracellular synthesis system, immobilization of metal ions in suitable carrier or support is achieved (Afshar and Sedaghat 2016). The benefit of extracellular production of nanoscale material is that it is free of contaminants like intracellular proteins and not requires ultrasonic treatment with detergents. The nanoparticles synthesized extracellularly were stabilized by using proteins and enzymes secreted by the fungal biomass. As far as fungal synthesis is concerned, it is proposed that extracellular metabolites include different enzymes secreted by fungi for their survival when exposed to the diverse environmental stresses that are typically responsible for the reduction of metal ions to metallic solid nanoparticles by the catalytic effect (Yadav et al. 2015; Elamawi et al. 2018). The protein isolated from fungal biomass was successfully used for the synthesis of metal nanoparticles with cationic proteins nanocrystalline zirconium at room temperature. *Aspergillus* was the most studied genus for the mycosynthesis of nanoparticles (Hulkoti and Taranath 2014). For example, *Aspergillus fumigatus* was reported for the extracellular production of

silver nanoparticles (AgNPs) (Bhainsa and D'Souza 2006). Gade et al. (2008) produced silver nanoparticles from *Aspergillus niger* isolated from the soil. Furthermore, hydrogenases, flavin adenine dinucleotide (FAD)-dependent glutathione reductase, also play a role in the biological synthesis of metal nanoparticles through fungi. On the other hand, studies have revealed that metal reduction involves an electron shuttle in the reductase enzyme system proposed by their possible mechanism action of nitrate reductase, electron shuttle quinones or both. It has been reported that mainly nitrate and α-NADPH-dependent reductases were responsible for the synthesis of nanoparticle in bacteria as well as fungi. Mukherjee et al. (2001) reported that fungal cell is a site for precipitation of heavy metals forming nanoparticles, where Ag nanoparticles were synthesized by the fungus *Verticillium* sp. Metuku et al. (2013) studied that by extracellular biomineral formation of Ag ions, *Schizophyllum radiatum* (white rot fungus) can produce well-dispersed stable nanoparticles (size 10–40 nm). These nanoparticles have strong antibacterial action against various Gram-negative and Gram-positive bacteria. In the production of metal nanoparticles by fungus, the fungal mycelium is exposed to the metal salt solution. That prompts the fungus to produce enzymes as well as metabolites for its own survival. In this process, the toxic metal ions are reduced nontoxic metallic solid nanoparticles through the catalytic effect of the extracellular enzyme and the metabolites of fungus.

Fungi produce nanoparticles through a range of bioreduction and other mechanisms involving proteins and extracellular or intracellular enzymes. Many fungi produce extracellular enzymes that act as reducing agents in the formation of nanoparticles. The examples for extracellular enzymes are acetyl xylan esterase, D, glucosidase, cellobiohydrolase and beta-glucosidase (Ovais et al. 2018). The nitrate reductase, an nicotinamide adenine dinucleotide + hydrogen (NADH)-dependent reductase secreted by *Fusarium oxysporum*, is involved in the bioreduction (M^+ ions to M^0) and extracellular production of metal nanoparticles, such as silver (Ag) and cadmium selenide (CdSe) nanoparticles (Kumar et al. 2007a, b). Besides extracellular mechanisms, few mechanisms were also proposed for the intracellular mycosynthesis of metal nanoparticles. During intracellular fungal synthesis, metal nanoparticles usually formed below the cell surface due to the reduction of metal ions by enzymes present cell membrane. In general, two-step mechanisms were proposed for the intracellular mycosynthesis of nanoparticles. In the first step, an aqueous metal ion attached to the surface of fungal cell by the electrostatic interaction between lysine residues and metal ions (Riddin et al. 2006). In second step, actual synthesis of nanoparticles took place with enzymatic reduction of metal ions, which leads to the aggregation and creation of nanoparticles. It also demonstrated that cell wall sugars play a major role in the reduction of metal ions to the metal nanoparticles (Mukherjee et al. 2001). Both the above-mentioned mechanisms proposed for the extracellular and intracellular mycosynthesis of few metals.

5.6 Applications of Mycogenic Nanoparticles

Mycogenesis of nanoparticle is an emerging and new-fangled field of nano biotechnology because of the wide spectrum diversity and availability of fungi (Rai et al. 2012). The nanoparticles have numerous applications in various fields such as medicine, drug designing, drug delivery, environment, textiles, cosmetics, food industry, optics and optical devices (Suman et al. 2010). Synthesis of nanoparticles by microorganisms has a great potential and enormous benefits to human, because they reduce the use of toxic chemicals and minimize the production cost.

5.7 In Cancer Therapy

The cancer has become one of the most life-threatening issues all over the world. According to a World Health Organization (WHO) statistic, each year, more than 6,000,000 deaths from and 10,000,000 new cases of cancer are reported (Steward and Kleihues 2003). Cancer is characterized by uncontrolled cell growth and attainment of metastatic properties. In most cases, the activation of oncogenes or deactivation of tumour suppressor genes lead to an uncontrolled cell cycle progression and inactivation of apoptosis. Cancer nano-medicine is a fast and advancing field, which employed nanoparticles to diagnose and treat the cancer disease (Rhodes and Green 2018). Nanoparticles are able to deliver normally insoluble drugs to local and distant tumour sites in a better way, as a result reducing the systemic side effects that are generally linked with conventional drug therapies. Breast cancer is most frequently diagnosed in women globally, with 2.26 million new cases in 2020 (Ferlay et al. 2020). In the United States (US), breast cancer alone is expected to account for 29% of all new cancers in women (De Santis et al. 2015).

The nanoparticles had proven to be particularly helpful in diverse medical applications, from diagnosis to cancer therapy (Horikoshi and Serpone 2013). The nanoparticles size is almost similar to the most of the biological structures and molecules. Hence, they confer functional properties for both in vivo and in vitro cancer research (Almeida et al. 2014). Synthesis of fungal-based tellurium nanoparticles was reported by Vahidi et al. (2020). These nanoparticles show cytotoxicity against breast cancer cell line MCF-7. Furthermore, these tellurium nanoparticles showed important antioxidant potential. *Penicillium oxalicum* and *Fusarium hainanense* derived silver nanoparticles exhibiting antimicrobial, larvicidal, antioxidant and anticancer potency (Thakor et al. 2022). Gold (Au) nanoparticles (40–45 nm) were synthesized *using the Fusarium solani* isolated from the plant *Chonemorpha fragrans*. Their anticancer efficiency was tested on cervical cancer cells (He La) and against human breast cancer cells (MCF-7), and the obtained results demonstrate the dose-dependent toxicity and nanoparticles induced cell apoptosis. The fungal-based production of nanoparticles by *Penicillium brevicompactum* (MTCC-1999) showed anticancer activity against the MCF-7 breast cancer cell line with IC50 values of 70 μg/mL and 50 μg/mL after 24 h and 48 h, respectively, and also inhibited the growth of numerous pathogenic bacteria

(Majeed et al. 2016). Furthermore, *Penicillium italicum*-mediated synthesized silver nanoparticles showed potential antimicrobial activity and cytotoxic effects against human breast cancer cells (MCF-7) (Taha et al. 2019). Several reports showed that mycosynthesized silver (Ag) nanoparticles have antibacterial, antifungal, antioxidant, larvicidal, anticancer and other properties, and the same nanoparticles showed a wide variety of biological activities. For instance, silver nanospheres obtained by using *Flammulina velutipes* had bactericidal, fungicidal, anticancer, antioxidant anti-Alzheimer and antidiabetic activities, and good biocompatibility against the human red blood cells (Faisal et al. 2021).

5.8 In Agriculture

The agricultural production is reduced globally every year due to plant diseases and thus, millions of dollars have been invested to control plant diseases. Different natural and artificial methods have been used for the protection of plants from these diseases. Amongst the methods for disease control, the use of pesticides is the most prevalent. But the use of nanoparticles could provide numerous advantages to agriculture as well as horticulture. Nanoparticles play a crucial role in the development of crop and improving the nutritive benefits in the agricultural sector (Osherov et al. 2023). Nanoparticles have been used as components of novel fertilizers in the agricultural field (Elmer and White 2016), herbicides (Maruyama et al. 2016), substances for crop protection (Worrall et al. 2018) and preparations for prolonging cut flower durability (He et al. 2018). In recent decades, the search for alternatives for disease control in agriculture has been gaining importance because some of the fungal pathogens increase antifungal resistance and few synthetic chemicals were banned due to their pollutive and toxic nature (Card et al. 2016). The fungal-mediated control of pathogenic fungi is eco-friendly, biocompatible and cost-effective approach to managing the phytopathogens (Abd-Elsalam et al. 2021; Dhiman et al. 2022, 2023; Gaba et al. 2023; Shelke et al. 2023). The use of fungal-mediated green chemistry methods for nanoparticles synthesis improves the yield potential as lowering the input costs (Singh et al. 2016). Due to their high processing capacity, large surface area recovery and outstanding mycelial growth, fungi are efficient as well as easy biosynthetic scaling agents (Balakumaran et al. 2016). The mycogenic nanoparticles synthesized by useful fungi are a potential environmentally acceptable approach for large-scale production of different nanoparticles. One of the important plant species in agriculture is *Trichoderma harzianum*, which serves as a biological control agent against phytopathogens. *Trichoderma* is the most widely used biocontrol agent, which shows characteristic features like pathogen antagonism, stimulation of systemic resistance in the host, nutrition competition and plant growth enhancement (Ahluwalia et al. 2014). One of the main advantages of biosynthesis of metal nanoparticles is their immense role in the protection of the environment, which is also the ultimate target of other green technologies (Ottoni et al. 2017; Omidi et al. 2018). The silver is known as a health additive in the traditional ayurvedic medicine. It has been known as effective antimicrobial agent

since ancient times (Klasen 2000). The biosynthesized silver nanoparticles thus serve as an important source of different therapeutic agents primarily as antimicrobial agents. The use of silver nanoparticles emerged as promising approach for overcoming the antibiotic resistance of microbes. *Trichoderma harzianum* is used for the stabilization of green synthesis of biogenic silver nanoparticles. *Trichoderma harzianum* cell filtrate is used to produce biogenic silver nanoparticles in an easy, green and eco-friendly approach without the use of any toxic-reducing, -capping or -dispersion agents (Ahluwalia et al. 2014; Rai and Prasad 2023). As this fungus has a range of qualities that aid with agricultural commodities, *Trichoderma*-based products contribute to more than half of the overall worldwide biopesticide industry, employed for improving the growth of plant, efficiency of nutrient use as well as physiological response to biotic and abiotic stresses (Meher et al. 2020; Prasad and Rai 2023). The application of green silver nanoparticles as antifungal agents is environmentally benign resource, cost-effective and alternative to the fungicides (Hirpara and Gajera 2020; Elamawi and El-Shafey 2013). The silver nanoparticles (AgNPs) produced from fungi are applied in the agriculture and show good potential against plant pathogenic insects, bacteria, fungi and viruses. Silver nanoparticles prepared by *Fusarium solani* from wheat are very effective against different pathogens of wheat, maize and barley (Abd El-Aziz et al. 2015). Silver nanoparticles synthesized from the fungus *Aspergillus versicolor* exhibit concentration-dependent activity against *Sclerotinia sclerotiorum* and *Botrytis cinerea* on a strawberry plant (Elgorban et al. 2016a, b). Fungus *Epicoccum nigrum* is used to synthesize silver nanoparticles against *Candida albicans* and *Fusarium solani* (Qian et al. 2013). Potential roles of fungus *Guignardia mangiferae*-derived silver nanoparticles were tested to manage plant pathogens *Colletotrichum* sp., *Curvularia lunata* and *Rhizoctonia solani* (Balakumaran et al. 2015). Raliya et al. (2016) produced ZnO nanoparticles using *Aspergillus fumigatus*, and these nanoparticles are applied to soil for enhancing the phosphorous uptake by mung bean (*Vigna radiata*).

5.9 In Drug Delivery Systems

There have been enormous developments in the sector of delivery systems to provide therapeutic agents or natural-based active compounds to its target location for the treatment of different aliments (Obeid et al. 2017; Miele et al. 2012). In the recent times, the number of drug delivery systems was successfully employed, but there are still certain challenges that need to be addressed and the advanced technology is essential for the successful delivery of drugs to its target sites. Therefore, the nano-based drug delivery systems are currently being studied, which facilitate the advancement drug delivery system. There are two ways through which nanostructures deliver drugs: passive as well as self-delivery. In the former, drugs are incorporated in the inner cavity of the structure mainly by the hydrophobic effect. When the nanostructure materials are targeted to particular sites, the proposed amount of drug is released due to the low content of drugs, which encapsulated in a hydrophobic environment (Lu et al. 2016). On the other hand, in the latter, the

drugs intended for the release are directly conjugated with carrier nanostructure material for easy delivery. In this approach, the timing of release is important as the drug will not reach the target site and it quickly detaches from the carrier, and on the contrary, its bioactivity and efficiency decreased if it is released from its nano-carrier system at right time (Lu et al. 2016). The multi-shaped gold nanoparticles derived from the fungus *Helminthosporium solani* were conjugated to anticancer drug doxorubicin. Conjugated drug was readily taken into the HEK293 cells with cytotoxicity when compared with doxorubicin (Kumar et al. 2008). Khan et al. (2014) that gadolinium oxide nanoparticle produced by thermophilic fungus *Humicola* sp. was bioconjugated with anti-cancer drug taxol to increase its efficacy against anti-tumour cells using these nanoparticles as the drug delivery applications. Likewise, *Humicola* derived gold nanoparticles conjugated with doxorubicin were used in targeted drug delivery for the treatment hepatic cancer (Syed et al. 2013).

5.10 In Cosmetics

The term cosmetics derived from Greek word Kosmetikos means "have the power to arrange, skilled in the decoration", to give "kosmein", to adorn and "kosmos", order, harmony (Butler 1993). The United States Federal Food, Drug, and Cosmetic Act describes cosmetics as articles intended to apply to human body by being rubbed, poured, sprayed or sprinkled for beautifying, cleansing, promoting the attractiveness or changing the appearance (U.S. Food and Drug Administration 2016; Singh et al. 2020). The nanotechnology is recognized as one of the developing technologies and is extensively studied in the area of cosmetics as well as cosmeceuticals (Raj et al. 2012; Kaul et al. 2018). Incorporation of the nanotechnology lead to the advancements in the cosmetic science, resulting in increased consumer demand globally (Ajazzuddin et al. 2015). More than last 30 years, the nano-based ingredients are being used in the cosmetic industry (Pastrana et al. 2018; Revia et al. 2019; Carrouel et al. 2020). The nanomaterial-based cosmetics have a few unique advantages in comparison compared with microscale cosmetics. The application of nanomaterials by the cosmetic industry aims for long-lasting effects as well as increased stability. The high surface area of nanomaterials allows for more effective transport of ingredients by the skin (Ahmad et al. 2018). The nanotechnology is currently utilized in beauty care products and dermatological items, such as cleansers, against wrinkle creams, lipsticks, aromas, toothpaste, lotions, hair care items, sunscreens, skin-cleaning agents and nail care bosom cream. The silver nanoparticles are currently usually utilized as additives due to their antimicrobial properties. These nanoparticles are usually utilized in beauty care products like antiperspirants, face packs and against maturing creams. The silver nanoparticles are currently in use as additives in toothpaste and shampoos because of their antibacterial properties. *Penicillium* is an endophytic fungus, which is used to synthesize silver nanoparticles. The phytochemicals identified in the *Penicillium* extracts include tannins, terpenoids, saponins and flavonoids. These substances can act as reducing and capping agents in the conversion of silver particles into

nanoparticles (Govindappa et al. 2016). Furthermore, it has been reported that the capping agents, such as the amide and carbonyl groups detected in silver nanoparticles of 10–60 nm biosynthesized from *Fusarium semitectum*, are stable for 6–8 weeks. The capping agents are essential to avoid the agglomeration of nanoparticles and they also provide stability to the product (Rai et al. 2009). These stable properties contribute to the appearance of the cosmetic products and also improve the sensory properties of product, because they support the product's homogeneous appearance and avoid sedimentation of the product for more than one year (Kokura et al. 2010).

5.11 Conclusion

The fungi are promising biological agents for green synthesis of the nanoparticles. Throughout the world, today, several species of fungi are of great importance in nano-biotechnology because of the safe, amenable, eco-friendly and important nanoparticles they produced. Many fungal species are able to form nanoparticles, which predominantly belong to the ascomycota and basidiomycota. The biological synthesis of nanoparticles is safe and inexpensive. The synthesis of metallic nanoparticles by microorganisms had shown to possess a strong potential with different applications. The utilization of fungi to fabricate the nanoparticles had greatly considered sequel to several advantages, including easy handling as well as downstream processing. The fungal nano-biotechnology has several applications in the agricultural, medical and industrial sectors for goods and services improvement and delivery to mankind. In the agriculture, it has found applications in the management of plant diseases. Currently, the most interesting is the so-called biogenic synthesis, which reduces the application of toxic reagents and extends the pharmacological activity of NPs. Considering the green chemistry requirements, the biogenic synthesis of NPs belongs to future trends.

References

Abd El-Aziz A, Al-Othman M, Mahmoud M, Metwaly H (2015) Biosynthesis of silver nanoparticles using *Fusarium solani* and its impact on grain borne fungi. Dig J Nanomater Biostruct 10:655–662

Abd-Elsalam KA, Periakaruppan R, Rajeshkumar S (2021) Agri-waste and microbes for production of sustainable nanomaterials. Elsevier, Amsterdam. 772 p

Afshar P, Sedaghat S (2016) Bio-synthesis of silver nanoparticles using water extracts of Saturejahortensis L and evaluation of the antibacterial properties. Curr Nanosci 12(1):90–93

Ahluwalia V, Kumar J, Sisodia R, Shakil NA, Walia S (2014) Green synthesis of silver nanoparticles by *Trichoderma harzianum* and their bio-efficacy evaluation against *Staphylococcus aureus* and *Klebsiella pneumonia*. Ind Crop Prod 55:202–206

Ahmad U, Ahmad Z, Khan AA, Akhtar J, Singh SP, Ahmad FJ (2018) Strategies in development and delivery of nanotechnology based cosmetic products. Drug Res 68:545–552

Ajazzuddin M, Jeswani G, Jha A (2015) Nanocosmetics: past, present and future trends. Recent Pat Nanomed 5:3–11

Almeida JP, Lin AY, Langsner RJ, Eckels P, Foster AE, Drezek RA (2014) In vivo immune cell distribution of gold nanoparticles in naive and tumor bearing mice. Small 10:812–819

Asmathunisha N, Kathiresan K (2013) A review on biosynthesis of nanoparticles by marine organisms. Colloids Surf B: Biointerfaces 103:283–287

Atwater HA (2007) The promise of plasmonics. Sci Am 296(4):56–63

Aziz N, Pandey R, Barman I, Prasad R (2016) Leveraging the attributes of *Mucor hiemalis*-derived silver nanoparticles for a synergistic broad-spectrum antimicrobial platform. Front Microbiol 7:1984. https://doi.org/10.3389/fmicb.2016.01984

Aziz N, Faraz M, Sherwani MA, Fatma T, Prasad R (2019) Illuminating the anticancerous efficacy of a new fungal chassis for silver nanoparticle synthesis. Front Chem 7:65. https://doi.org/10.3389/fchem.2019.00065

Balakumaran MD, Ramachandran R, Kalaichelvan PT (2015) Exploitation of endophytic fungus, Guignardia mangiferae for extracellular synthesis of silver nanoparticles and their in vitro biological activities. Microbiol Res 178:9–17

Balakumaran MD, Ramachandran R, Balashanmugam P, Mukeshkumar DJ, Kalaichelvan PT (2016) Mycosynthesis of silver and gold nanoparticles: optimization, characterization and antimicrobial activity against human pathogens. Microbiol Res 182:8–20

Balzani V (2005) Nanoscience and nanotechnology: a personal view of chemist. Small 1(3): 278–283

Barber DJ, Freestone IC (1990) An investigation of the origin of the colour of the Lycurgus Cup by analytical transmission electron microscopy. Archaeometry 32(1):33–45

Barhoum A, El-Maghrabi HH, Nada AA, Sayegh S, Roualdes S, Renard A, Iatsunskyi I, Coy E, Bechelany M (2021) Simultaneous hydrogen and oxygen evolution reactions using free-standing nitrogen-doped-carbon–Co/CoOx nanofiber electrodes decorated with palladium nanoparticles. J Mater Chem A 9:17724–17739

Bawendi M, Carroll P, Wilson W, Brus L (1992) Luminescence properties of CdSe quantum crystallites: resonance between interior and surface localized states. J Chem Phys 96(2): 946–954

Bhainsa KC, D'Souza SF (2006) Extracellular biosynthesis of silver nanoparticles using the fungus *Aspergillus fumigatus*. Colloids Surf B: Biointerfaces 47:160–164

Bharde A, Rautaray D, Bansal V et al (2006) Extracellular biosynthesis of magnetite using fungi. Small 2(1):135–141

Bhardwaj K, Sharma A, Tejwan N, Bhardwaj S, Bhardwaj P, Nepovimova E, Shami A, Kalia A, Kumar A, Abd-Elsalam KA (2020) Pleurotus macrofungi-assisted nanoparticle synthesis and its potential applications: a review. J Fungi 6:351

Buszewski B, Railean-Plugaru V, Pomastowski P, Rafínska K, Szultka-Mlynska M, Golinska P, Wypij M, Laskowski D, Dahm H (2018) Antimicrobial activity of biosilver nanoparticles produced by a novel Streptacidiphilus durhamensis strain. J Microbiol Immunol Infect 51:45–54

Butler H (1993) Microbiological control of cosmetics. In: Butler H (ed) Poucher's perfumes, cosmetics and soaps, vol 3. Springer, Dordrecht, pp 572–606

Card S, Johnson L, Teasdale S, Caradus J (2016) Deciphering endophyte behaviour: the link between endophyte biology and efficacious biological control agents. FEMS Microbiol Ecol 92:114

Carrouel F, Viennot S, Ottolenghi L, Gaillard C, Bourgeois D (2020) Nanoparticles as anti-microbial, anti-inflammatory, and remineralizing agents in oral care cosmetics: a review of the current situation. Nanomaterials 10:140

Castro L, Blázquez ML, González FG, Ballester A (2014) Mechanism and applications of metal nanoparticles prepared by bio-mediated process. Rev Adv Sci Eng 3:199–216

Chan WCW (2020) Nano research for COVID-19. ACS Nano 14:3719–3720

Chauhan A, Anand J, Parkash V, Rai N (2022) Biogenic synthesis: a sustainable approach for nanoparticles synthesis mediated by fungi. Inorg Nano-Metal Chem 53:460–473

De Santis CE, Fedewa SA, Sauer AG, Kramer JL, Smith RA, Jemal A (2015) Breast cancer statistics, 2015: convergence of incidence rates between black and white women. CA Cancer J Clin 66:31–42

Dhiman S, Varma A, Prasad R, Goel A (2022) Mechanistic insight of the antifungal potential of green synthesized zinc oxide nanoparticles against *Alternaria brassicae*. J Nanomater 2022:7138843, 13. https://doi.org/10.1155/2022/7138843

Dhiman S, Varma A, Rao M, Prasad R, Goel A (2023) Deciphering the fertilizing and disease suppression potential of phytofabricated zinc oxide nanoparticles on *Brassica juncea*. Environ Res. https://doi.org/10.1016/j.envres.2023.116276

Drexler KE, Peterson C (1989) Nanotechnology and enabling technologies. Foresight Briefing

Duran N, Marcato PD, Alves OL, DeSouza G, Esposito E (2005) Mechanistic aspects of biosynthesis of silver nanoparticles by several *Fusarium oxysporum* strains. J Nanobiotechnol 3:8

Dykman L, Khlebtsov N (2012) Gold nanoparticles in biomedical applications: recent advances and perspectives. Chem Soc Rev 41(6):2256–2282

Elamawi R, El-Shafey RA (2013) Inhibition effects of silver nanoparticles against rice blast disease caused by Magnaporthe grisea. Egypt J Agric Res 91:1271–1283

Elamawi RM, Al-Harbi RE, Hendi AA (2018) Biosynthesis and characterization of silver nanoparticles using *Trichoderma longibrachiatum* and their effect on phytopathogenic fungi. Egypt J Biol Pest Contr 28:28

Elgorban A, Aref S, Seham S, Elhindi K, Bahkali A, Sayed S (2016a) Extracellular synthesis of silver nanoparticles using aspergillus versicolor and evaluation of their activity on plant pathogenic fungi. Mycosphere 7:844–852

Elgorban AM, Al-Rahmah AN, Sayed SR, Hirad A, Mostafa AAF, Bahkali AH (2016b) Antimicrobial activity and green synthesis of silver nanoparticles using *Trichoderma viride*. Biotechnol Equip 30:299–304

Elmer WH, White JC (2016) The use of metallic oxide nanoparticles to enhance growth of tomatoes and eggplants in disease infested soil or soilless medium. Environ Sci Nano 3:1072–1079

Faisal S, Khan MA, Jan H, Shah SA, Abdullah Shah S, Rizwan M, Wajidullah Akbar MT (2021) Redaina edible mushroom (Flammulina velutipes) as biosource for silver nanoparticles: from synthesis to diverse biomedical and environmental applications. Nanotechnology 32:065101

Fariq A, Khan T, Yasmin A (2017) Microbial synthesis of nanoparticles and their potential applications in biomedicine. J Appl Biomed 15:241–248

Fayaz AM, Balaji K, Girilal M, Yadav R, Kalaichelvan PT, Venketesan R (2010) Biogenic synthesis of silver nanoparticles and their synergistic effect with antibiotics: a study against gram-positive and gram-negative bacteria. Nanomedicine 6(1):103

Ferlay J, Ervik M, Lam F, Colombet M, Mery L, Piñeros M, Znaor A, Soerjomataram I, Bray F (2020) Global cancer observatory: cancer today. International Agency for Research on Cancer, Lyon. https://gco.iarc.fr/today. Accessed 9 Jul 2021

Feynman RP (1960) There's plenty of room at the bottom. Eng Sci 23:22–36

Filipponi L, Nicolau DV (2006) Cell patterning. Wiley encyclopedia of biomedical engineering. John Wiley and Sons, New York, NY

Fouda A, Saad E, Salem SS, Shaheen TI (2018) In-vitro cytotoxicity, antibacterial, and UV protection properties of the biosynthesized zinc oxide nanoparticles for medical textile applications. Microb Pathog 125:252–261

Gaba S, Prasad L, Varma A, Rai AK, Prasad R, Goel A (2023) Leveraging of mycogenic copper oxide nanostructures for disease management of Alternaria blight of *Brassica juncea*. Green Processing Synth 12:20230015. https://doi.org/10.1515/gps-2023-0015

Gade AK, Bonde P, Ingle AP, Marcato PD, Duran N, Rai MK (2008) Exploitation of Aspergillus niger for synthesis of silver nanoparticles. J Biobased Mater Bioenergy 2(3):243–247

Gajbhiye MB, Kesharwani JG, Ingle AP, Gade AK, Rai MK (2009) Fungus mediated synthesis of silver nanoparticles and its activity against pathogenic fungi in combination of fluconazole. Nanomedicine: NBM 5:282–286

Gaur M, Misra C, Yadav AB, Swaroop S, Maolmhuaidh F, Bechelany M, Barhoum A (2021) Biomedical applications of carbon nanomaterials: fullerenes, quantum dots, nanotubes, nanofibers, and graphene. Materials 14:5978

Govindappa M, Farheen H, Chandrappa CP, Channabasava Rai RV, Raghavendra VB (2016) Mycosynthesis of silver nanoparticles using extract of endophytic fungi, Penicillium species of Glycosmis mauritiana, and its antioxidant, antimicrobial, anti-inflammatory and tyrokinase inhibitory activity. Adv Nat Sci Nanosci Nanotechnol 7:035014

Guilger-Casagrande M, Lima RD (2019) Synthesis of silver nanoparticles mediated by fungi: a review. Front Bioeng Biotechnol 7:287

He Y, Qian L, Liu X, Hu R, Huang M, Liu Y, Chen G, Losic D, Zhu H (2018) Graphene oxide as an antimicrobial agent can extend the vase life of cut flowers. Nano Res 11:6010–6022

Hemath KS, Naveen G, Kumar L, Karthik KVB, Rao E (2010) Extracellular biosynthesis of silver nanoparticles using the filamentous fungus *Penicillium* sp. Arch App Sci Res 2(6):161

Hirpara DG, Gajera HP (2020) Green Synthesis and Antifungal Mechanism of Silver nanoparticles derived from Chitin-induced Exometabolites of *Trichoderma interfusant*. Appl Organomet Chem 34:5407

Honary S, Barabadi H, Gharaei-Fatahabad E, Naghibi F (2013) Green synthesis of silver nanoparticles induced by the fungus *Penicillium citrinum*. Trop J Pharm Res 12:7–11

Horikoshi S, Serpone N (2013) Introduction to nanoparticles. In: Horikoshi S, Serpone N (eds) Microwaves in nanoparticle synthesis: fundamentals and applications. Wiley-VCH Verlag GmbH and Co. KGaA, Weinheim, pp 1–24

Hulkoti NI, Taranath TC (2014) Biosynthesis of nanoparticles using microbes - a review. Colloids Surf B: Biointerfaces 121:474–483

Ingle A, Gade A, Pierrat S, Sonnichsen C, Rai M (2008) Mycosynthesis of silver nanoparticles using the fungus *Fusarium acuminatum* and its activity against some human pathogenic bacteria. Curr Nanosci 4:141–144

Ingle A, Rai M, Gade A, Bawaskar M (2009) *Fusarium solani*: a novel biological agent for the extracellular synthesis of silver nanoparticles. J Nanopart Res 11:2079–2085

Jaidev LR, Narasimha G (2010) Fungal mediated biosynthesis of silver nanoparticles, characterization and antimicrobial activity. Colloids Surf B: Biointerfaces 81(2):430

Jain N, Bhargava A, Majumdar S, Tarafdar JC, Panwar J (2011) Extracellular biosynthesis and characterization of silver nanoparticlesusing *Aspergillus flavus* NJP08: a mechanism perspective. Nanoscale 3:635

Jang HD, Kim SK, Chang H, Choi JH, Cho BG, Jo EH, Choi JW, Huang J (2015) Three-dimensional crumpled graphenebased platinum–gold alloy nanoparticle composites as superior electrocatalysts for direct methanol fuel cells. Carbon 93:869–877

Jeevanandam J, Barhoum A, Chan YS, Dufresne A, Danquah MK (2018) Review on nanoparticles and nanostructured materials: history, sources, toxicity and regulations. Beilstein J Nanotechnol 9:1050–1074

Kathiresan K, Manivannan S, Nabeel MA, Dhivya B (2009) Studies on silver nanoparticles synthesized by a marine fungus, *Penicillium fellutanum* isolated from coastal mangrove sediment. Colloids Surf B: Biointerfaces 71:1133–1137

Kaul S, Gulati N, Verma D, Mukherjee S, Nagaich U (2018) Role of nanotechnology in cosmeceuticals: a review of recent advances. J Pharm 2018:3420204

Khan SA, Gambhir S, Ahmad A (2014) Extracellular biosynthesis of gadolinium oxide (Gd2O3) nanoparticles, their biodistribution and bioconjugation with the chemically modified anticancer drug taxol. Beilstein J Nanotechnol 5:249–257

Khandel P, Shahi SK (2018) Mycogenic nanoparticles and their bioprospective applications: current status and future challenges. J Nanostruct Chem 8(4):369–391

Klasen HJ (2000) A historical review of the use of silver in the treatment of burns II. Renewed interest for silver. Burns 26:131–138

Koch N, Sonowal S, Prasad R (2023) Elucidate the smart tailored biogenic nanoparticles and their applications in remediation. Biotechnol Genet Eng Rev. https://doi.org/10.1080/02648725.2023.2219942

Kokura S, Handa O, Takagi T, Ishikawa T, Naito Y, Yoshikawa T (2010) Silver nanoparticles as a safe preservative for use in cosmetics. Nanomed Nanotechnol Biol Med 6:570–574

Kumar N, Kumbhat S (2010) Essentials in nanoscience and nanotechnology, 1st edn. Wiley, Hoboken, NJ

Kumar SA, Ansary AA, Ahmad A, Khan MI (2007a) Extracellular biosynthesis of CdSe quantum dots by the fungus, *Fusarium Oxysporum*. J Biomed Nanotechnol 3:190–194

Kumar SA, Abyaneh MK, Gosavi SW, Kulkarni SK, Pasricha R, Ahmad A, Khan MI (2007b) Nitrate reductase-mediated synthesis of silver nanoparticles from AgNO3. Biotechno Lett 29:439–445

Kumar SA, Peter YA, Nadeau JL (2008) Facile biosynthesis, separation and conjugation of gold nanoparticles to doxorubicin. Nanotechnology 19:495–101

Lombardo D, Kiselev MA, Caccamo MT (2019) Smart nanoparticles for drug delivery application: development of versatile nanocarrier platforms in biotechnology and nanomedicine. J Nanomater 12:1–26

Lu H, Wang J, Wang T, Zhong J, Bao Y, Hao H (2016) Recent progress on nano-structures for drug delivery applications. J Nanomater 2016:5762431

Majeed S, Abdullah MS, Nanda A, Ansari MT (2016) In vitro study of the antibacterial and anticancer activities of silver nanoparticles synthesized from *Penicillium brevicompactum* (MTCC-1999). J Taibah Univ Sci 10:614–620

Maruyama CR, Guilger M, Pascoli M, Bileshy-José N, Abhilash PC, Fraceto LF, De Lima R (2016) Nanoparticles based on chitosan as carriers for the combined herbicides Imazapic and Imazapyr. Sci Rep 6:19768

Meher J, Rajput RS, Bajpai R, Teli B, Sarma BK (2020) *Trichoderma*: a globally dominant commercial biofungicide. In: Soil biology. Springer, Cham, pp 195–208

Metuku RP, Pabba S, Burra S, Hima Bindu N et al (2013) Biosynthesis of silver nanoparticles from Schizophyllum radiatum HE 863742.1: their characterization and antimicrobial activity. 3 Biotech 4:227–234

Miele E, Spinelli GP, Miele E, Di Fabrizio E, Ferretti E, Tomao S, Gulino A (2012) Nanoparticle-based delivery of small interfering RNA: challenges for cancer therapy. Int J Nanomedicine 7:3637

Mohanpuria P, Rana NK, Yadav SK (2008) Biosynthesis of nanoparticles technological concepts and future applications. J Nanopart Res 10(3):507–517

Molnár Z, Bódai V, Szakacs G (2018) Green synthesis of gold nanoparticles by Thermophilic flamentous fungi. Sci Rep 8:3943

Mughal B, Zaidi SZJ, Zhang X, Hassan SU, Mukherjee P, Ahmad A, Mandal D, Senapati S, Sainkar SR, Khan MI, Ramani RP (2021) Biogenic nanoparticles: synthesis, characterisation and applications. Appl Sci 11(6):2598

Mukherjee P, Ahmad A, Mandal D, Senapati S, Sainkar SR, Khan MI, Ramani R, Pasricha R, Ajayakumar PV, Alam M (2001) Bioreduction of AuCl4–Ions by the fungus, Verticillium sp. and surface trapping of the gold nanoparticles formed. Angew Chem Int Ed 40:3585–3588

Narayanan KB, Sakthivel N (2010) Biological synthesis of metal nanoparticles by microbes. Adv Colloid Interf Sci 156:1–13

Nithya R, Ragunathan R (2009) Synthesis of silver nanoparticle using Pleurotus sajor caju and its antimicrobial study. Digest J Nanomater Biostruct 4(4):623

Obeid MA, Al Qaraghuli MM, Alsaadi M, Alzahrani AR, Niwasabutra K, Ferro VA (2017) Delivering natural products and biotherapeutics to improve drug efficacy. Ther Deliv 8:947–956

Omidi S, Sedaghat S, Tahvildari K, Derakhshi P, Motiee F (2018) Biosynthesis of silver nanocomposite with Tarragon leaf extract and assessment of antibacterial activity. J Nanostruct Chem 8(2):171–178

Osherov A, Prasad R, Chrzanowski W, New EJ, Brazaca L, Sadik O, Haynes CL, Maine E (2023) Responsible nanotechnology for a sustainable future. One Earth 6(7):763–766. https://doi.org/10.1016/j.oneear.2023.06.010

Ottoni CA, Simões MF, Fernandes S, Dos Santos JG, Da Silva ES, de Souza RFB, Maiorano AE (2017) Screening of flamentous fungi for antimicrobial silver nanoparticles synthesis. AMB Express 7(1):31

Ovais M, Khalil AT, Ayaz M, Ahmad I, Nethi SK, Mukherjee S (2018) Biosynthesis of metal nanoparticles via microbial enzymes: a mechanistic approach. Int J Mol Sci 19:4100

Pastrana H, Avila A, Tsai CSJ (2018) Nanomaterials in cosmetic products: the challenges with regard to current legal frame works and consumer exposure. Nano Ethics 12:123–137

Paul S, Chugh A (2011) Assessing the role ayurvedic bhasmas as ethano-nanomedicine in the metal based nanomedicine patent regime. J Intell Prop Rights 16:509–515

Prasad R (2016) Advances and applications through fungal nanobiotechnology. Springer, International Publishing Switzerland. (ISBN: 978-3-319-42989-2)

Prasad R (2017) Fungal nanotechnology: applications in agriculture, industry, and medicine. Springer Nature Singapore Pte Ltd. (ISBN 978-3-319-68423-9)

Prasad R (2019a) Microbial nanobionics: basic research and applications. Springer International Publishing. (ISBN 978-3-030-16534-5) https://www.springer.com/gp/book/9783030165338

Prasad R (2019b) Microbial nanobionics: state of art. Springer International Publishing. (ISBN 978-3-030-16383-9) https://www.springer.com/gp/book/9783030163822

Prasad R, Rai S (2023) Trichoderma for biotechnological applications: current insight and future prospects. Elsevier

Qian Y, Yu H, He D, Yang H, Wang W, Wan X (2013) Biosynthesis of silver nanoparticles by the endophytic fungus Epicoccum nigrum and their activity against pathogenic fungi. Bioprocess Biosyst Eng 36:1613–1619

Rai S, Prasad R (2023) Nanoparticle producing trichoderma for sustainable agriculture: current understanding, opportunities, and challenges. In: Prasad R and Rai S (eds) New and future developments in microbial biotechnology and bioengineering: trichoderma for biotechnological applications: current insight and future prospects 203-222

Rai M, Yadav A, Gade A (2009) Silver nanoparticles as a new generation of antimicrobials. Biotechnol Adv 27:76–83

Rai MK, Deshmukh SD, Ingle AP, Gade AK (2012) Silver nanoparticles: the powerful nanoweapon against multidrug-resistant bacteria. J Appl Microbiol 112(5):841–852

Raj S, Jose S, Sumod US, Sabitha M (2012) Nanotechnology in cosmetics: opportunities and challenges. J Pharm Bioall Sci 4:186–193

Raliya R, Tarafdar JC (2013) ZnO nanoparticle biosynthesis and its effect on phosphorous-mobilizing enzyme secretion and gum contents in Clusterbean (Cyamopsis tetragonoloba L.). Agirc Res 2:48–57

Raliya R, Tarafdar JC, Biswas P (2016) Enhancing the mobilization of native phosphorus in the mung bean rhizosphere using ZnO nanoparticles synthesized by soil fungi. J Agric Food Chem 64:3111–3118

Revia RA, Wagner BA, Zhang MA (2019) Portable electrospinner for nanofiber synthesis and its application for cosmetic treatment of alopecia. Nanomaterials 9:1317

Rhodes KR, Green JJ (2018) Nanoscale artificial antigen presenting cells for cancer immunotherapy. Mol Immunol 98:13–18

Riddin TL, Gericke M, Whiteley CG (2006) Analysis of the inter- and extracellular formation of platinum nanoparticles by *Fusariumoxysporum* f. sp. lycopersici using response surface methodology. Nanotechnology 17:3482–3489

Saha S, Pal A, Kundu S, Basu S, Pal T (2010) Photochemical green synthesis of calcium-alginate stabilized Ag and Au nanoparticles and their catalytic application to 4-nitrophenol reduction. Langmuir 26:2885–2893

Salem SS, Fouda A (2021) Green synthesis of metallic nanoparticles and their prospective biotechnological applications: an overview. Biol Trace Elem Res 199:344–370

Sanaeimehr Z, Javadi I, Namvar F (2018) Antiangiogenic and antiapoptotic effects of green-synthesized zinc oxide nanoparticles using sargassum muticum algae extraction. Cancer Nanotechnol 9:1–16

Saravanan M, Barik SK, Mubarak Ali D, Prakash P, Pugazhendhi A (2018) Synthesis of silver nanoparticles from bacillus brevis (ncim 2533) and their antibacterial activity against pathogenic bacteria. Microb Pathog 116:221–226

Saravanan A, Kumar PS, Karishma S, Vo DVN, Jeevanantham S, Yaashikaa PR (2020) A review on biosynthesis of metal nanoparticles and its environmental applications. Chemosphere 264: 128580

Šebesta M, Urík M, Bujdoš M, Kolenčík M, Vávra I, Dobročka E, Kim H, Matúš P (2020) Fungus Aspergillus niger processes exogenous zinc nanoparticles into a biogenic oxalate mineral. J Fungi 6:210

Shankar SS, Ahmad A, Pasricha R, Sastry M (2003) Bioreduction of chloroaurate ions by geranium leaves and its endophytic fungus yields gold nanoparticles of different shapes. J Mater Chem 13: 1822–1826

Shelke DB, Islam NF, Chambhare MR, Sonawane HB, Patowary R, Prasad R, Sarma H (2023) Enhancing secondary metabolites and alleviating environmental stress in crops with mycogenic nanoparticles: a comprehensive review. Biocatal Agric Biotechnol. https://doi.org/10.1016/j.bcab.2023.102805

Singh P, Kim YJ, Zhang D, Yang DC (2016a) Biological synthesis of nanoparticles from plants and microorganisms. Trends Biotechnol 34(7):588–599

Singh J, Kaur G, Kaur P, Bajaj R, Rawat M (2016b) A review on green synthesis and characterization of silver nanoparticles and their applications: a green nanoworld. World J Pharm Sci 7:730–762

Singhal U, Khanuja M, Prasad R, Varma A (2017) Impact of synergistic association of ZnO-nanorods and symbiotic fungus *Piriformospora indica* DSM 11827 on *Brassica oleracea* var. botrytis (Broccoli). Front Microbiol 8:1909. https://doi.org/10.3389/fmicb.2017.01909

Singh S, Dhanjal DS, Thotapalli S, Sharma P, Singh J (2020) Importance and recent aspects of fungi-based food ingredients. In: New and future developments in microbial biotechnology and bioengineering. Elsevier, Amsterdam, pp 245–254

Spagnoletti FN, Spedalieri C, Kronberg F, Giacometti R (2019) Extracellular biosynthesis of bactericidal Ag/AgCl nanoparticles for crop protection using the fungus *Macrophomina phaseolina*. J Environ Manag 231:457–466

Steward BW, Kleihues P (2003) World cancer report. IARC Press, Lyon

Subbaiya R, Saravanan M, Priya AR, Shankar KR, Selvam M, Ovais M (2017) Biomimetic synthesis of silver nanoparticles from Streptomyces atrovirens and their potential anticancer activity against human breast cancer cells. IET Nanobiotechnol 11:965–972

Suman V, Prasad R, Jain VK, Varma A (2010) Role of nanomaterials in symbiotic fungus growth enhancement. Curr Sci 99:1189–1191

Syed A, Raja R, Kundu GC, Gambhir S, Ahmad A (2013) Extracellular biosynthesis of monodispersed gold nanoparticles, their characterization, cytotoxicity assay, biodistribution and conjugation with the anticancer drug doxorubicin. J Nanomed Nanotechnol 4:156–161

Taha ZK, Hawar SN, Sulaiman GM (2019) Extracellular biosynthesis of silver nanoparticles from *Penicillium italicum* and its antioxidant, antimicrobial and cytotoxicity activities. Biotechnol Lett 41:899–914

Thakkar KN, Mhatre SS, Parikh RY (2010) Biological synthesis of metallic nanoparticles. Nanomedicine 6:257–262

Thakor R, Mistry H, Patel H, Jhala D, Parmar N, Bariya H (2022) Biogenic synthesis of silver nanoparticles mediated by the consortium comprising the marine fungal filtrates of *Penicillium oxalicum* and *Fusarium hainanense* along with their antimicrobial, antioxidant, larvicidal and anticancer potency. J Appl Microbiol 133:857–869

Thirumurugan G, Shaheedha SM, Dhanaraju MD (2009) Invitro evaluation of anti-bacterial activity of silver nanoparticles synthesised by using *Phytophthora infestans*. Int J Chem Tech Res 1(3): 714

Tolochko NK (2009) History of nanotechnology (Chapter 1). In: Kharkin V, Bai C, Kapitza S, Awadelkarim OO (eds) Nanoscience and nanotechnologies, vol 1. UNESCO, Oxford. ISBN 978-1-78021-531-0. https://www.eolss.net/ebooklib/bookinfo/nanoscience-nanotechnologies.aspx

U.S. Food and Drug Administration (2016) Is it a cosmetic, a drug, or both? (Or is it soap?). FDA, Silver Spring, MD. http://www.fda.gov/cosmetics/guidancecomplianceregulatoryinformation/ucm074201.htm

Vahabi K, Mansoori GA, Karimi S (2011) Biosynthesis of silver nanoparticles by fungus *Trichoderma Reesei* (A Route for Large-Scale Production of AgNPs). Insciences J 1(1):65

Vahidi H, Kobarfard F, Alizadeh A, Saravanan M, Barabadi H (2020) Green nanotechnology-based tellurium nanoparticles: exploration of their antioxidant, antibacterial, antifungal and cytotoxic potentials against cancerous and normal cells compared to potassium tellurite. Inorg Chem Commun 124:108385

Vala AK, Shah S, Patel R (2014) Biogenesis of silver nanoparticles by marine derived fungus *Aspergillus flavus* from Bhavnagar Coast, Gulf of Khambhat, India. J Mar Biol Oceanogr 3(1): 1–3

Verma VC, Singh SK, Solanki R, Prakash S (2011) Biofabrication of anisotropic gold nanotriangles us extract of endophytic *Aspergillus clavatus* as a dual functional reductant and stabilizer. Nanoscale Res Lett 6:16

Walter P, Welcomme E, Hallégot P, Zaluzec NJ, Deeb C, Castaing J (2006) Early use of PbS nanotechnology for an ancient hair dyeing formula. Nano Lett 6(10):2215–2219

Wang L, Liu X, Lee DJ, Tay JH, Zhang Y, Wan CL (2018) Recent advances on biosorption by aerobic granular sludge. J Hazard Mater 357:253–270

Worrall EA, Hamid A, Mody KT, Mitter N, Pappu HR (2018) Nanotechnology for plant disease management. Agronomy 8:285

Yadav A, Kon K, Kratošová G, Durán N, Ingle AP, Rai M (2015) Fungi as an efficient mycosystem for the synthesis of metal nanoparticles: progress and key aspects of research. Biotechnol Lett 37:2099–2120

Zhang MAM, Yu Y, Shen W, Zhang HY, Gu HQN (2008) Preparation and characterization of magnetite nanoparticles coated by amino silane. Colloids Surf A Physicochem Eng Asp 212(2): 219–226

Synthesis of Nanoparticles in Biofilms

6

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Abstract

Nanoparticles are of great interest in material science due to their characteristics, such as high surface area, biocompatibility, and unique optical properties. Within the search for more ecological and efficient pathways to synthesize nanoparticles, there is a special interest in the synthesis of bacterial biofilms. Biofilms are self-organized communities of homogeneous or heterogeneous microorganisms that grow on a surface. Naturally, bacteria organize themselves by forming biofilms as a survival mechanism, which is why they are found in different ecosystems. Synthesis of nanoparticles assisted by biofilms is exceptionally a particular methodology in which it is possible to produce nanoparticles with high purity, selectivity, and uniformity, taking advantage of in vivo synthesis. Some of the recent findings in the synthesis of nanoparticles by using biofilms have been

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focused on the synthesis, mechanism, and stabilization, in which the stabilization represents one of the most critical factors. From a biological point of view, the use of nanoparticles synthetized by using biofilm represents an innovator and direct practical application especially in drug delivery and biocatalysis. In this chapter, a general description of nanoparticles and their different synthesis routes are made, as well as basic concepts of biofilms and their formation processes, to finally present in detail the method of synthesis of nanoparticles into biofilms and their applications. In this order, the first part of the chapter will focus on concepts and methodologies to synthetize nanoparticles, followed by a general description of biofilms. In the third part, an introduction about synthesis of nanoparticles assisted by biofilms will be present. Finally, general applications (agriculture, medicine, and catalysis) will be discussed.

Keywords

Biofilms · Nanoparticles synthesis · Drug-delivery systems · EPS matrix

6.1 Nanoparticles Synthesis

Nanotechnology refers to the manipulation of matter at the nanoscale, i.e., at dimensions around 10^{-9} m. Solids with at least one dimension between 1 and 100 nm are called nanomaterials (Laurent et al. 2010). At this scale, solids might show different properties regarding their macroscopic analogous. Thus, the interest in developing synthesis routes for obtaining nanomaterials has gained attention during the last decades (Li et al. 2013; Shkodenko et al. 2020). In that regard, several experimental protocols, at the laboratory and even pilot scale, have been proposed.

Depending on the composition, nanomaterials are classified as organic or inorganic, and the synthesis route strongly depends on this parameter. Among the most used inorganic nanomaterials, transition metal-based particles are the most used. Metals such as iron, zinc, and copper (Shkodenko et al. 2020) are the most widely used due to their versatile properties and application. Taking advantage of the redox properties of transition metals, common synthesis routes are based on them.

6.1.1 Chemical Routes

For instance, nowadays it is quite common to favor the reduction, nucleation, and growth of transition metal-based nanoparticles using a proper reducing agent. Briefly, a metal source is solubilized on a specific solvent, commonly water, and then the called reducing agent is added, which produces the reduction of the oxidized metal to a reduced state (or combination of them) as shown in Reaction (6.1) (Lu et al. 1997).

$$M^{+n} + \text{Reducing agent} \rightarrow M^{+n-x} + \text{subproducts} \quad (6.1)$$

where *M* stands for the oxidized metal atom, *n* for the initial oxidation state, and *x* is the modification on this parameter based on the reducing capacity of the reducing agent. Regarding the subproducts, they depend on the nature of the reducing agent. This simple approach has been widely used in the literature (Lu et al. 1997; Dong et al. 2009; Mercado and Weiss 2018). For instance, for obtaining zero-valent iron nanoparticles, sodium borohydride ($NaHB_4$) has been reported following Reaction (6.2).

$$4Fe^{3+} + 3BH_4^- + 9H_2O \rightarrow 4Fe^0{}_{(S)} + 3H_2BO_3^- + 12H^+ + 6H_2 \quad (6.2)$$

In this case, the subproducts are $3H_2BO_3^- + 12H^+ + 6H_2$. More importantly, the reduction from Fe^{3+} to Fe^0 is due to the relatively high standard reduction potential of BH_4^-, varying from −1.24 V vs SHE (Standard Hydrogen Electrode) at pH 14 to −0.48 V vs SHE at pH 0 (Lu et al. 1997), when compared to the −0.036 V to the Fe^{3+}/Fe^0 pair. Thus, selecting the proper reducing agent to promote the formation of zero-valent transition metal nanoparticles depends on the standard reduction potential of the reducing agent and both the initial and final oxidation state of the transition metal. Nevertheless, zero-valent iron nanoparticles are susceptible to oxidation in an air atmosphere. Thus, to obtain air-stable zero-valent iron nanoparticles, the use of an additional functionalization protocol is required. In this way, dicarboxylic acids such as succinic acid have been proven to chelate the surface of the material enhancing their oxidation stability (Mercado and Weiss 2018).

Another example of the previous protocol route is the well-known production of zero-valent gold or silver nanoparticles using the citrate anion as a reducing agent (Turkevich and Copper 1951; Dong et al. 2009). Due to their relatively higher standard reduction potential, Au^{3+}/Au^0 (1.52 V vs SHE) and Ag^+/Ag^0 (0.80 V vs SHE) do not require strong reducing agents such as $NaBH_4$ and citrate anion could be used instead. Moreover, compared to the Fe/$NaBH_4$ system, the Au or Ag/citrate systems do not require the use of an additional surface stabilizer because the oxidized organic subproducts which can be adsorbed on the surface and act as a stabilizer. For instance, the common route to obtain gold nanoparticles is by using $AuCl_4^-$ ($AuCl_4^-/Au^0$ 1.002 V vs SHE) reduced by citrate which results in the obtention of nanospheres with a mean diameter of 12 nm (De Freitas et al. 2018).

Moving toward a circular economy concept, the use of agro-industrial wastes as feedstock or additives for the synthesis of transition metal oxide nanoparticles has gained interest in the academic community due to its relative simplicity. The reducing agents are typically substituted by an extract from the organic wastes, and the principle of the synthesis is the one previously mentioned. For instance, zero-valent silver nanoparticles have been obtained, instead of using the citrate protocol, avocado seed extracts were suitable as a reducing and stabilization agents. The involved reactive pathway is represented in Fig. 6.1. Immediately after adding the avocado seed extract in contact with the silver ions, the suspension turns

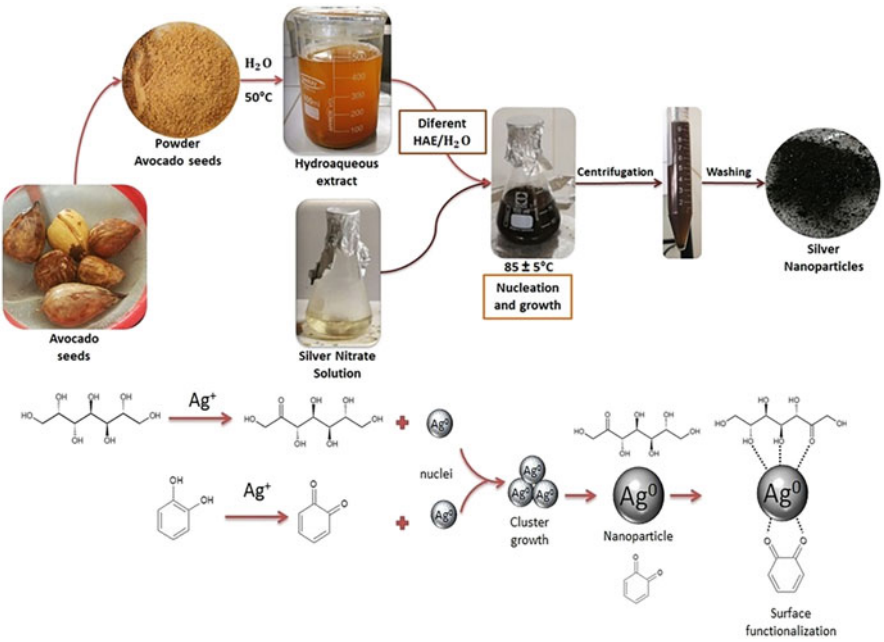

Fig. 6.1 Proposed mechanism for the synthesis of zero-valent silver nanoparticles using avocado seed aqueous extract as a reducing and stabilization agent

brownish-black, which indicates the start of the reduction of the Ag ions. In this case, the nuclei formation of the nanoparticle is given by the interaction of metal ions with organic molecules from avocado extract; mainly hydroxylated molecules, polyphenolic compounds, and organic acids such as perseitol ($C_7H_{16}O_7$) or pyrocatechol ($C_6H_6O_2$), many of which have enough redox potential to complex and reduce Ag^+ to Ag^0 (Figueroa et al. 2018).

Nevertheless, non-reductive pathways for obtaining transition metal-oxide-based nanomaterials using agroindustrial wastes have been also reported. Monje et al. have studied the use of *Ilex paraguariensis,* commonly known as Yerba mate, as both precipitation and dispersion matrix for embedding iron/copper oxide nanomaterials (Monje et al. 2022) as shown in Fig. 6.2. Similar to the case of dicarboxylic acid-coated zero-valent iron nanoparticles, the organic matter acts as a stabilization agent. In this case, the organic compounds on the extract do not completely reduce the metallic ions and the final state corresponds to mixed oxides. They suggest that nanoparticle nucleation and growth depend on the formation of monomers of iron-polyphenol complexes and thus pH synthesis is a crucial parameter to control the final size.

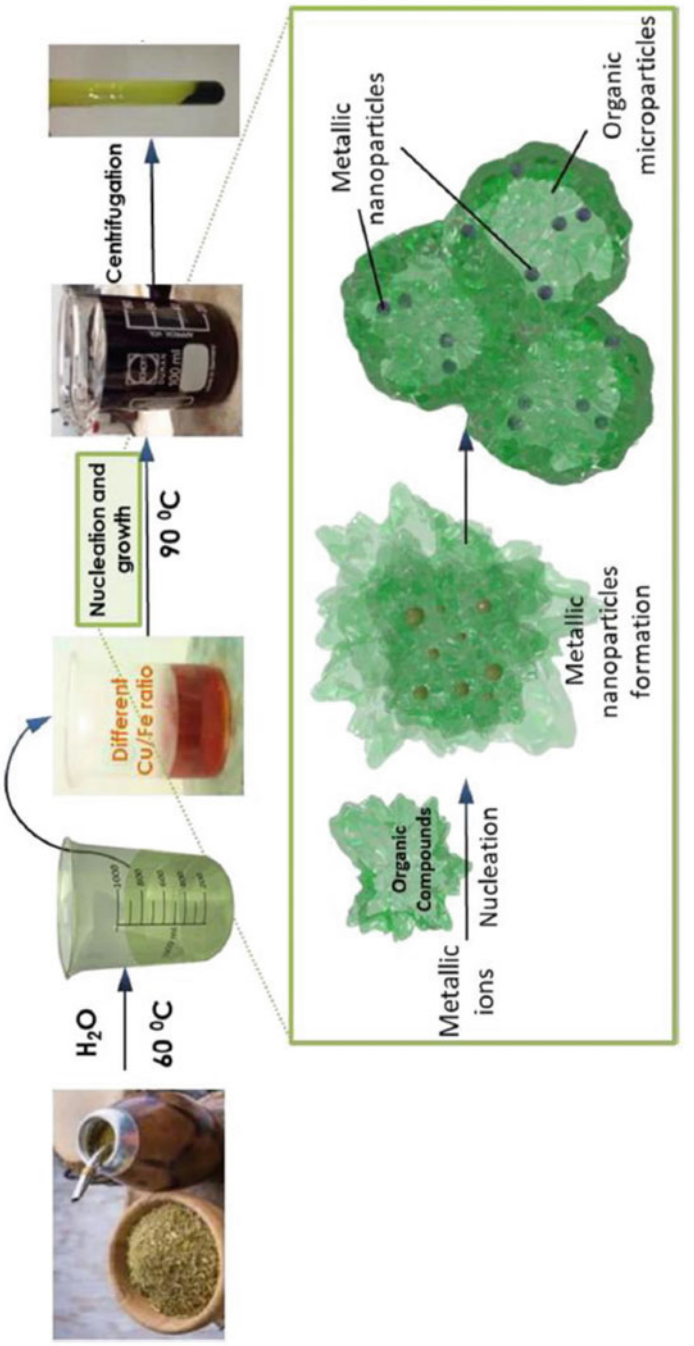

Fig. 6.2 Proposed mechanism for the synthesis of mixed iron–copper oxide nanoparticles embedded on organic microparticles from *Ilex paraguariensis*

6.1.2 Microorganisms-Based Route

A relatively new approach to nanoparticle synthesis is through biological processes taking advantage of extracellular redox reactions (similar to those discussed above) in microorganisms. This approach is of interest due to the decrease in the use of harmful reagents and its low cost. Moreover, at the end of the synthesis, the obtained materials are coated with biogenic capping agents due to the interaction with the biomass (Tanzil et al. 2016; Prasad et al. 2016; Srivastava et al. 2021; Eftekhari et al. 2023; Kisimba et al. 2023) which avoids its oxidation (*vide supra*). Among all microorganisms, bacteria and their biofilms have gained attention as nanomaterials synthesis platforms due to their inherent metal resistance and rapid extracellular metal reduction (Ramanathan et al. 2013). From the kinetic aspect of nanoparticle production, biofilms are superior to their bacteria due to their higher metal resistance properties (Tanzil et al. 2016).

As for the chemical route, the nanomaterial synthesis (Reaction (6.1)) requires the use of metal ions and a reducing agent. This latter reagent is provided indirectly by the bacteria. Thus, the production mechanism varies among the used bacteria according to their reducing metabolites secreted (or even in their intracellular space). Nevertheless, some parameters have been identified to control the size of the nanoparticles, such as the pH, incubation time, composition of the growth medium, and metal concentration (Klaus et al. 1999). In fact, the metal concentration is a key parameter to control. Metal ions might be consumed by the microorganism for biochemical reaction such as oxygenic photosynthesis, nitrogen fixation, and hydrogel assimilation (Klaus et al. 1999). Thus, to avoid high metal concentration, it is necessary that the bacteria adopt a resistive state such as complexation, precipitation, or reduction (Tanzil et al. 2016). This last case is responsible for the production of metal-based nanoparticles. The required electrons are provided by the oxidation of reduced organic matter through electron transfer system mediated by multihaeme cytochromes, which prevail in the membrane (Tanzil et al. 2016).

6.2 Biofilms

Biofilms are self-organized communities of homogeneous or heterogeneous microorganisms that grow on a surface. Naturally, bacteria organize themselves by forming biofilms as a survival mechanism, which is why they are found in different ecosystems, but it was not until 1970 that Nils Hoiby linked chronic infections with bacterial biofilms (Vestby et al. 2020). Currently, it is known that approximately 65% of bacterial infections involve the formation of a biofilm; the strains mainly found in humans are *Staphylococcus aureus* and *epidermidis*, *Acinetobacter*, *Bacteroides fragilis, Klebsiella pneumonia*, *Pseudomonas aeruginosa*, and *Escherichia coli* (Joshi and Litake 2013; Khan et al. 2017). Biofilms can form on different surfaces, such as living tissues, polymeric devices, pipes, or aquatic systems (natural or synthetic) (Schiebel et al. 2020). The developing environment of the biofilm will largely determine the composition and the growth rate.

Biofilms are formed by the adhesion of planktonic bacteria to a surface, acquiring a characteristic structure in which they are covered with an extracellular matrix that provides protection. That matrix is generally formed by a mixture of proteins, mainly rigid such as fibrin, polysaccharides, and polynucleotides. The exact composition of the biofilm matrix depends on the strains that make it up and the developing medium. The extracellular matrix constitutes between 50 and 90% of the biofilm and is usually made up mostly of neutral or anionic polysaccharides that allow the association of cations that provide strength to the biofilm structure (Karygianni et al. 2020). This physical barrier provides the pathogen resistance against antibiotics and host defenses. Some of the mechanisms that have been studied to explain this resistance are: (1) slow and incomplete penetration of antimicrobial agents since the matrix neutralizes and dilutes them, decreasing their effect; (2) decreases the metabolic rate of bacteria, which allows them to survive in conditions of nutrient deficiency; and (3) gene changes that lead to the formation of persistent cells, which occurs due to the slow rate of growth that allows variations in the bacterial phenotype (Percival et al. 2015; Sonawane et al. 2022).

The formation of biofilms is a process that involves three parameters: the substrate, the medium, and the microorganism. Regarding the substrate, the properties of the surface, such as surface energy, polarity, charge, and morphology, are determinants for bacterial fixation since it is the surface that predisposes to the adhesion of external agents by providing binding sites. Some studies found that rough surfaces increase microbial colonization, as were polar, high surface tension, and charged surfaces (De-la-Pinta et al. 2019; Zheng et al. 2021). According to Belfort et al., nonpolar surfaces facilitate the conformational reorientation of proteins since they exert a destabilizing effect, which allows greater interaction with the surface and favors the creation of a conditioning layer that promotes the microorganism adhesion (Nakanishi et al. 2001).

The medium is a factor of great importance for the development of biofilms since it determines the composition of the conditioning film and the stabilization of the microcolonies. When a surface comes into contact with an aqueous medium, it is initially coated with components found in it, such as proteins, polymers, or salts, creating a conditioning film that will affect the shape, speed, and intensity of microorganism attachment. In addition, the physical-chemical conditions of the medium, such as pH, ionic strength, temperature, and the concentration and type of nutrients, are essential for the development of the biofilm. Cowan et al. demonstrated in in vitro tests that the increase in the concentration of nutrients in the medium increases the number of attached microorganisms (Cowan et al. 1991). Additionally, the hydrodynamics of the medium also plays an important role, and the flow velocity limits sedimentation and association of bacteria cells with the surface (Donlan 2002).

Finally, the composition of the surface of the microorganism also affects the rate and intensity of binding to the substrate. In general, bacteria have a highly hydrophobic and negatively charged surface, given to a large extent by the fimbriae or flagellar appendages, which are the first to adhere to the substrate and facilitate the approach of the microorganism for its subsequent fixation. In addition to fimbriae,

recent studies have shown that some proteins, mycolic acid, lipopolysaccharide, and other flagella also affect the adhesion process (Srinivasan et al. 2021).

Within a biofilm, there may be more than one bacterial strain, which usually enter into a competition that ends in the strain elimination or coexistence. Mixed biofilms are syntrophic communities, in which several microorganisms coexist, giving them high resistance. It is estimated that between 60 and 80% of biofilm infections correspond to mixed biofilms (Rao et al. 2020). Cooperation between mixed species can also improve adhesion or produce cross-feeding increasing community growth. Yuan et al. reported that biofilms formed *by Lactococcus lactis* and *Pseudomonas fluorescens* have an approximately 20,000 and 100-fold increase in adhesiveness when compared to their pure strains, respectively (Yuan et al. 2020).

The reason why the mixed biofilms present greater resistance is still a field of study, among the proposed speculations is the three-dimensional structuring that allows the protection of the weakest microbial strains and the development of denser, thicker, and more adaptable extracellular matrices. The extracellular matrix thickness largely determines the ability of the biofilm to block harmful substances and maintain good bacterial development (Rao et al. 2020).

6.2.1 Life Cycle of a Biofilm

The study of biofilms is recent, even though bacteria have been studied for several centuries. The first reports of the observation of these structures date back to 1684 when Anthony van Leeuwenhoek observed this behavior in bacteria attached to teeth. However, it was until 1970 that the adhesion of bacteria to pacemaker leads was observed and associated with persistent infections, awakening medical interest in this type of bacterial conformation (Bjarnsholt 2013). Since then, different models have been proposed to try to understand how the formation of biofilms occurs and what is the cause of their particular characteristics. Currently, the biofilm life cycle is made up of three stages: adhesion, growth, and separation. Figure 6.3 shows the process.

The adhesion process is the first phase (I) of biofilm development; this involves the conditioning of the surface and the accumulation and union of a small population of microorganisms. When a medical device is put in contact with tissues, the surface is covered with proteins and other molecules from the medium, which when adhered form a conditioning film that allows a more friendly interaction between the material

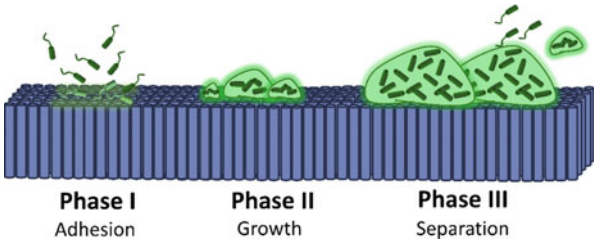

Fig. 6.3 Life cycle of a biofilm

and microorganisms. Thus, when the bacteria find a conditioned solid surface, they proceed to form a union via appendages (fibrins, flagella) or by secretion of proteins that facilitate adhesion. This union is reversible and requires interaction time for the microorganisms to cement themselves to the substrate and begin to form aggregates that drive the irreversible union of the bacterium to the surface. At this stage, the gene expression of the flagellum is not distinguished, and the bacteria begin to segregate the base substances that will form the extracellular matrix of the biofilm. The second phase (II) corresponds to the growth or maturation of the microorganism; once the bacterium adheres to the surface, it initiates cell division forming clusters of several layers of cells, which form microcolonies with a protective extracellular barrier, which will depend on the type of bacteria and the conditions in which it grows. In the final stage (III), the separation or dispersion of the biofilm occurs; at this point the bacteria are released from the surface, either individually or by conglomerates that can colonize the surface again, closing the cycle, and causing the propagation of bacterial infection. When biofilms dissociate, their structure becomes unstable, and the cells inside them acquire some mobility, which allows separation through biofilm erosion (Palmer et al. 2007; Francolini and Donelli 2010; Sonawane et al. 2022).

The biofilm formation model was developed based on in vitro studies of *P. aeruginosa*, which has practical and observable management, and initially included five steps; however, said model did not describe the behavior of complex systems such as industrial, natural, and clinical environments, nor did it find the great diversity of biofilm structures that can be formed, so the model was extended leaving the current model that encompasses the three basic events described above, this model gives a general idea of the behavior of this type of structure, allowing its expansion and adaptation to different environments and behavior (Sauer et al. 2022).

6.2.2 Beneficial Uses of Biofilms

Although biofilms are normally associated with the development of infections and damage to health and industry, they can be used for the benefit of society. Among the beneficial applications of this type of structure are antibacterial potential, fermentation capacity, biofertilizer, filtration, anticorrosive effect, and bioremediation (Qureshi et al. 2005; Todhanakasem 2013). All these characteristics can be exploited mainly by the agricultural and food industry. Some beneficial microorganisms can be expressed as biofilms, which improves their application. For example, in the food and agricultural industry, the production of probiotics in the form of biofilms from different strains of *Lactobacillus* has shown technological advantages the manufacture, since biofilms avoid the contamination and deterioration of the strain, as well as improve the characteristics of the final product and also have greater resistance to changes in temperature, pH, and mechanical wear (Jones and Versalovic 2009). Probiotics are microorganisms that improve human health by helping to treat and prevent gastrointestinal diseases, so their production and use are highly desired. Another use of biofilm in the food industry is for the manufacture of fermented

products (dairy, meat, and pickles) to maintain the quality of the product as aromas and textures. Thus, to produce Ragusano cheese, a vat with a biofilm of fermentative microflora is used; the milk is added to the vat where fermentation and curing of the cheese can take place. In addition, in the traditional formation of cheese, the formation of biofilms on wooden utensils improves the production of lactic acid (Ünal Turhan et al. 2019).

On the other hand, an application related with the bioremediation is still more interesting. Bioremediation deals with the use of microorganisms to treat contaminants, transforming them into less toxic substances. Biofilms have been used for the bioremediation of recalcitrant substances, due to their high biomass, biofilms can immobilize the compounds; in addition, this structure is more resistant to toxic environments (Singh et al. 2006). In agriculture, the formation of biofilms on different parts of the plants can produce symbiotic effects and bring biological control to the crop; among the bacteria that fulfill this function are *Bacillus subtilis* and *Pseudomonas* that on the root gives the plant robustness and protection. *Rhizobium* in the root of the legumes produces symbiosis, and *Gluconacetobacter diazotrophicus* benefits sugar cane (Rudrappa et al. 2008). Biofilms have also been used for the development of bioreactors, which are used in a wide range of industrial applications. By the way, the formation of biofilms in reactors has shown an increase in productivity, providing advantages such as a higher amount of biomass and greater efficiency in the process. These types of reactors have been used for water treatment and the manufacture of biofuels, enzymes, and fatty acids. One of the best-known processes that use this type of bioreactor is the manufacture of vinegar, which uses *Acetobacter* biofilms on pieces of wood to speed up the production process (Zottola and Sasahara 1994).

6.3 Nanoparticles Synthesis by Using Biofilms

There are a lot of strategies that can be adequate to synthetize nanoparticles or to improve their dispersion for several catalytic applications. Among these, biofilms are a good option to control the synthesis (biosynthesis) of nanoparticles. The use of these materials present different and relevant advantages which some of them are related with the low precursor concentrations that can be used during the synthesis, the evident large surface area and besides the inert atmosphere which can produce a resistance of different agents (highly charged) in where evidently can decrease the effective synthesis of the nanoparticles. In general, biofilms minimize the risk of contamination by oxidation suggesting a good way to synthetize and incorporate metallic particles into biofilms (Tanzil et al. 2016).

In this way, the synthesis of nanoparticles using biological pathways (by means bacteria and biofilms) has gained more attention because of the application of green chemical routes which effectively reduce the contamination charge. Effective supporting or adhesion of nanoparticles in the matrix of the biofilms can represent a challenge because sometimes can help to reduce its low biocompatibility. In this way, synthetisizing nanoparticles in the wall or inside of the biofilm is of interest.

Besides, biofilms have been used to produce nanoparticles, however, the mechanistic details of its formation are not well understood.

Some of the recent findings in the synthesis of nanoparticles by using biofilms have been focused on the synthesis, mechanism, and stabilization, in which the last represents one of the most critical factors. From a biological point of view, the use of nanoparticles synthetized by using biofilm represents an innovate and direct practical application especially in drug delivery and biocatalysis. Although negative effects of biofilms have been reported, their use in many applications including nanotechnology-based drug delivery is still of interest (Dos Santos Ramos et al. 2018). The use of nanoparticles such as liposomes, microemulsions, polymeric, and metallic nanoparticles could help to control the evident negative effect that can represent the microbial biofilms for a specific application (Thambirajoo et al. 2021). To solve this, the use of nanoparticles as a carrier is widely used to avoid any damage and increase biological activities in comparison with biofilms (Thambirajoo et al. 2021). The modification of biofilms with the use of nanoparticles could avoid the adhesion of bacteria or other phenomena in the surface and within the biological behavior of the cell. In addition, nanoparticles could cause an increasing in the resistance to different vectors coming from antimicrobial agents and helping in the multidrug-resistance strains.

For example, recently the synthesis has been described in a single step of extracellular silver nanoparticles through an in-situ bio-reduction of aqueous solution of silver nitrate using *Psidium guayaba L.* Nanoparticles were obtained by the reduction pathway starting from $AgNO_3$ solution and periodically monitored by using UV-vis (Gupta et al. 2014). Besides, they were well characterized by TEM obtaining a size particle distribution at around 59.39 nm. In comparison, significant Au nanoparticles were synthetized using marine actinomycete of *Nocardiopsis* sp. *GRG1* (KT235640) as biological stabilizing and reducing agent. In this case, these nanoparticles were evaluated as a potential antibiofilm (up to 91% against biofilm-forming MR-CoNS) (Rajivgandhi et al. 2019). Comparatively, ZnO nanoparticles were synthesized using green chemical synthesis with sodium hydroxide as a reducing agent (Velsankar et al. 2022). These nanoparticles were deposited into a biofilm which was tested as a matrix in biomedical field. The biofilm activity confirmed the antibacterial properties of green-ZnO nanoparticles on both Gram-negative (*S. typhi*) and Gram-positive (*B. subtilis and S. aureus*) bacteria by films previously disintegrated. As verification of the potential activity of these nanoparticles, the antioxidant, ant-diabetic, and anti-inflammatory activities were tested showing relevant results.

Following the reported literature, a recent study was focused on the effect of molecular weight starting from chitosan depolymerization products on the synthesis and production of silver nanoparticles (AgNPs) as well as chitosan/AgNPs blend films (Affes et al. 2020). In comparison with the films constituted by only chitosan, the properties of most of them were enhanced when the mixture of chitosan/AgNPs was tested. Then, the light barrier, opacity, elongation at break, as well as bioactivities were improved, thus suggesting that films could be used as novel alternative food packaging applications (Chausali et al. 2022).

Among a lot of applications with nanoparticles by the use of biofilms, an antibacterial study was performed to see whether the effect of polymeric PolymP-n Active nanoparticles would present a significant contribution by using an in vitro subgingival biofilm model (Sánchez et al. 2019). Interestingly, the in vitro investigation demonstrated that the coating surface with both nanoparticles and ions from metallic sources could have an impact on the biofilm formation reducing in some ways the vitality and weakness. In other terms, decreases the contact between matrix and colonizer and being more susceptible to detachment.

Comparatively, ultra-small nanoparticles (USNPs) coming from noble metals could represent a great potential in different applications. This fact is related with their high surface areas and high reactivity, increasing its potential interest in biology. Several pathways have been reported, however, the electrochemical route has been reported recently to obtain USNPs (Au, Pd, Pt) using single bacterium strain of *Shewanella loihica* PV-4; comparatively, these USNPs had a size range between 2 and 7 nm and showed to be active as potential catalysts for dye degradation (Ahmed et al. 2018).

The mechanism of the interaction of the nanoparticles in systems involving the drug delivery on biofilm formation process is divided into different stages involving, among other, the adherence of microbial cells, the reversible adhesion, irreversible adhesion, maturation, and finally the detachment of cells (Martin et al. 2015).

6.4 General Applications (Fig. 6.4)

6.4.1 Nanomedicine

6.4.1.1 Oral Treatments

Nanoparticles have significant promise for addressing the challenges of oral biofilm drug delivery. The chemical flexibility and relative ease of nanoparticle preparation enable the development of unique biofilm treatments. Nanoparticles can either be directly bactericidal or be designed to enhance drug aqueous solubility and transport

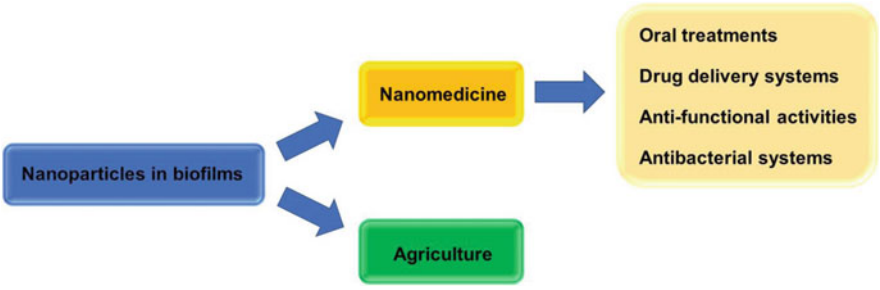

Fig. 6.4 General applications of nanoparticles in biofilms

into bacterial cells. Antibiofilm nanoparticles can be developed from metals or metal oxides, synthetic or natural polymers, or hybrids therein. Furthermore, by modifying chemical compositions, size, surface charge, and other properties, nanoparticles provide great flexibility to ensure robust biofilm targeting and retention through biofilm matrix interactions, thereby enhancing substantivity and antibiofilm efficacy. Nanoparticles' high surface-area-to-volume ratios enable robust drug or drug combination loading that may result in synergistic antibiofilm efficacy. Data suggest that nanoparticles can also lower the potential for bacterial resistance and protect conventional drugs from pH and/or enzymatic degradation in the harsh biofilm microenvironments (Wang et al. 2016; Benoit et al. 2019).

6.4.1.2 Drug Delivery Systems

Biofilms can help nanoparticles to improve the aqueous solubility of drugs. Through fine adjustments to chemical compositions such as size, surface charge, and other properties, biofilms together with nanoparticles can provide flexibility for transport, retention, and deliver drugs (Wang et al. 2016). For example, depending on the shape and morphology of nanoparticle, can penetrate the bacterial biofilm, making resistant bacteria more sensitive to breaking the film, thus improving the penetration of antibacterial agents (Shah et al. 2022), in general shape, size, and morphology are the most important parameters for determining the property of nanoparticles (Velsankar et al. 2022).

6.4.1.3 Anti-Functional Activities

In the recent years, the synthesis of metal oxide nanoparticles has attained much interest in a scientific community. Among them, the ZnO nanostructures are most preferable and attractable due to its cost-effective and easily accessible dynamic nature in emerging bio-sensing, photocatalytic, optical, and electronic device applications (Yadav et al. 2019; Velsankar et al. 2022; Bhuyan et al. 2015).

ZnO nanostructures are nontoxic and a biocompatible material and are used in drug delivery, pharmaceutical, and biomedical fields, for example, some uses are antioxidant, anti-inflammatory, and antidiabetic activities (Kavitha et al. 2023).

The antioxidant activity has been ascribed to a variety of mechanisms, including transition metal ion catalyst binding, chain initiation prevention, hydrogen abstraction prevention, radical scavenging activity, breakdown of peroxides, and reductive capacity. The antioxidants play a significant role in all the living organisms due to the interaction of biomolecules with molecular oxygen. The different chemical entities that consist of unpaired electrons are known as free radicals. These are highly unstable in nature. They extract electrons from neighboring molecules to attain stability and causing damage to them. They are highly reactive, causing severe damage to short-lived chemical species, which results in degradation of biomolecules. These free radicals are essential to human body for detoxification, energy supply, chemical signaling, and immune function, and they are produced continuously in our human body. The antioxidant activity of any studied material is mostly owing to their redox property, which can help in the absorption and

neutralization of free radicals, as well as quenching of singlet and triplet oxygen (Rehana et al. 2017; Rajakumar et al. 2018; Velsankar et al. 2022).

6.4.1.4 Antibacterial Systems

Silver nanoparticles have become the focus of intensive research due to their applications in different areas such as antimicrobials and biomaterial production. Recently nanoparticles have been successfully used for the delivery of therapeutic agents in chronic disease diagnostics, to reduce bacterial infections in skin and burn wounds, to prevent bacterial colonization on medical devices, and in food and clothing industries as an antimicrobial agent (Gupta et al. 2014; Prasad et al. 2020, Inamuddin et al. 2021).

It must be considered that to deliver the antimicrobial agents to the infected area, the dense physical obstacle presented by biofilms must be overcome. Antimicrobial agents administered systemically are not able to effectively reach the infected areas. In addition to the presence of biofilms, in infected wounds, the necrotic tissue covering the wound bed is another issue to consider in the treatment process. Antimicrobial agents delivered from conventional topical dosage forms have been found to display poor penetration due to this obstruction, leading to low concentrations of the antimicrobial agents in the infected area. One way to improve these systems is by developing films from chitosan laden with silver NPs as a delivery system, this allows for improved treatment of chronic wounds with the presence of bacterial biofilms (Permana et al. 2021; Prasad et al. 2020).

Other uses of AgNPs in biomedical applications are antiviral, antifungal, antiparasitic, and antifouling activity (Almatroudi 2020).

6.4.2 Agriculture

In agriculture, applications of nanomaterials include efficient, slow-releasing plant growth, and protection products such as fertilizers, pesticides, seed cover treatments, improved pathogen detection systems, and improved delivery systems (Prasad et al. 2014, 2017a, b; Bhattacharyya et al. 2016). One potential benefit of nanoparticles is their use for control of pathogenic microorganisms that pose a major threat to crop productivity (Ismail et al. 2017; Gupta et al. 2018; Prasad et al. 2017c). Biological control of pathogens is an effective alternative that also provides the benefit of soil sustainability (Osherov et al. 2023). Biocontrol agents are self-replicating and therefore limit the need for repeated application. The problem of resistance to these agents of disease control is also not encountered. The immobilization of nanoparticles in polymeric matrices helps to improve biocompatibility, control release, and reduce toxicity levels (Bhatia et al. 2021).

6.5 Summary

In this contribution, we have described most of the basic concepts to understand different synthetic pathways for the synthesis of nanoparticles and also their stabilization in matrices as biofilms. Synthesis of nanoparticles assisted by biofilms is

currently an exceptional methodology emerging from another because of the low environmental impact. Recent advances in the use of biofilms as biological carrier for the delivery and synthesis of particles at the nano size have been described focused on the mechanism and stabilization, highlighted the most critical factors. On the other hand, description about its chemical flexibility and relative introduction in biological applications were introduced using examples such as oral treatments, agriculture, antibacterial, and drug delivery systems. In general, nanoparticles as a carrier are widely used to avoid any damage and increasing biological activities in comparison with biofilms which open new synthetic methodologies to apply in materials science. In the same way, modification of biofilms with the use of nanoparticles could avoid the adhesion of bacteria or other phenomena in the surface and within the biological behavior of the cell giving more resistance against diseases, aggregations, and among others. In general, nanoparticles synthetized by using biofilms can generate an increase in the substrate interactions toward the typical properties of these films such as surface energy, polarity, charge, and morphology. The critical factors are determinants for bacterial fixation since it is the surface that predisposes to the adhesion of external agents by providing binding sites. In summary, nanoparticles within the use of biofilms are an emerging topic with critical and potential applications in connection with biology, chemistry, and material science.

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References

Affes S, Maalej H, Aranaz I et al (2020) Controlled size green synthesis of bioactive silver nanoparticles assisted by chitosan and its derivatives and their application in biofilm preparation. Carbohydr Polym 236:116063. https://doi.org/10.1016/j.carbpol.2020.116063

Ahmed E, Kalathil S, Shi L et al (2018) Synthesis of ultra-small platinum, palladium and gold nanoparticles by Shewanella loihica PV-4 electrochemically active biofilms and their enhanced catalytic activities. J Saudi Chem Soc 22:919–929. https://doi.org/10.1016/j.jscs.2018.02.002

Almatroudi A (2020) Silver nanoparticles: synthesis, characterisation and biomedical applications. Open Life Sci 15:819–839. https://doi.org/10.1515/biol-2020-0094

Benoit DSW, Sims KR, Fraser D (2019) Nanoparticles for oral biofilm treatments. ACS Nano 13: 4869–4875. https://doi.org/10.1021/acsnano.9b02816

Bhattacharyya A, Duraisamy P, Govindarajan M, Buhroo AA, Prasad R (2016) Nano-biofungicides: emerging trend in insect pest control. In: Prasad R (ed) Advances and applications through fungal nanobiotechnology. Springer International Publishing Switzerland, pp 307–319

Bhatia R, Gulati D, Sethi G (2021) Biofilms and nanoparticles: applications in agriculture. Folia Microbiol 66:159–170. https://doi.org/10.1007/s12223-021-00851-7

Bhuyan T, Mishra K, Khanuja M, Prasad R, Varma A (2015) Biosynthesis of zinc oxide nanoparticles from *Azadirachta indica* for antibacterial and photocatalytic applications. Mater Sci Semicond Process 32:55–61

Bjarnsholt T (2013) The role of bacterial biofilms in chronic infections. APMIS Suppl 136:1–51. https://doi.org/10.1111/apm.12099

Chausali N, Jyoti Saxena J, Prasad R (2022) Recent trends in nanotechnology applications of bio-based packaging. J Agric Food Res. https://doi.org/10.1016/j.jafr.2021.100257

Cowan MM, Warren TM, Fletcher M (1991) Mixed-species colonization of solid surfaces in laboratory biofilms. Biofouling 3:23–34. https://doi.org/10.1080/08927019109378159

De Freitas LF, Varca GHC, Batista JGDS, Lugão AB (2018) An overview of the synthesis of gold nanoparticles using radiation technologies. Nano 8:939. https://doi.org/10.3390/nano8110939

De-la-Pinta I, Cobos M, Ibarretxe J et al (2019) Effect of biomaterials hydrophobicity and roughness on biofilm development. J Mater Sci Mater Med 30:77. https://doi.org/10.1007/s10856-019-6281-3

Dong X, Ji X, Wu H et al (2009) Shape control of silver nanoparticles by stepwise citrate reduction. J Phys Chem C 113:6573–6576. https://doi.org/10.1021/jp900775b

Donlan RM (2002) Biofilms: microbial life on surfaces. Emerg Infect Dis 8:881–890. https://doi.org/10.3201/eid0809.020063

Dos Santos Ramos MA, Da Silva PB, Spósito L et al (2018) Nanotechnology-based drug delivery systems for control of microbial biofilms: a review. Int J Nanomedicine 13:1179–1213. https://doi.org/10.2147/IJN.S146195

Eftekhari A, Khalilov R, Kavetskyy T, Keskin C, Prasad R, Rosic GL (2023) Biological/chemical-based metallic nanoparticles synthesis, characterization, and environmental applications. Front Chem 11:1191659. https://doi.org/10.3389/fchem.2023.1191659

Figueroa JG, Borrás-Linares I, Lozano-Sánchez J, Segura-Carretero A (2018) Comprehensive characterization of phenolic and other polar compounds in the seed and seed coat of avocado by HPLC-DAD-ESI-QTOF-MS. Food Res Int 105:752–763. https://doi.org/10.1016/j.foodres.2017.11.082

Francolini I, Donelli G (2010) Prevention and control of biofilm-based medical-device-related infections. FEMS Immunol Med Microbiol 59:227–238. https://doi.org/10.1111/j.1574-695X.2010.00665.x

Gupta K, Hazarika SN, Saikia D et al (2014) One step green synthesis and anti-microbial and anti-biofilm properties of Psidium guajava L. leaf extract-mediated silver nanoparticles. Mater Lett 125:67–70. https://doi.org/10.1016/j.matlet.2014.03.134

Gupta N, Upadhyaya CP, Singh A, Abd-Elsalam KA, Prasad R (2018) Applications of silver nanoparticles in plant protection. In: Abd-Elsalam K, Prasad R (eds) Nanobiotechnology applications in plant protection. Springer International Publishing AG, pp 247–266

Inamuddin, Ahamed MI, Prasad R (2021) Advanced antimicrobial materials and applications. Springer Singapore. (ISBN: 978-981-15-7098-8) https://www.springer.com/gp/book/9789811570971

Ismail M, Prasad R, Ibrahim AIM, Ahmed ISA (2017) Modern prospects of nanotechnology in plant pathology. In: Prasad R, Kumar M, Kumar V (eds) Nanotechnology. Springer Nature Singapore Pte Ltd, pp 305–317

Jones SE, Versalovic J (2009) Probiotic Lactobacillus reuteribiofilms produce antimicrobial and anti-inflammatory factors. BMC Microbiol 9:35. https://doi.org/10.1186/1471-2180-9-35

Joshi S, Litake G (2013) Acinetobacter: an emerging pathogenic threat to public health. World J Clin Infect Dis 3(3):25–36. https://doi.org/10.5495/wjcid.v3.i3.25

Karygianni L, Ren Z, Koo H, Thurnheer T (2020) Biofilm matrixome: extracellular components in structured microbial communities. Trends Microbiol 28:668–681. https://doi.org/10.1016/j.tim.2020.03.016

Kavitha A, Doss A, Pole RPP, Pushpa Rani TPK, Prasad R, Satheesh S (2023) A mini review on plant-mediated zinc oxide nanoparticles and their antibacterial potency. Biocatal Agric Biotechnol. https://doi.org/10.1016/j.bcab.2023.102654

Khan HA, Baig FK, Mehboob R (2017) Nosocomial infections: epidemiology, prevention, control and surveillance. Asian Pac J Trop Biomed 7:478–482. https://doi.org/10.1016/j.apjtb.2017.01.019

Kisimba K, Krishnan A, Faya M, Byanga K, Kasumbwe K, Vijayakumar K, Prasad R (2023) Synthesis of metallic nanoparticles based on green chemistry and their medical biochemical applications: synthesis of metallic nanoparticles. J Renew Mater 11(6):2575–2591. https://doi.org/10.32604/jrm.2023.026159

Klaus T, Joerger R, Olsson E, Granqvist CG (1999) Silver-based crystalline nanoparticles, microbially fabricated. Proc Natl Acad Sci U S A 96:13611–13614. https://doi.org/10.1073/pnas.96.24.13611

Laurent S, Forge D, Port M et al (2010) Erratum: Magnetic iron oxide nanoparticles: synthesis, stabilization, vectorization, physicochemical characterizations, and biological applications (Chemical Reviews (2008) 108 (2064)). Chem Rev 110:2574. https://doi.org/10.1021/cr900197g

Li Y, Liu H, Song C et al (2013) The dehydration of fructose to 5-hydroxymethylfurfural efficiently catalyzed by acidic ion-exchange resin in ionic liquid. Bioresour Technol 133:347–353. https://doi.org/10.1016/j.biortech.2013.01.038

Lu J, Dreisinger DB, Cooper WC (1997) Cobalt precipitation by reduction with sodium borohydride. Hydrometallurgy 45:305–322. https://doi.org/10.1016/S0304-386X(96)00086-2

Martin C, Low WL, Gupta A et al (2015) Strategies for antimicrobial drug delivery to biofilm. Curr Pharm Des 21:43–66. https://doi.org/10.2174/1381612820666140905123529

Mercado DF, Weiss RG (2018) Polydimethylsiloxane as a matrix for the stabilization and immobilization of zero⇑valent iron nanoparticles. Applications to dehalogenation of environmentally deleterious molecules. J Braz Chem Soc 29:1427–1439. https://doi.org/10.21577/0103-5053.20180006

Monje DS, Ruiz OS, Valencia GC, Mercado DF (2022) Iron oxide nanoparticles embedded in organic microparticles from Yerba Mate useful for remediation of textile wastewater through a photo-Fenton treatment: ilex paraguariensis as a platform of environmental interest – part 1. Environ Sci Pollut Res 29:57127–57146. https://doi.org/10.1007/s11356-022-19744-4

Nakanishi K, Sakiyama T, Imamura K (2001) On the adsorption of proteins on solid surfaces, a common but very complicated phenomenon. J Biosci Bioeng 91:233–244. https://doi.org/10.1016/S1389-1723(01)80127-4

Osherov A, Prasad R, Chrzanowski W, New EJ, Brazaca L, Sadik O, Haynes CL, Maine E (2023) Responsible nanotechnology for a sustainable future. One Earth 6(7):763–766. https://doi.org/10.1016/j.oneear.2023.06.010

Palmer J, Flint S, Brooks J (2007) Bacterial cell attachment, the beginning of a biofilm. J Ind Microbiol Biotechnol 34:577–588. https://doi.org/10.1007/s10295-007-0234-4

Percival SL, Suleman L, Vuotto C, Donelli G (2015) Healthcare-associated infections, medical devices and biofilms: risk, tolerance and control. J Med Microbiol 64:323–334. https://doi.org/10.1099/jmm.0.000032

Permana AD, Anjani QK, Sartini et al (2021) Selective delivery of silver nanoparticles for improved treatment of biofilm skin infection using bacteria-responsive microparticles loaded into dissolving microneedles. Mater Sci Eng C 120:111786. https://doi.org/10.1016/j.msec.2020.111786

Prasad R, Kumar V, Prasad KS (2014) Nanotechnology in sustainable agriculture: present concerns and future aspects. Afr J Biotechnol 13(6):705–713

Prasad R, Pandey R, Barman I (2016) Engineering tailored nanoparticles with microbes: quo vadis. WIREs Nanomed Nanobiotechnol 8:316–330. https://doi.org/10.1002/wnan.1363

Prasad R, Bhattacharyya A, Nguyen QD (2017a) Nanotechnology in sustainable agriculture: recent developments, challenges, and perspectives. Front Microbiol 8:1014. https://doi.org/10.3389/fmicb.2017.01014

Prasad R, Kumar M, Kumar V (2017b) Nanotechnology: an agriculture paradigm. Springer Nature Singapore Pte Ltd. (ISBN: 978-981-10-4573-8)

Prasad R, Gupta N, Kumar M, Kumar V, Wang S, Abd-Elsalam KA (2017c) Nanomaterials act as plant defense mechanism. In: Prasad R, Kumar M, Kumar V (eds) Nanotechnology. Springer Nature Singapore Pte Ltd, pp 253–269

Prasad R, Siddhardha B, Dyavaiah M (2020) Nanostructures for antimicrobial and antibiofilm applications. Springer International Publishing. (ISBN 978-3-030-40336-2) https://www.springer.com/gp/book/9783030403362

Qureshi N, Annous BA, Ezeji TC et al (2005) Biofilm reactors for industrial bioconversion processes: employing potential of enhanced reaction rates. Microb Cell Factories 4:24. https://doi.org/10.1186/1475-2859-4-24

Rajakumar G, Thiruvengadam M, Mydhili G et al (2018) Green approach for synthesis of zinc oxide nanoparticles from Andrographis paniculata leaf extract and evaluation of their antioxidant, anti-diabetic, and anti-inflammatory activities. Bioprocess Biosyst Eng 41:21–30. https://doi.org/10.1007/s00449-017-1840-9

Rajivgandhi G, Maruthupandy M, Muneeswaran T et al (2019) Biosynthesized silver nanoparticles for inhibition of antibacterial resistance and biofilm formation of methicillin-resistant coagulase negative Staphylococci. Bioorg Chem 89:103008. https://doi.org/10.1016/j.bioorg.2019.103008

Ramanathan R, Field MR, O'Mullane AP et al (2013) Aqueous phase synthesis of copper nanoparticles: a link between heavy metal resistance and nanoparticle synthesis ability in bacterial systems. Nanoscale 5:2300–2306. https://doi.org/10.1039/c2nr32887a

Rao Y, Shang W, Yang Y et al (2020) Fighting mixed-species microbial biofilms with cold atmospheric plasma. Front Microbiol 11:1000. https://doi.org/10.3389/fmicb.2020.01000

Rehana D, Mahendiran D, Kumar RS, Rahiman AK (2017) Evaluation of antioxidant and anticancer activity of copper oxide nanoparticles synthesized using medicinally important plant extracts. Biomed Pharmacother 89:1067–1077. https://doi.org/10.1016/j.biopha.2017.02.101

Rudrappa T, Biedrzycki ML, Bais HP (2008) Causes and consequences of plant-associated biofilms. FEMS Microbiol Ecol 64:153–166. https://doi.org/10.1111/j.1574-6941.2008.00465.x

Sánchez MC, Toledano-Osorio M, Bueno J et al (2019) Antibacterial effects of polymeric PolymP-n active nanoparticles. An in vitro biofilm study. Dent Mater 35:156–168. https://doi.org/10.1016/j.dental.2018.11.015

Sauer K, Stoodley P, Goeres DM et al (2022) The biofilm life cycle: expanding the conceptual model of biofilm formation. Nat Rev Microbiol 20:608–620. https://doi.org/10.1038/s41579-022-00767-0

Schiebel J, Noack J, Rödiger S et al (2020) Analysis of three-dimensional biofilms on different material surfaces. Biomater Sci 8:3500–3510. https://doi.org/10.1039/D0BM00455C

Shah S, Famta P, Bagasariya D et al (2022) Nanotechnology based drug delivery systems: does shape really matter? Int J Pharm 625:122101. https://doi.org/10.1016/j.ijpharm.2022.122101

Shkodenko L, Kassirov I, Koshel E (2020) Metal oxide nanoparticles against bacterial biofilms: perspectives and limitations. Microorganisms 8:1–21. https://doi.org/10.3390/microorganisms8101545

Singh R, Paul D, Jain RK (2006) Biofilms: implications in bioremediation. Trends Microbiol 14:389–397. https://doi.org/10.1016/j.tim.2006.07.001

Sonawane JM, Rai AK, Sharma M, Tripathi M, Prasad R (2022) Microbial biofilms: recent advances and progress in environmental bioremediation. Sci Total Environ 824:153843. https://doi.org/10.1016/j.scitotenv.2022.153843

Srinivasan R, Santhakumari S, Poonguzhali P et al (2021) Bacterial biofilm inhibition: a focused review on recent therapeutic strategies for combating the biofilm mediated infections. Front Microbiol 12:676458. https://doi.org/10.3389/fmicb.2021.676458

Srivastava S, Usmani Z, Atanasov AG, Singh VK, Singh NP, Abdel-Azeem AM, Prasad R, Gupta G, Sharma M, Bhargava A (2021) Biological nanofactories: using living forms for metal nanoparticle synthesis. Mini-Rev Med Chem 21(2):245–265

Tanzil AH, Sultana ST, Saunders SR et al (2016) Biological synthesis of nanoparticles in biofilms. Enzym Microb Technol 95:4–12. https://doi.org/10.1016/j.enzmictec.2016.07.015

Thambirajoo M, Maarof M, Lokanathan Y et al (2021) Potential of nanoparticles integrated with antibacterial properties in preventing biofilm and antibiotic resistance. Antibiotics 10:111338. https://doi.org/10.3390/antibiotics10111338

Todhanakasem T (2013) Microbial biofilm in the industry. Afr J Microbiol Res 7:1625–1634. https://doi.org/10.5897/AJMR12.2146

Turkevich J, Copper PHJ (1951) A study of the nucleation and growth processes in the synthesis of colloidal gold. Discuss Faraday Soc 11:55–75

Ünal Turhan E, Erginkaya Z, Korukluoğlu M, Konuray G (2019) Beneficial biofilm applications in food and agricultural industry. In: Malik A, Erginkaya Z, Erten H (eds) BT—health and safety aspects of food processing technologies. Springer, Cham, pp 445–469

Velsankar K et al (2022) Green inspired synthesis of ZnO nanoparticles and its characterizations with biofilm, antioxidant, anti-inflammatory, and anti-diabetic activities. J Mol Struct 1255: 132420. https://doi.org/10.1016/j.molstruc.2022.132420

Vestby LK, Grønseth T, Simm R, Nesse LL (2020) Bacterial biofilm and its role in the pathogenesis of disease. Antibiotica 9:20059. https://doi.org/10.3390/antibiotics9020059

Wang LS, Gupta A, Rotello VM (2016) Nanomaterials for the treatment of bacterial biofilms. ACS Infect Dis 2:3–4. https://doi.org/10.1021/acsinfecdis.5b00116

Yadav LSR, Pratibha S, Manjunath K et al (2019) Green synthesis of AgZnO nanoparticles: structural analysis, hydrogen generation, formylation and biodiesel applications. J Sci Adv Mater Devices 4:425–431. https://doi.org/10.1016/j.jsamd.2019.03.001

Yuan L, Hansen MF, Røder HL et al (2020) Mixed-species biofilms in the food industry: current knowledge and novel control strategies. Crit Rev Food Sci Nutr 60:2277–2293. https://doi.org/10.1080/10408398.2019.1632790

Zheng S, Bawazir M, Dhall A et al (2021) Implication of surface properties, bacterial motility, and hydrodynamic conditions on bacterial surface sensing and their initial adhesion. Front Bioeng Biotechnol 9:643722. https://doi.org/10.3389/fbioe.2021.643722

Zottola EA, Sasahara KC (1994) Microbial biofilms in the food processing industry–should they be a concern? Int J Food Microbiol 23:125–148. https://doi.org/10.1016/0168-1605(94)90047-7

Microbial Enzymes in Nanoparticle Synthesis

7

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Abstract

Due to numerous applications of nanoparticles in biomedical, agricultural, bioremediation, and other fields, the field of nanotechnology is growing quickly. Compared to physical and chemical processes, nano-biosynthesis is a more environmentally benign way to create nanoparticles. Microorganisms, microbial enzymes, bioactive substances, and plant extracts are used in green nanosynthesis to create nanoparticles. In response to a toxic metal environment, microorganisms reduce heavy metals to nanoparticles as a type of defense response. The production of nanoparticles can take place intracellularly or extracellularly and involves enzymes such as cytochrome oxidase, iron reductase, NADH-dependent reductase, and fumarate reductase. This chapter gives an insight into the microbes and their enzymes involved in metal nanoparticle synthesis and its applications.

Keywords

Nanotechnology · Microbes · NADH reductase · Microbial enzymes · Metal nanoparticles

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7.1 Introduction

Nanotechnology: The branch that deals with the synthesis and applications of nanoscale structures, the size of nanoparticles ranges from 10 to 100 nm with properties like high surface-area-to-volume ratio, high reactivity, and magnified catalytic and biological properties (Rai et al. 2021). Nanoparticles find their applications in antimicrobial applications, drug delivery, biomedical applications, imaging, and biosensing (Suman et al. 2010; Saglam et al. 2021).

Based on their size, morphology, and physical and chemical characteristics, nanoparticles are divided into various categories Some of the classes of nanoparticles include carbon nanoparticles, metal nanoparticles, polymeric nanoparticles, and lipid-based nanoparticles (Khan et al. 2019).

The majority of the synthesis of nanoparticles is done by the physical and chemical methods which follow the top-down approach or the bottom-up approach. The biological, physical, and chemical approaches of nanoparticle synthesis belong to either the top-down or bottom-up methods.

The top-down method is a mechanical method of the gradual reduction in size by the breakdown of bulk materials into nanoparticles. Besides, the bottom-up method involves the formation of molecular structures in the nanoscale range by the assembly of atoms or molecules. The bottom-up method is generally followed in chemical and biological synthesis, whereas the top-down approach is generally preferred by the physical or chemical route (Gan and Li 2012; Lombardo et al. 2020).

The physical methods include vapor phase, lithography, pyrolysis, attrition, grinding, and milling; the chemical methods include sol-gel method, electrochemical reduction, microwave-assisted synthesis, and photocatalytic reduction; these methods involve the usage of toxic chemicals and generate baneful byproducts which may result in environmental pollution (Ahmed et al. 2016).

The biological approach to synthesizing nanoparticles—green nano-synthesis—has caught a lot of attention in recent years, the reason being, rapid nanoparticle synthesis, ease of culturing microbes in different conditions, ease of gene manipulation in microbes, and their eco-friendly nature compared to physical and chemical methods (Rai et al. 2021; Sarma et al. 2021).

Nanobiotechnology is an environment-friendly method using bacteria, fungi, viruses, algae, and plant extracts. As we know, microbes are ubiquitous and are responsible for causing harmful diseases. The fact that it is also involved in providing beneficial products such as antibiotics, organic acids, enzymes, and vitamins cannot be ignored. It is known for its important role in bioremediation, biotransformation, biosorption, and biomineralization (Koch et al 2023). However, microbial synthesis of nanoparticles is a relatively new and largely unexplored research area. Various prokaryotic (bacteria and actinomycetes), eukaryotic (such as yeast and fungi), and viral biogenic potentials have been investigated for the synthesis of nanoparticles (Singh et al. 2015; Sarma et al. 2021). This chapter mainly focuses on the microorganisms and microbial enzymes involved in nanoparticle biosynthesis.

7.2 Green Synthesis of Nanoparticles

Microorganisms are present everywhere and constantly exposed to diverse environments in their natural habitats. Examples of these environmental changes are nutrient limitation, osmolarity fluctuations, temperature, pH, desiccation, radiation, and other harmful agents such as the excessive amount of heavy metals and superoxides. When microbes are exposed to these adverse environmental conditions, they undergo a variety of transcription regulatory mechanisms, depending on the type of external stimuli the cell receives, an altered gene expression is performed by the cell, and a variety of proteins are produced to cope with the external environment. Exploring these mechanisms can help us understand the physiology of microorganisms and pave the way to their applications in environment protection, food industries, health care, and others (Gao et al. 2011).

In the environment, the biogeochemical cycles of metals and elements by microorganisms involve a process of biomineralization, studies have shown the implicit applications of nanoparticle synthesis through biomineralization (Liu et al. 2021a).

The use of microorganisms to synthesize nanoparticles (nanoparticles) has gained considerable interest worldwide. The microbial transformation of metals and metal salts into respective nanoparticles can be achieved under eco-friendly conditions, providing a better alternative to the physical and chemical methods of nanoparticle synthesis (Rajput et al. 2021; Prasad 2016, 2017, 2019a, b; Prasad and Aranda 2018).

The preferred sources for nanoparticle biosynthesis involve bacteria, fungi, and yeasts because of their easy cultivation, faster-multiplying rate, and ability to grow at various pH, temperature, pressure, and other parameters. Due to their adaptability to toxic metal environments, microorganisms possess the intrinsic ability to synthesize nanoparticles of inorganic materials by following reduction mechanisms via the intracellular and extracellular routes (Ajnai et al. 2014; Prasad et al. 2016, 2018; Srivastava et al. 2021; Kisimba et al. 2023).

The synthesis of nanoparticles is a result of a resistance or defense mechanism shown by a microbe when it encounters an environment with high metal concentration. The metal ions are reduced to their elemental form (nontoxic) through the enzymes produced by cellular activities. The site of nanoparticle synthesis may be intracellular or extracellular. The intracellular method involves the transport of metal ions inside the cell and reducing it by enzymatic action. The extracellular synthesis of nanoparticles involves capturing the metal ions on the cell surface and reducing the metal ions enzymatically. Another pathway involves the attachment of metal ions to microorganisms resulting in the formation of nanoparticles without the expenditure of energy (Zhang et al. 2011).

7.3 Microbial Enzymes in Nanoparticle Synthesis

Heavy metals like silica, gold, silver, selenium, cadmium, platinum, and alloys of heavy metals are biologically reduced to their respective metal nanoparticles. The bioproduction of metals involves the use of microbes like bacteria, actinomycetes,

cyanobacteria, fungi yeast and molds, and viruses. Various bioreduction pathways are followed by microorganisms to synthesize nanoparticles intracellularly or extracellularly (Egan-Morriss et al. 2022).

The microorganisms contribute to the biogeochemical cycling of trace elements by metal bioreduction on a wide range of metal species. Microbes perform certain mechanisms like bioaccumulation, chelation, metal complexation, extracellular precipitation, and biosorption for the synthesis of nanoparticles the enzymes involved in these processes include nitrate reductase, sulfite reductase, and cysteine desulfhydrase (Ovais et al. 2018; Prasad et al. 2016).

The advantage of green nano-synthesis involves the conversion of metal ions into zero-valent metals with the help of enzymatic reduction and excluding the use of toxic chemical reagents or long physical procedures. When a microorganism is employed for the synthesis of nanoparticles, the requirement it demands is a sterile environment to avoid cross-contamination, a suitable media, and ambient culture conditions which include optimum pH, temperature, light, and nutrients (Sachin and Karn 2021).

Microbial biomineralization and metal reduction occur through two processes where the site of extracellular nanoparticle synthesis is not controlled by the cell, whereas intracellular nanoparticle synthesis is a controlled process occurring inside the cell's compartments (Qin et al. 2020). The size, orientation, and texture of the nanoparticle can be controlled in the intracellular method by regulating factors such as the pH, salt concentration, temperature, concentration of the precursor, and reaction kinetics (Poulose et al. 2014).

7.3.1 Intracellular Synthesis of Nanoparticles

The pathway of intracellular synthesis in microbes like bacteria and fungi plays a remarkable role in the production of nanoparticles involving the production of enzymes and polysaccharides. Significantly among microorganisms, the bacterial members are most commonly employed for the bioreduction of Ag, Au, Cd, Se, Ni, Pt, Se, Hg, Fe, and other metals. The primary method for obtaining metallic ions from the media and reducing them inside the cell is interactions between intracellular enzymes and positively charged groups. Metal nanoparticles are deposited in the cytoplasmic membrane, the cell wall, and the periplasm when these structures are examined under a microscope. This is brought on by the passage of metal ions across the membranes and the creation of metal nanoparticles as a result of enzymatic reduction.

The mechanism through which the intracellular synthesis of nanoparticles occurs is unclear because different microbes, metals, and biomolecules are used in its synthesis. It is shown that due to the opposite charge: positive metal ions get trapped in the negatively charged layers of the microbial cell. These metal cations undergo reduction resulting in the emergence of their subsequent nanoparticles (Golinska et al. 2014; Manivasagan et al. 2016).

Several studies have shown the reduction of metal ions to nanoparticles by intracellular enzymes such as cytochrome oxidase. The mechanism involved in this reduction involves electron transport across cytoplasmic components such as NADH, NADPH, proteins, organic acids, and vitamins. Unlike chemical and physical nanoparticle synthesis methods, green nanoparticle synthesis mechanisms do not require stabilizers. Intracellular reductase enzymes are involved in the formation and stabilization of nanoparticles in the following ways (1) reduction of M^{2+} to M^{+} in the cytoplasm leading to the formation of metal nanoparticles, (2) direct reduction of heavy metals into nanoparticles further in the cytoplasm or periplasm by periplasmic reductase (Klaus et al. 1999; Mishra et al. 2016; Lv et al. 2018; Siddiqi et al. 2018).

The magnetotactic bacteria mostly belong to the α-Proteobacteria group following anaerobic or microaerophilic metabolism, comprises of organelles called magnetosomes which help in the navigation of the earth's magnetic field. Magnetosomes contain magnetic crystals of magnetite or greigite, which are surrounded by membranes made of phospholipids, proteins, and glycolipids. Magnetosomes are the natural magnetic nanoparticles synthesized by magnetotactic bacteria in nature, their synthesis depends on a wide range of factors like environmental stress, cell proliferation cycle, and cellular stress (Vargas et al. 2018).

The alpha proteobacterium *Magnetospirillum gryphiswaldense* synthesizes natural magnetic nanoparticles consisting of a monocrystalline core of magnetite (Fe_3O_4) enveloped by a protein-containing phospholipid bilayer. The bacteria follow a highly controlled biomineralization process due to which the naturally synthesized nanoparticles exhibit uniform size, shape, high purity, and strong magnetic properties (Brachhold et al. 2017).

In bacteria like *Magnetospirillum magneticum,* the encapsulation of Fe_2O_3 nanoparticles is carried out by intracellular magnetosomes, with the help of an enzyme iron reductase and ferritin protein. The formation of magnetosomes involves the transport of iron through vesicles to the outer layers of the bacterial cell leading to magnetosomes being aligned like a chain, later maturing into crystals (Kuzajewska et al. 2020).

The research on the biosynthesis of gold nanoparticles was first conducted by Beveridge and Murray in 1980 on the bacterium *Bacillus subtilis.* Later many research studies have worked on different bacteria for investigating the synthesis and applications of gold nanoparticles in the field of biomedicine it was found that gold nanoparticles (AuNPs) find their applications in diagnostics, and therapeutics, and also show antimicrobial action.

In a study, the effect of pH in relation to the synthesis of gold nanoparticles was studied. It was seen that, in a mesophilic bacterium *Shewanella* sp., the gold nanoparticle size ranging from 10 to 20 nm was observed in the periplasmic space of the bacterial cell. The size and site of nanoparticles synthesis were influenced by the pH of the solution, at a neutral pH-7 the synthesised AuNPs size was in the range of 10–20 nm and the site of synthesis is intracellular, but when the pH of the solution was dropped to 1 the nanoparticle size increased to 50–500 nm and the site of synthesis was extracellular. A similar pattern of nanoparticles biosynthesis in response to pH was also seen in the bacterium *Rhodopseudomonas capsulate,* by

He et al., in their study they subjected aqueous chloroauric acid solution to a range of pH from 4 to 7 using the bacterium *Rhodopseudomonas capsulate* it was observed by them that spherical gold nanoparticles ranging in the size from 10 to 20 nm were formed at a pH of 7.0, whereas at a pH of 4 gold nanoplates were formed, perhaps this study shows the influence of pH on the size, shape, and site of nanoparticle biosynthesis in a bacterium (He et al. 2008).

Gajbhiye et al. (2009) worked on the synthesis of silver nanoparticles using the fungus *Verticillium species.* Due to the electrostatic interaction between negatively charged carboxylate enzymes of the fungal cell and the positively charged silver ions, the reduction of silver ions takes place leading to silver nanoparticle synthesis beneath the surface of the cell wall.

Bacterial nanocellulose has biomedical applications such as antibacterial action, certain drug delivery systems, the field of tissue engineering, and the field of biosensors (supporting immobilization of nanocomposites and biological recognition elements) (Saxena and Brown 2005). Aerobic acetobacteria, such as the genus Gluconacetobacter, the most effective bacteria for producing nanocellulose, form a three-dimensional network of cellulose nanofibrils called bacterial nanocellulose. Bacterial nanocellulose has greater purity, crystallinity, and mechanical stability than nanocrystalline and nano-fibrillated cellulose (Golmohammadi et al. 2017).

The Blue-Green Algae Bhadury Wright (2004) listed the applications of cyanobacteria in biotechnology. Lately, cyanobacteria have obtained much attention as a source of diverse bioactive compounds and have been considered one of the most promising groups of organisms in the production of antibacterial, antifungal, antiplasmodial, and antiviral agents. The synthesis of metal nanoparticles in cyanobacteria is a newly emerging area of research it has been investigated that a few cyanobacterial members like *Plectonema* sp., *Calothrix* sp., *Anabaena* sp., and *Leptolyngbya* sp have shown the ability to synthesize gold nanoparticles (Govindaraju et al. 2008).

A study was conducted by Younis et al. on the cyanobacterial member *Synechocystis* sp. It is a unicellular organism belonging to the family Merismopediacea. It was investigated that *Synechocystis* sp. has the ability to produce silver nanoparticles from $AgNO_3$ solution. The study also proved the applications of the silver nanoparticles synthesized by *Synechocystis* sp. in angiogenesis promotion in diabetic wounded mice, antimicrobial, anti-inflammatory, and antimicrobial (Younis et al. 2022).

Genetic engineering is the area of biology that involves the manipulation and production of recombinant gene products which are of great importance to mankind, this method of gene manipulation or recombination can be done in prokaryotes and lower eukaryotes with ease.

Chen et al. were the first to make use of genetic engineering in nanobiotechnology. In their study, the researchers isolated the gene phytochelatin synthase along with modified g-glutamylcysteine synthetase (GSHI*) from *Schizosaccharomyces pombe* (SpPCS) into *Escherichia coli* JM109.

Schizosaccharomyces pombe when grown in a toxic metal environment has the ability to form nanoparticles, the enzyme g-glutamylcysteine synthetase catalyzes the synthesis of glutathione (GSH) which is the precursor for phytochelatin, this compound behaves as an agent for capping in the synthesis of cadmium nanocrystals in *S. pombe*. This property of cadmium nanoparticle synthesis was genetically engineered in *E. coli* JM109 and *E. coli* R189 which showed positive results forming cadmium nanocrystals in the size range of 3–4 nm (Kang et al. 2008). In another study *Klebsiella aerogenes*, yeasts such as *Schizosaccharomyces pombe* and *Candida glabrata* were studied by Holmes et al. for the production of cadmium sulfide nanoparticles. The effect of buffer composition of the growth medium on the growth and formation of the cadmium sulfide crystals were studied in *k.aerogenes* (Holmes et al. 1995).

It has been suggested by Sinha et al. that strains of *Enterobacter* sp. could be helpful for mercury clean up and nanoparticle manufacturing. Low concentrations of mercury with a pH of 8.0 in the culture medium encourage the creation of 2–5 nm sized, spherical, and monodispersed intracellular Hg nanoparticles.

NPs of tellurium and selenium—selenium is used in photocopiers and microelectronic circuitry because of its photo-optical and semiconducting characteristics. A promising transition of selenite (Se_2O_3) to elemental selenium (Se^0) was demonstrated by *Stenotrophomonas maltophilia* SELTE02, which concentrated selenium particles inside the cell's cytoplasm or in the extracellular space. Additionally, it has been discovered that *Desulfovibrio desulfuricans*, *Rhodospirillum rubrum*, and *Enterobacter cloacae* SLD1a-1 all reduce selenite to selenium inside as well as outside the cell, with a wide range of nano-morphologies including spherical, fibrillar, and granular structure or small atomic aggregates (Narayanan and Sakthivel 2010).

7.3.2 Extracellular Nanoparticle Synthesis

In comparison with the intracellular synthesis of nanoparticles, the extracellular NPs synthesis is beneficial as the bioproduction of heavy metals occurs outside or on the cell surface of the microorganism, the microorganisms absorb heavy metal ions onto their cell surface and convert them into nanomaterials with the aid of enzymes and other bioactive compounds (Li et al. 2011).

Nonetheless, the extracellular site of synthesis of metal nanoparticles is a desirable feature due to easy extraction in situations involving extensive scale of manufacturing. Exopolysaccharides (EPS) are negatively charged and released by microorganisms. Alternatively, few peripheral proteins aid in sequestering metal ions via ionic interactions which serve as nucleation sites for biologically driven mechanisms. Metal cation uptake occurs via specialized ion channels or transporters in membrane-bound vesicles for intracellular biofabrication. One good example for the interplay between internal and external processes is magnetite biomineralization in magnetotactic bacteria. Metal complex formation is also facilitated by certain metal-binding proteins such as phytochelatins and metallothioneins (Cobbett and Goldsbrough 2002).

The biosynthesis of extracellular nanoparticles includes the following steps—selecting a suitable medium for microbial growth and maintaining optimum pH and temperature. The culture medium is centrifuged to separate the supernatant containing the microbial reductase enzymes that catalyze the formation of nanoparticles. Furthermore, the supernatant is transferred to a separate vessel for metal ion reduction leading to further nanoparticle formation.

The work of Carlos Pernas et al. shows the effect of the concentration of NaCl on the speed of synthesis of nanoparticles by *Pseudomonas alloputida.* It was observed that the media containing NaCl showed faster silver nanoparticle synthesis, whereas the media without NaCl showed a slower rate of nanoparticle synthesis (Pernas-Pleite et al. 2022).

The members of Actinomycetes can produce different bioactive compounds like antibiotics with different chemical structures and mechanisms of action apart from having biomedical applications and the members of actinomycetes have applications in the synthesis of nanoparticles. Ahmad and co-workers investigated an alkalothermophilic actinomycete *Thermomonospora* sp. can synthesize gold nanoparticles (AuNP) from gold ions under alkaline conditions.

Biosynthesis of silver nanoparticles of size 40 nm extracellularly was observed in *Bacillus licheniformis* cellfree extract (Kalishwaralal et al. 2008). Saifuddin et al. investigated a unique method for the green biosynthesis of silver nanoparticles by employing a mixture of microwave irradiation in water and *Bacillus subtilis* culture supernatant. They reported the extracellular biosynthesis of uniformly dispersed silver NPs (5–50 nm) using *B. subtilis* supernatants, but they also used microwave radiation to speed up the reaction and reduce NP aggregation, which may provide uniform heating around the NPs and aid in the further maturation of particles without accumulation (Saifuddin et al. 2009).

Silver nanoparticles (6–13 nm) using five psychrophilic bacteria (*Phaeocystis antarctica*, *Pseudomonas proteolytica*, *Pseudomonas meridiana*, *Arthrobacter kerguelensis*, and *Arthrobacter gangotriensis*) and two mesophilic bacteria (*Bacillus indicus* and *Bacillus cecembensis*) were synthesized and showed a shelf life of 8 months. Temperature, pH, or the type of bacteria used to prepare the supernatant all appeared to affect the production and stability of silver nanoparticles, this study provided important evidence that different bacterial species produce different components which later in the cell-free culture supernatants support the synthesis of silver nanoparticles (Shivaji et al. 2011).

It is believed that oxidoreductases and quinones, among other enzymes, are crucial in the production of nanoparticles. In a study on the oxidoreductase enzyme, Mandal et al. and Jha et al. found that the enzyme is sensitive to pH, activating the oxidase under low pH settings and the reductase under high pH conditions. It has been demonstrated that the use of Cerium oxide nanoparticles mimics oxidoreductase enzymes by catalyzing the breakdown of organic substrates and reactive oxygen species (Baldim et al. 2020).

It is of great importance to study marine resources for the production of various metallic nanoparticles, as marine microorganisms can easily adapt to harsh environmental conditions. Additionally, marine bacteria are known to produce active

biomolecules that are beneficial to human health. This study focuses on the innovative eco-friendly microbial production of AuNPs by *P. haeundaensis* strain BC74171T. Synthesis of astaxanthin gives the marine bacterium *Paracoccus haeundaensis* an orange pigment and rod-like structure (Manivasagan et al. 2015). This is the first report on the extracellular synthesis of AuNPs from the supernatant of a new marine bacterium. Controlling morphology and maximizing nanoparticle production depends on various reaction parameters such as reaction time, temperature, and reactants (Patil et al. 2019).

In another study conducted by Rajasekar et al., it was observed that extracellular metabolites of marine bacteria (*Rastrelliger kanagurta*, *Selachimorpha* sp., and *Panna microdon*) were used for the synthesis of gold nanoparticles (Rajasekar et al. 2020).

According to Zafrilla et al. (2010), haloarchaea, which make up the majority of the population in saltwater body settings with salinities up to 300 g/L, are responsible for the water's red hue. These organisms increase the potassium ion concentration in their cells to maintain osmotic balance in the hypersaline environment (Oren 2008). Haloarchaea is also known to come into contact with metals in their environment, although little is known about how they react to metals (Srivastava et al. 2013). Model organism Halobacterium sp. strain NRC-1 possesses metal resistance genes annotated (Ng et al. 2000), however, only arsenic resistance has been experimentally proven (Wang et al. 2004). The third domain of life, archaea, is a member of the halophilic archaea (Haloarchaea), the subject of study by Srivastava and colleagues, who found that *H. salifodinae* can reduce Ag^{+} to elemental Ag0 nanoparticles (Srivastava et al. 2013).

Extracellular Mycosynthesis of Nanoparticles

Fungi are considered to be a diverse biological system, including the ability to synthesize metal nanoparticles inside and outside of the cell. Mostly fungi are preferred above other microorganisms due to their ubiquitous presence in the environment. A variety of fungal species like *Penicillium fellutanum*, *Fusarium semitectum*, *Fusarium solani*, *Cladosporium cladosporioides*, *Aspergillus fumigates*, and *Coriolus versicolor* have been explored for extracellular synthesis of silver nanoparticles (Ingle et al. 2009; Balaji et al. 2009).

Fungi exhibit many advantages over other biological producers for nanoparticle synthesis, including production of bioactive metabolites, enhanced production, and high synthesis (Castro-Longoria et al. 2011; Alghuthaymi et al. 2015; Aziz et al. 2016, 2019; Shelke et al. 2023). Fusarium is one such fungal member which has been used for the synthesis of many metal nanoparticles (Yadav et al. 2015; Ahmad et al. 2003). The employment of *Fusarium* spp in the synthesis of nanoparticles is because they come with the advantage of the ease in culturing, produce nanoparticles in colloidal form, follow both extracellular and intracellular routes of nanoparticle synthesis, produce a variety of nanoparticles and bioactive compounds, and easy downstream processing (Rai et al. 2021).

The extracellular mycosynthesis involves the production of various metabolites by fungi (*Fusarium* spp.). These metabolites include proteins, polysaccharides,

enzymes, alkaloids, flavonoids, organic acids, and phenolic compounds. When the fungal cell is exposed to a stressful environment (heavy metal environment), these compounds help in coping with the stress leading to the formation of metal nanoparticles (Srivastava et al. 2019; Koch et al. 2023).

The exact mechanism of extracellular nanoparticle synthesis remains unclear, but the involvement of the NADH-dependent denitrification enzyme is widely accepted. It was observed that in *F.oxysporum*, the NADH-dependent nitrate reductase enzyme caused the reduction of silver ions in an aqueous solution to silver nanoparticles (AgNPs) (Ahmad et al. 2003).

Among fungi, *Aspergillus flavus*, when incubated with silver nitrate solution, has the ability to synthesize silver nanoparticles on the cell wall surface. Extracellular nanoparticles are stabilized by enzymes and reducing agents secreted by the fungus. A similar approach to reducing nanoparticles via enzymes has been observed in *Bacillus licheniformis*. The NADH cofactor and NADH-dependent enzymes secreted by bacteria play a role in the formation of silver nanoparticles (Kalimuthu et al. 2008).

In a study conducted by Pei-jun Li et al. (2015) on the fungi *Aspergillus japonicus* PJO1, the organism was used for the production of a multienzyme complex following solid-state fermentation. An extracellular extract was derived containing enzymes such as xylanase, pectinase, CMcase, and other reducing sugars and carbohydrates were also found to be present and involved in the synthesis of silver nanoparticles.

Other fungal enzymes involved in green nano synthesis include hydrolase (cellobiohydrolase D), esterase (acetyl xylan esterase), and glucosidase enzymes (Rai et al. 2021), other bioactive compounds like toluquinones, and hydroxy, methoxy derivatives of benzoquinones have shown to play a role in the synthesis of nanoparticles in lower fungi like Ascomycetes.

Algae in the Biosynthesis of Nanoparticles

The production of nanoparticles from algae is a bottom-up process. The most common nanoparticles made using algae include gold, silver, copper oxide, and zinc oxide. First, an algae extract is prepared, preferably an aqueous or ethanolic extract. When the extract is combined with a specific metal solution (specific to the type of nanoparticles desired), the algae reduce the metal ions to produce metal nanoparticles. Electrostatic interactions between positively charged functional groups or peptides in algae and negatively charged ions in the metal solution cause reduction (Vijayaraghavan et al. 2011; Aziz et al. 2014, 2015).

The degradation of dyes is one of the uses for nanoparticles made from algae. In a few studies, it was discovered that silver particles made from the red alga *Hypnea musciformis* work as a photocatalyst and aid in the decomposition of the dye methyl orange when exposed to light (Ganapathy Selvam and Sivakumar 2015). Malachite green dye can be broken down by silver nanoparticles made from the red algae *Gracilaria corticate*. Rhodamine B and Sulforhodamine are discovered to be

degraded by brown algal *Turbinaria conoides* and *Sargassum tenerrimum* gold nanoparticles (Poornima and Valivittan 2017).

7.4 Applications of Nanoparticles

The applications of nanoparticles are immense due to their unique shape, size, and biophysical properties. Nanoparticles find their applications in the food industry, pharmaceuticals-drug delivery, biosensors, cancer therapy, disease diagnosis (theranostics), gene delivery, heavy metal recycling, etc. (Koul et al. 2021; Thangadurai et al. 2020a, b).

7.5 Application of Nanoparticles in the Food Industry

The applications of nanoparticles in the food industry are food packaging and food processing. Among metal NPs, silver nanoparticles are efficiently used because of their antimicrobial activity.

Edible coatings encoded with nanomaterials have also demonstrated potential in food preservation and packaging. Fruits and vegetables wrapped in perishables can be eaten during storage and transportation. Longer transport and storage times can lead to higher postharvest losses as well as reduced nutritional and cosmetic quality of the item due to active respiratory processes. Preventing this loss of nutritional value and mass is essential in prolonging the shelf life of fresh food products. Temperature and relative humidity are the two main issues (He et al. 2008).

Because the material used for food packaging comes into direct contact with the food substance, it is an important phase in the food manufacturing process. In recent years, the transition from traditional to cutting-edge food packaging techniques has happened quickly. Nanoclay is one of the nanomaterials that is utilized in food packaging because of its low cost, mechanical, and thermal barrier qualities (Karlo et al. 2023; Chausali et al. 2022).

Inorganic (metal and metal oxide NPs), organic (mostly natural product NPs), and mixed nanomaterials have all been tested in the food business (i.e., clay). The use of titanium dioxide nanoparticles as a food additive (white color pigment), disinfectant, and flavor enhancer is also well-researched. Natural products (NPs) are typically used in the food business as ingredients or supplements as well as delivery systems.

Due to the ultra-sensitive characteristics of nanomaterials, other applications in food contact packaging include the detection of pesticides, diseases, and poisons (He et al. 2019). These applications are also actively being researched and developed. According to a recent study by Sahoo et al. (2018), ZnO quantum dots (QD) can be utilized to detect a variety of pesticides, such as aldrin.

7.5.1 Applications of Nanoparticles in Agriculture

Chemical pesticides are used in the control of pests and plant pathogens in agriculture. Chemical pesticides include DTD, BHC, aldrin, dieldrin, captan, 2,4-D, etc, the problem with pesticides is their recalcitrant nature. Pesticides can also establish themselves in food, harm pollinators, and cause harm to our ecosystems. It is proven that pesticides have been a cause of reproductive and developmental effects, cancer, kidney and liver damage, and endocrine disruption in order to avoid the use of pesticides the agriculture industry needs an eco-friendly alternative where nanobiotechnology can prove to be of great use.

Macronutrients and micronutrients are two categories of nano-fertilizer, which are mineral nutrients produced mostly through encapsulation with NPs. Different nanomaterials have been used to encapsulate macronutrients like carbon (C), nitrogen (N), potassium (K), phosphorus (P), calcium (Ca), sulfur (S), and magnesium (Mg) in order to increase crop fertilizer uptake and reduce fertilizer outflow. While these substances are easily transported into plant cells, fertilizers enclosed by nanoparticles, particularly porous nanoparticles, are scarcely destroyed by external elements such as rain and wind. This characteristic increases the physical and chemical characteristics of the soil while delaying the release of fertilizer. It's interesting to note that all nanomaterial fertilizers have smaller particle sizes and more particles per unit, which results in high specific surface areas.

Since their commercial production, herbicides, which are frequently employed to eradicate weeds, have demonstrated a variety of negative side effects, including toxicity to living things, water pollution, soil contamination, and air pollution. Herbicides can be encapsulated by nanoparticles, which has the potential to reduce environmental herbicide residues and improve weed control effectiveness. Among many types of NPs, solid lipids are the most ideal nanocarriers for nano-herbicides due to their excellent chemical stability and easy metabolism (Liu et al. 2021b).

Nanotechnology has been used in various agricultural production processes, such as seed germination and plant growth, to improve crop yield and quality (Prasad et al. 2014, 2017a, b). Nanoparticles such as carbon nanotubes, silicon dioxide (SiO_2), zinc oxide (ZnO), titanium dioxide (TiO_2), and even gold (Au) NPs have been shown to improve seed germination in agricultural plants such as tomatoes, wheat, rice, and pearl millet. It has recently been shown to promote soybeans, barley, and corn. For example, silver nanoparticles dramatically improved the germination rate of pearl millet compared to untreated plants.

Mediating abiotic stress tolerance through nanotechnology Due to their stemless nature, plants are highly susceptible to external stimuli such as cold, heat, drought, salinity, alkaline soil, and metal contamination. According to several studies, various nanomaterials, such as ZnO NPs, TiO_2 NPs, Fe_2O_3 NPs, silicon (Si) NPs, nanoceria, graphene oxides, and MWCNTs, mitigate the negative effects of abiotic stress on crop plant species like potato, barley, alfalfa, sugar beet, flax, maize, Arabidopsis thaliana, and rice. The NPs mainly increased antioxidant enzyme activity and plant tolerance to abiotic stress by scavenging reactive oxygen species. Recent studies have demonstrated that graphene nanoparticles (NPs) enhance the antioxidant

enzyme activity of alfalfa and increase fresh weight, dry weight, and seedling weight to increase tolerance of alfalfa under alkaline conditions.

7.5.2 Applications of Nanoparticles in Theranostics

Theranostics The unification of therapy and diagnostics is theranostics. Theranostic nanoparticles are extensively being used in disease diagnosis, identification of the stage of disease, reporting the disease location, and treatment. Apart from these, the nanoparticles can carry the drug to the site of infection by the means of external stimulation (Chen et al. 2014).

Magnetotactic bacteria carry a natural ability to synthesize nanoparticles of iron oxide (magnetite) and iron sulfide (greigite) in their lipid layers. The structures in which nanoparticles reside are called magnetosomes, and these nanoparticles help position bacterial cells for their nutritional needs. Nanoparticles of magnetite and greigite can be harvested from bacterial cells and they can be used for medical applications such as drug delivery and drug development (Tanaka et al. 2006; Dai et al. 2017; Long et al. 2016).

The combination of gold nanorods with folic acid proved to be an excellent theranostic agent in locating and destructing breast cancer cells (Nima et al. 2019). Silver nanomaterials have vast applications in the biomedical area. AgNPs are used in wound dressing for faster healing of the wound and reduction in the bacterial load (Huang et al. 2007), antibiotics are used in catheters to control the bacterial load and biofilm formation, the use of antibiotics in catheters had led to the gain of antimicrobial resistance in bacteria, and a study proved the use of silver nanoparticles in catheters to reduce the number of *Staphylococcus aureus* (Fichtner et al. 2010).

Among nanoparticles, gold and silver NPs have a lot of applications however due to their cost the use of gold and silver is restricted. On the other hand, copper nanoparticles are used widely as they are cost-effective and have many biomedical applications. Copper nanoparticles can be used as antimicrobial agents (Ullah et al. 2017; Yadav et al. 2017).

7.5.3 Role of Nanoparticles in Bioremediation

The process that involves biological systems like bacteria, fungi, algae, and plants for the removal of environmental pollutants like pesticides, chemical fertilizers, herbicides, heavy metals, etc. is called bioremediation.

The development of metallic (mono/bi) nanomaterials including nanowires, nanorods, and nanospheres in conjunction with electrochemical biosensors offers different benefits such as high accuracy and easy detection of heavy metals (Gunti et al. 2015).

Eukaryotic microorganisms have an advantage over prokaryotic cells in the detection of pesticides and heavy metals, which is another area where microbial

biosensors have potential applications (Gutiérrez et al. 2015). This is mostly attributable to the benefit of creating whole-cell biosensors with selective and sensitive applications linked to the detection of heavy metal and pesticide toxicity (Gutiérrez et al. 2015). Future applications for these microbial biosensors (Sun et al. 2015) will include monitoring environmental metal pollution and the creation of renewable energy.

Metal nanoparticles like TiO_2, ZnO, and other nobel nanoparticles have shown their role in the biodegradation of organic pollutants in the environment. The combination of gold and palladium nanoparticles behaves as a catalyst in the oxidation of mercury and bioremediation of trichloroethane which is a water pollutant. The levels of carbon monoxide and oxides of nitrogen can be detected in the environment by employing silver nanoparticles as biosensors (Tripathi et al. 2018).

Carbon nanotubes (CNTs), magnetic nanoparticles, noble metal nanomaterials, and quantum dots are nanomaterials used for monitoring water quality, particularly those utilized for the detection of trace contaminants and pathogens (Kumari and Singh 2016; Xue et al. 2017).

7.5.4 Applications of Nanoparticles in Cancer

With more than 10 million deaths per year, cancer is one of the main causes of death worldwide. Current cancer treatments include surgery, radiation, and the use of chemotherapeutic medications, which frequently cause toxicity in patients and the death of healthy cells (Zaimy et al. 2017).

Gold Nanoparticles in Cancer Because of their surface plasmon resonance, optical, and tuneable features, gold nanoparticles have attracted the interest of scientists for their potential use as drug carriers. The wide variety of core sizes they can be manufactured in (1–150 nm) makes it simpler to manage their dispersion. Gold nanoparticles can be easily changed since they have a negative charge on their surface. This indicates that numerous biomolecules, like medicines, targeting ligands, and genes, can be added to easily functionalize them. Additionally, gold nanoparticles are a great choice to be used as medication carriers due to their biocompatibility and non-toxicity (Ajnai et al. 2014).

Patil's study highlights the novel strain *P. haeundaensis* BC74171T for environmentally friendly microbial synthesis of AuNPs. According to this study, this is the first report on the extracellular synthesis of AuNPs using a novel marine bacterial supernatant. Various reaction parameters such as reaction time, temperature, and reactant concentrations are important to control the morphology and optimize nanoparticle production. The AuNPs synthesized in this study were spherical with an average size of 20.93 nm. Haeundensis BC74171T. The prepared AuNPs are nontoxic to normal human cells and have concentration-dependent toxic and antiproliferative effects on cancer cells (Patil et al. 2019).

A promising nano-targeted therapy for ovarian cancer is provided by AgNPs, which are highly stable and greatly reduce the proliferation of ovarian cancer cells and tumor growth in tumor-bearing mice (Figs. 7.1 and 7.2; Table 7.1).

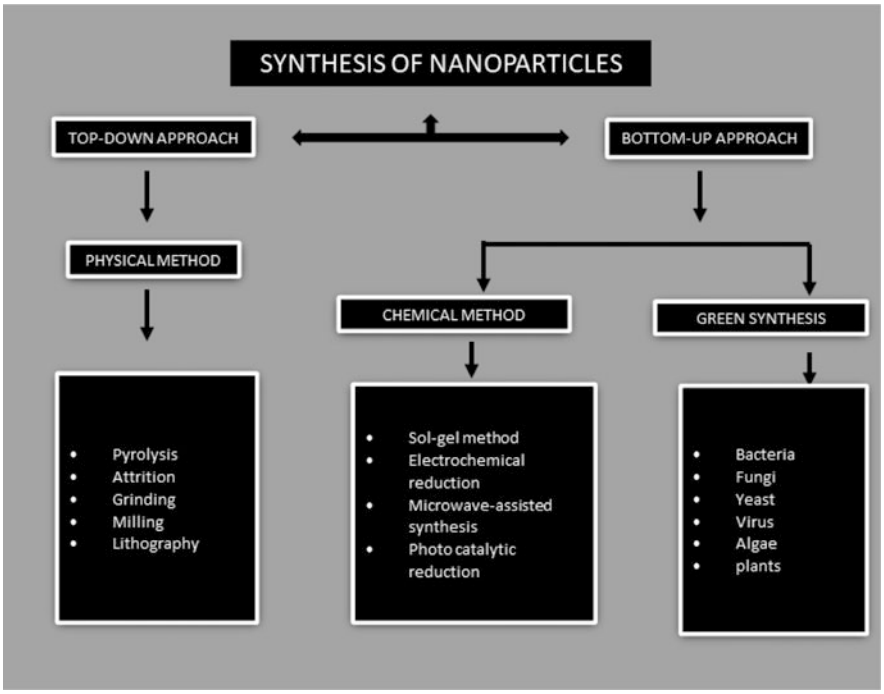

Fig. 7.1 Methods of nanoparticle synthesis

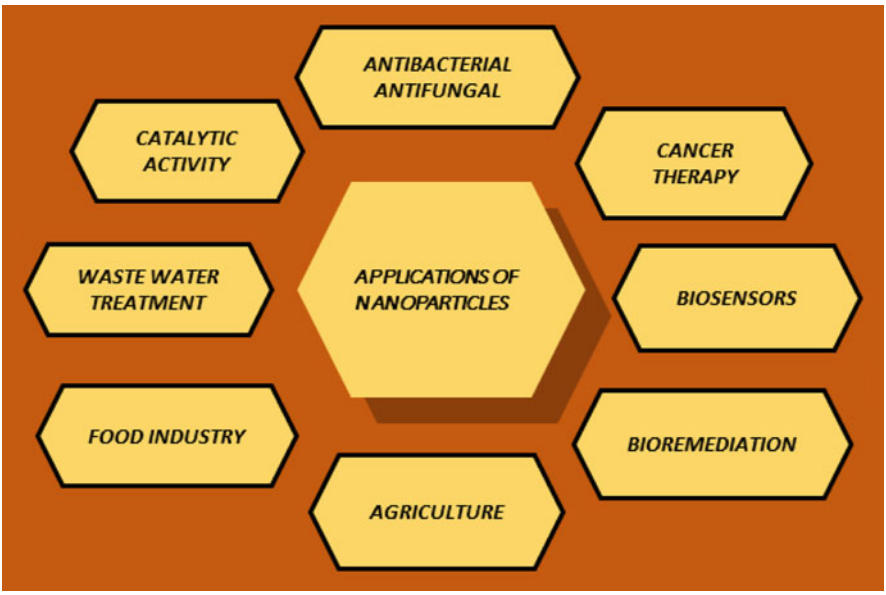

Fig. 7.2 Applications of nanoparticles

Table 7.1 Microbes involved in the synthesis of metal nanoparticles and their site of synthesis

Desulfovibrio desulfuricans	SeNP	Intracellular	Narayanan and Sakthivel (2010)
Rhodospirillum rubrum, *Enterobacter cloacae* SLD1a	SeNP	Intracellular	Narayanan and Sakthivel (2010)
Enterobacter cloacae SLD1a-1	SeNP	Intracellular	Narayanan and Sakthivel (2010)
Pseudomonas alloputida	AgNP	Extracellular	Pernas-Pleite et al. (2022)
Thermomonospora sp.	AuNP	Extracellular	Ahmad et al. (2003)
Bacillus licheniformis	AgNP	Extracellular	Kalishwaralal et al. (2008)
Phaeocystis antarctica	AgNP	Extracellular	Shivaji et al. (2011)
Pseudomonas proteolytica	AgNP	Extracellular	Shivaji et al. (2011)
Bacillus cecembensis	AgNP	Extracellular	Shivaji et al. (2011)
Bacillus indicus	AgNP	Extracellular	Shivaji et al. (2011)
Arthrobacter gangotriensis	AgNP	Extracellular	Shivaji et al. (2011)
Arthrobacter kerguelensis	AgNP	Extracellular	Shivaji et al. (2011)
Pseudomonas meridiana	AgNP	Extracellular	Shivaji et al. (2011)
Paracoccus haeundaensis	AuNP	Extracellular	Manivasagan et al. (2015)
Penicillium fellutanum	AgNP	Extracellular	Ingle et al. (2009), Balaji et al. (2009)
Fusarium semitectum	AgNP	Extracellular	Ingle et al. (2009), Balaji et al. (2009)
Aspergillus fumigates	AgNP	Extracellular	Ingle et al. (2009), Balaji et al. (2009)
Cladosporium cladosporioides	AgNP	Extracellular	Ingle et al. (2009), Balaji et al. (2009)
Fusarium solani	AgNP	Extracellular	Ingle et al. (2009), Balaji et al. (2009)
Aspergillus flavus	AgNP	Extracellular	Kalimuthu et al. (2008)

7.6 Conclusion and Future Aspects

Metallic nanoparticles produced by microorganisms are highly ordered structures composed of metal atoms and metal oxides and are expected to have wide-ranging applications in nanotechnology. This chapter enlightens the role of microorganisms, microbial enzymes, and their bioactive compounds used in the synthesis of nanoparticles.

Nanotechnology has found its way into almost all areas of biology majorly targeting the field of biomedicine.

The world needs newer technologies to combat new calamities arising at a faster pace, the sudden occurrence of the pandemic COVID-19 is the best example, microbial nanotechnology can be used to bring out sophisticated methods or

techniques to deal with antibiotic resistance, disease diagnosis early stages, vaccinations, elimination of harmful compounds from the environment. This is a booming area in biology where there is room for many as quoted by Richard Feynman "There is plenty of room at the bottom".

References

Ahmad A, Mukherjee P, Senapati S, Mandal D, Khan MI, Kumar R, Sastry M (2003) Extracellular biosynthesis of silver nanoparticles using the fungus Fusarium oxysporum. Colloids Surf B Biointerfaces 28(4):313–318. https://doi.org/10.1016/S0927-7765(02)00174-1

Ahmed S, Ahmad M, Swami BL, Ikram S (2016) A review on plants extract mediated synthesis of silver nanoparticles for antimicrobial applications: a green expertise. J Adv Res 7(1):17–28. https://doi.org/10.1016/j.jare.2015.02.007

Ajnai G, Chiu A, Kan T, Cheng C-C, Tsai T-H, Chang J (2014) Trends of gold nanoparticle-based drug delivery system in cancer therapy. J Exp Clin Med 6(6):172–178. https://doi.org/10.1016/j.jecm.2014.10.015

Alghuthaymi MA, Almoammar H, Rai M, Said-Galiev E, Abd-Elsalam KA (2015) Myconanoparticles: synthesis and their role in phytopathogens management. Biotechnol Biotechnol Equip 29(2):221–236. https://doi.org/10.1080/13102818.2015.1008194

Aziz N, Fatma T, Varma A, Prasad R (2014) Biogenic synthesis of silver nanoparticles using Scenedesmus abundans and evaluation of their antibacterial activity. J Nanoparticles 2014:689419. https://doi.org/10.1155/2014/689419

Aziz N, Faraz M, Pandey R, Sakir M, Fatma T, Varma A, Barman I, Prasad R (2015) Facile algae-derived route to biogenic silver nanoparticles: synthesis, antibacterial and photocatalytic properties. Langmuir 31:11605–11612. https://doi.org/10.1021/acs.langmuir.5b03081

Aziz N, Pandey R, Barman I, Prasad R (2016) Leveraging the attributes of *Mucor hiemalis*-derived silver nanoparticles for a synergistic broad-spectrum antimicrobial platform. Front Microbiol 7:1984. https://doi.org/10.3389/fmicb.2016.01984

Aziz N, Faraz M, Sherwani MA, Fatma T, Prasad R (2019) Illuminating the anticancerous efficacy of a new fungal chassis for silver nanoparticle synthesis. Front Chem 7:65. https://doi.org/10.3389/fchem.2019.00065

Balaji DS, Basavaraja S, Deshpande R, Mahesh DB, Prabhakar BK, Venkataraman A (2009) Extracellular biosynthesis of functionalized silver nanoparticles by strains of Cladosporium cladosporioides fungus. Colloids Surf B: Biointerfaces 68(1):88–92. https://doi.org/10.1016/j.colsurfb.2008.09.022

Baldim V, Yadav N, Bia N, Graillot A, Loubat C, Singh S, Karakoti AS, Berret J-F (2020) Polymer-coated cerium oxide nanoparticles as oxidoreductase-like catalysts. ACS Appl Mater Interfaces 12(37):42056–42066. https://doi.org/10.1021/acsami.0c08778

Bhadury P, Wright PC (2004) Exploitation of marine algae: biogenic compounds for potential antifouling applications. Planta 219(4):561–578. https://doi.org/10.1007/s00425-004-1307-5

Brachhold K, et al (2017) Magnetosomes: natural magnetic nanoparticles for biomedical applications

Castro-Longoria E, Vilchis-Nestor AR, Avalos-Borja M (2011) Biosynthesis of silver, gold and bimetallic nanoparticles using the filamentous fungus Neurospora crassa. Colloids Surf B Biointerfaces 83(1):42–48. https://doi.org/10.1016/j.colsurfb.2010.10.035

Chausali N, Jyoti Saxena J, Prasad R (2022) Recent trends in nanotechnology applications of bio-based packaging. J Agric Food Res. https://doi.org/10.1016/j.jafr.2021.100257

Chen F, Ehlerding EB, Cai W (2014) Theranostic nanoparticles. J Nucl Med 55(12):1919–1922. https://doi.org/10.2967/jnumed.114.146019

Cobbett C, Goldsbrough P (2002) Phytochelatins and metallothioneins: roles in heavy metal detoxification and homeostasis. Annu Rev Plant Biol 53(1):159–182. https://doi.org/10.1146/annurev.arplant.53.100301.135154

Dai Q, Besla R, Ding D, Ouyang B, Li A, Chen J, Zheng G, Robbins C, Chan WCW et al (2017) Effect of removing Kupffer cells on nanoparticle tumor delivery. Proc Natl Acad Sci 114(51). https://doi.org/10.1073/pnas.1713390114

Egan-Morriss C, Kimber RL, Powell NA, Lloyd JR (2022) Biotechnological synthesis of Pd-based nanoparticle catalysts. Nanoscale Adv 4(3):654–679. https://doi.org/10.1039/D1NA00686J

Fichtner J, Güresir E, Seifert V, Raabe A (2010) Efficacy of silver-bearing external ventricular drainage catheters: a retrospective analysis. J Neurosurg 112(4):840–846. https://doi.org/10.3171/2009.8.JNS091297

Gajbhiye M, Kesharwani J, Ingle A, Gade A, Rai M (2009) Fungus-mediated synthesis of silver nanoparticles and their activity against pathogenic fungi in combination with fluconazole. Nanomedicine 5(4):382–386. https://doi.org/10.1016/j.nano.2009.06.005

Gan PP, Li SFY (2012) Potential of plant as a biological factory to synthesize gold and silver nanoparticles and their applications. Rev Environ Sci Biotechnol 11(2):169–206. https://doi.org/10.1007/s11157-012-9278-7

Ganapathy Selvam G, Sivakumar K (2015) Phycosynthesis of silver nanoparticles and photocatalytic degradation of methyl orange dye using silver (Ag) nanoparticles synthesized from Hypnea musciformis (Wulfen) J.V. Lamouroux. Appl Nanosci 5(5):617–622. https://doi.org/10.1007/s13204-014-0356-8

Gao H, Weitao T, He Q (2011) Coping with the environment: how microbes survive environmental challenges. Int J Microbiol 2011:1–2. https://doi.org/10.1155/2011/379519

Golinska P, Wypij M, Ingle AP, Gupta I, Dahm H, Rai M (2014) Biogenic synthesis of metal nanoparticles from actinomycetes: biomedical applications and cytotoxicity. Appl Microbiol Biotechnol 98(19):8083–8097. https://doi.org/10.1007/s00253-014-5953-7

Golmohammadi H, Morales-Narváez E, Naghdi T, Merkoçi A (2017) Nanocellulose in sensing and biosensing. Chem Mater 29(13):5426–5446. https://doi.org/10.1021/acs.chemmater.7b01170

Govindaraju K, Basha SK, Kumar VG, Singaravelu G (2008) Silver, gold and bimetallic nanoparticles production using single-cell protein (Spirulina platensis) Geitler. J Mater Sci 43(15):5115–5122. https://doi.org/10.1007/s10853-008-2745-4

Gunti S, Kumar A, Ram MK (2015) Comparative organics remediation properties of nanostructured graphene doped titanium oxide and graphene doped zinc oxide photocatalysts. Am J Anal Chem 06(08):708–717. https://doi.org/10.4236/ajac.2015.68068

Gutiérrez JC, Amaro F, Martin-Gonzalez A (2015) Heavy metal whole-cell biosensors using eukaryotic microorganisms: an updated critical review. Front Microbiol 6:48. https://doi.org/10.3389/fmicb.2015.00048

He S, Zhang Y, Guo Z, Gu N (2008) Biological synthesis of gold nanowires using extract of Rhodopseudomonas capsulata. Biotechnol Prog 24(2):476–480. https://doi.org/10.1021/bp0703174

He X, Deng H, Hwang H-M (2019) The current application of nanotechnology in food and agriculture. J Food Drug Anal 27(1):1–21. https://doi.org/10.1016/j.jfda.2018.12.002

Holmes JD, Smith PR, Evans-Gowing R, Richardson DJ, Russell DA, Sodeau JR (1995) Energy-dispersive X-ray analysis of the extracellular cadmium sulfide crystallites of Klebsiella aerogenes. Arch Microbiol 163(2):143–147. https://doi.org/10.1007/BF00381789

Huang Y, Li X, Liao Z, Zhang G, Liu Q, Tang J, Peng Y, Liu X, Luo Q (2007) A randomized comparative trial between Acticoat and SD-Ag in the treatment of residual burn wounds, including safety analysis. Burns 33(2):161–166. https://doi.org/10.1016/j.burns.2006.06.020

Ingle A, Rai M, Gade A, Bawaskar M (2009) Fusarium solani: a novel biological agent for the extracellular synthesis of silver nanoparticles. J Nanopart Res 11(8):2079–2085. https://doi.org/10.1007/s11051-008-9573-y

Kalimuthu K, Suresh Babu R, Venkataraman D, Bilal M, Gurunathan S (2008) Biosynthesis of silver nanocrystals by Bacillus licheniformis. Colloids Surf B Biointerfaces 65(1):150–153. https://doi.org/10.1016/j.colsurfb.2008.02.018

Kalishwaralal K, Deepak V, Ramkumarpandian S, Nellaiah H, Sangiliyandi G (2008) Extracellular biosynthesis of silver nanoparticles by the culture supernatant of Bacillus licheniformis. Mater Lett 62(29):4411–4413. https://doi.org/10.1016/j.matlet.2008.06.051

Kang SH, Bozhilov KN, Myung NV, Mulchandani A, Chen W (2008) Microbial synthesis of CdS nanocrystals in genetically engineered E. coli. Angew Chem Int Ed 47(28):5186–5189. https://doi.org/10.1002/anie.200705806

Karlo J, Prasad R, Singh SP (2023) Biophotonics in food technology: quo vadis? J Agric Food Res. https://doi.org/10.1016/j.jafr.2022.100482

Khan I, Saeed K, Khan I (2019) Nanoparticles: properties, applications and toxicities. Arab J Chem 12(7):908–931. https://doi.org/10.1016/j.arabjc.2017.05.011

Kisimba K, Krishnan A, Faya M, Byanga K, Kasumbwe K, Vijayakumar K, Prasad R (2023) Synthesis of metallic nanoparticles based on green chemistry and their medical biochemical applications: synthesis of metallic nanoparticles. J Renew Mater 11(6):2575–2591. https://doi.org/10.32604/jrm.2023.026159

Klaus T, Joerger R, Olsson E, Granqvist C-G (1999) Silver-based crystalline nanoparticles, microbially fabricated. Proc Natl Acad Sci 96(24):13611–13614. https://doi.org/10.1073/pnas.96.24.13611

Koch N, Sonowal S, Prasad R (2023) Elucidate the smart tailored biogenic nanoparticles and their applications in remediation. Biotechnol Genet Eng Rev. https://doi.org/10.1080/02648725.2023.2219942

Koul B, Poonia AK, Yadav D, Jin J-O (2021) Microbe-mediated biosynthesis of nanoparticles: applications and future prospects. Biomol Ther 11(6):886. https://doi.org/10.3390/biom11060886

Kumari B, Singh DP (2016) A review on multifaceted application of nanoparticles in the field of bioremediation of petroleum hydrocarbons. Ecol Eng 97:98–105. https://doi.org/10.1016/j.ecoleng.2016.08.006

Kuzajewska D, Wszołek A, Żwierełło W, Kirczuk L, Maruszewska A (2020) Magnetotactic bacteria and magnetosomes as smart drug delivery systems: a new weapon on the battlefield with cancer? Biology 9(5):102. https://doi.org/10.3390/biology9050102

Li X, Xu H, Chen Z-S, Chen G (2011) Biosynthesis of nanoparticles by microorganisms and their applications. J Nanomater 2011:1–16. https://doi.org/10.1155/2011/270974

Li PJ, Xia JL, Shan Y, Nie ZY (2015) Comparative study of multi-enzyme production from typical agro-industrial residues and ultrasound-assisted extraction of crude enzyme in fermentation with aspergillus japonicus PJ01. Bioprocess Biosyst Eng 38(10):2013–2022. https://doi.org/10.1007/s00449-015-1442-3

Liu F, Shah DS, Gadd GM (2021a) Role of protein in fungal biomineralization of copper carbonate nanoparticles. Curr Biol 31(2):358–368. https://doi.org/10.1016/j.cub.2020.10.044

Liu C, Zhou H, Zhou J (2021b) The applications of nanotechnology in crop production. Molecules 26(23):7070. https://doi.org/10.3390/molecules26237070

Lombardo D, Calandra P, Pasqua L, Magazù S (2020) Self-assembly of organic nanomaterials and biomaterials: the bottom-up approach for functional nanostructures formation and advanced applications. Materials 13(5):1048. https://doi.org/10.3390/ma13051048

Long R, Liu Y, Dai Q, Wang S, Deng Q, Zhou X (2016) A natural bacterium-produced membrane-bound nanocarrier for drug combination therapy. Materials 9(11):889. https://doi.org/10.3390/ma9110889

Lv Q, Zhang B, Xing X, Zhao Y, Cai R, Wang W, Gu Q (2018) Biosynthesis of copper nanoparticles using Shewanella loihica PV-4 with antibacterial activity: novel approach and mechanisms investigation. J Hazard Mater 347:141–149. https://doi.org/10.1016/j.jhazmat.2017.12.070

Manivasagan P, Venkatesan J, Kang K-H, Sivakumar K, Park S-J, Kim S-K (2015) Production of α-amylase for the biosynthesis of gold nanoparticles using Streptomyces sp. MBRC-82. Int J Biol Macromol 72:71–78. https://doi.org/10.1016/j.ijbiomac.2014.07.045

Manivasagan P, Nam SY, Oh J (2016) Marine microorganisms as potential biofactories for synthesis of metallic nanoparticles. Crit Rev Microbiol 42(6):1007–1019. https://doi.org/10.3109/1040841X.2015.1137860

Mishra A, Ahmad R, Perwez M, Sardar M (2016) Reusable green synthesized biomimetic magnetic nanoparticles for glucose and H2O2 detection. BioNanoScience 6(2):93–102. https://doi.org/10.1007/s12668-016-0197-x

Narayanan KB, Sakthivel N (2010) Biological synthesis of metal nanoparticles by microbes. Adv Colloid Interf Sci 156(1–2):1–13. https://doi.org/10.1016/j.cis.2010.02.001

Ng WV, Kennedy SP, Mahairas GG, Berquist B, Pan M, Shukla HD, Lasky SR, Baliga NS, Thorsson V, Sbrogna J, Swartzell S, Weir D, Hall J, Dahl TA, Welti R, Goo YA, Leithauser B, Keller K, Cruz R et al (2000) Genome sequence of Halobacterium species NRC-1. Proc Natl Acad Sci 97(22):12176–12181. https://doi.org/10.1073/pnas.190337797

Nima ZA, Watanabe F, Jamshidi-Parsian A, Sarimollaoglu M, Nedosekin DA, Han M, Watts JA, Biris AS, Zharov VP, Galanzha EI (2019) Bioinspired magnetic nanoparticles as multimodal photoacoustic, photothermal and photomechanical contrast agents. Sci Rep 9(1):887. https://doi.org/10.1038/s41598-018-37353-5

Oren A (2008) Microbial life at high salt concentrations: phylogenetic and metabolic diversity. Saline Syst 4(1):2. https://doi.org/10.1186/1746-1448-4-2

Ovais M, Khalil A, Ayaz M, Ahmad I, Nethi S, Mukherjee S (2018) Biosynthesis of metal nanoparticles via microbial enzymes: a mechanistic approach. Int J Mol Sci 19(12):4100. https://doi.org/10.3390/ijms19124100

Patil MP, Kang M-J, Niyonizigiye I, Singh A, Kim J-O, Seo YB, Kim G-D (2019) Extracellular synthesis of gold nanoparticles using the marine bacterium Paracoccus haeundaensis BC74171T and evaluation of their antioxidant activity and antiproliferative effect on normal and cancer cell lines. Colloids Surf B Biointerfaces 183:110455. https://doi.org/10.1016/j.colsurfb.2019.110455

Pernas-Pleite C, Conejo-Martínez AM, Marín I, Abad JP (2022) Green extracellular synthesis of silver nanoparticles by Pseudomonas alloputida, their growth and biofilm-formation inhibitory activities and synergic behavior with three classical antibiotics. Molecules 27(21):7589. https://doi.org/10.3390/molecules27217589

Poornima S, Valivittan K (2017) Degradation of malachite green (dye) by using photo-catalytic biogenic silver nanoparticles synthesized using red algae (Gracilaria corticata) aqueous extract. Int J Curr Microbiol App Sci 6(1):62–70. https://doi.org/10.20546/ijcmas.2017.601.008

Poulose S, Panda T, Nair PP, Theodore T (2014) Biosynthesis of silver nanoparticles. J Nanosci Nanotechnol 14(2):2038–2049. https://doi.org/10.1166/jnn.2014.9019

Prasad R (2016) Advances and applications through fungal nanobiotechnology. Springer, International Publishing Switzerland. (ISBN: 978-3-319-42989-2)

Prasad R (2017) Fungal nanotechnology: applications in agriculture, industry, and medicine. Springer Nature Singapore Pte Ltd. (ISBN 978-3-319-68423-9)

Prasad R (2019a) Microbial nanobionics: basic research and applications. Springer International Publishing. (ISBN 978-3-030-16534-5) https://www.springer.com/gp/book/9783030165338

Prasad R (2019b) Microbial nanobionics: state of art. Springer International Publishing. (ISBN 978-3-030-16383-9) https://www.springer.com/gp/book/9783030163822

Prasad R, Aranda E (2018) Approaches in bioremediation. Springer International Publishing. https://www.springer.com/de/book/9783030023683

Prasad R, Kumar V, Prasad KS (2014) Nanotechnology in sustainable agriculture: present concerns and future aspects. Afr J Biotechnol 13(6):705–713

Prasad R, Pandey R, Barman I (2016) Engineering tailored nanoparticles with microbes: quo vadis. WIREs Nanomed Nanobiotechnol 8:316–330. https://doi.org/10.1002/wnan.1363

Prasad R, Kumar M, Kumar V (2017a) Nanotechnology: an agriculture paradigm. Springer Nature Singapore Pte Ltd. (ISBN: 978-981-10-4573-8)

Prasad R, Bhattacharyya A, Nguyen QD (2017b) Nanotechnology in sustainable agriculture: recent developments, challenges, and perspectives. Front Microbiol 8:1014. https://doi.org/10.3389/fmicb.2017.01014

Prasad R, Jha A, Prasad K (2018) Exploring the realms of nature for nanosynthesis. Springer International Publishing. (ISBN 978-3-319-99570-0) https://www.springer.com/978-3-319-99570-0

Qin W, Wang C, Ma Y, Shen M, Li J, Jiao K, Tay FR, Niu L (2020) Microbe-mediated extracellular and intracellular mineralization: environmental, industrial, and biotechnological applications. Adv Mater 32(22):1907833. https://doi.org/10.1002/adma.201907833

Rai M, Bonde S, Golinska P, Trzcińska-Wencel J, Gade A, Abd-Elsalam KA, Shende S, Gaikwad S, Ingle AP (2021) Fusarium as a novel fungus for the synthesis of nanoparticles: mechanism and applications. J Fungi 7(2):139. https://doi.org/10.3390/jof7020139

Rajasekar T, Karthika K, Muralitharan G, Maryshamya A, Sabarika S, Anbarasu S, Revathy K, Prasannabalaji N, Kumaran S (2020) Green synthesis of gold nanoparticles using extracellular metabolites of fish gut microbes and their antimicrobial properties. Braz J Microbiol 51(3):957–967. https://doi.org/10.1007/s42770-020-00263-8

Rajput VD, Minkina T, Kimber RL, Singh VK, Shende S, Behal A, Sushkova S, Mandzhieva S, Lloyd JR (2021) Insights into the biosynthesis of nanoparticles by the Genus Shewanella. Appl Environ Microbiol 87:22. https://doi.org/10.1128/AEM.01390-21

Sachin K, Karn SK (2021) Microbial fabricated nanosystems: applications in drug delivery and targeting. Front Chem 9:617353. https://doi.org/10.3389/fchem.2021.617353

Saglam N, Korkusuz F, Prasad R (2021) Nanotechnology Applications in Health and Environmental Sciences. Springer International Publishing. (ISBN: 978-3-030-64410-9) https://www.springer.com/gp/book/9783030644093

Sahoo D, Mandal A, Mitra T, Chakraborty K, Bardhan M, Dasgupta AK (2018) Nanosensing of pesticides by Zinc Oxide Quantum Dot: an optical and electrochemical approach for the detection of pesticides in water. J Agric Food Chem 66(2):414–423. https://doi.org/10.1021/acs.jafc.7b04188

Saifuddin N, Wong CW, Yasumira AAN (2009) Rapid biosynthesis of silver nanoparticles using culture supernatant of bacteria with microwave irradiation. J Chem 6(1):61–70. https://doi.org/10.1155/2009/734264

Sarma H, Joshi S, Prasad R, Jampilek J (2021) Biobased nanotechnology for green applications. Springer International Publishing. (ISBN 978-3-030-61985-5) https://www.springer.com/gp/book/9783030619848

Saxena IM, Brown RM (2005) Cellulose biosynthesis: current views and evolving concepts. Ann Bot 96(1):9–21. https://doi.org/10.1093/aob/mci155

Shelke DB, Islam NF, Chambhare MR, Sonawane HB, Patowary R, Prasad R, Sarma H (2023) Enhancing secondary metabolites and alleviating environmental stress in crops with mycogenic nanoparticles: a comprehensive review. Biocatal Agric Biotechnol. https://doi.org/10.1016/j.bcab.2023.102805

Shivaji S, Madhu S, Singh S (2011) Extracellular synthesis of antibacterial silver nanoparticles using psychrophilic bacteria. Process Biochem 46(9):1800–1807. https://doi.org/10.1016/j.procbio.2011.06.008

Siddiqi KS, Husen A, Rao RAK (2018) A review on biosynthesis of silver nanoparticles and their biocidal properties. J Nanobiotechnology 16(1):14. https://doi.org/10.1186/s12951-018-0334-5

Singh S, Vidyarthi AS, Dev A (2015) Microbial synthesis of nanoparticles. In: Bio-nanoparticles. Wiley, Hoboken, pp 155–186. https://doi.org/10.1002/9781118677629.ch8

Srivastava P, Bragança J, Ramanan SR, Kowshik M (2013) Synthesis of silver nanoparticles using haloarchaeal isolate Halococcus salifodinae BK3. Extremophiles 17(5):821–831. https://doi.org/10.1007/s00792-013-0563-3

Srivastava S, Bhargava A, Pathak N, Srivastava P (2019) Production, characterization and antibacterial activity of silver nanoparticles produced by Fusarium oxysporum and monitoring of protein-ligand interaction through in-silico approaches. Microb Pathog 129:136–145. https://doi.org/10.1016/j.micpath.2019.02.013

Srivastava S, Usmani Z, Atanasov AG, Singh VK, Singh NP, Abdel-Azeem AM, Prasad R, Gupta G, Sharma M, Bhargava A (2021) Biological nanofactories: using living forms for metal nanoparticle synthesis. Mini-Rev Med Chem 21(2):245–265

Suman V, Prasad R, Jain VK, Varma A (2010) Role of nanomaterials in symbiotic fungus growth enhancement. Curr Sci 99:1189–1191

Sun J-Z, Peter Kingori G, Si R-W, Zhai D-D, Liao Z-H, Sun D-Z, Zheng T, Yong Y-C (2015) Microbial fuel cell-based biosensors for environmental monitoring: a review. Water Sci Technol 71(6):801–809. https://doi.org/10.2166/wst.2015.035

Tanaka M, Okamura Y, Arakaki A, Tanaka T, Takeyama H, Matsunaga T (2006) Origin of magnetosome membrane: proteomic analysis of magnetosome membrane and comparison with cytoplasmic membrane. Proteomics 6(19):5234–5247. https://doi.org/10.1002/pmic.200500887

Thangadurai D, Sangeetha J, Prasad R (2020a) Functional bionanomaterials. Springer International Publishing. (ISBN 978-3-030-41464-1) https://www.springer.com/gp/book/9783030414634

Thangadurai D, Sangeetha J, Prasad R (2020b) Nanotechnology for food, agriculture, and environment. Springer International Publishing. (ISBN 978-3-030-31937-3) https://www.springer.com/gp/book/9783030319373

Tripathi S, Sanjeevi R, Anuradha J, Chauhan DS, Rathoure AK (2018) Nano-bioremediation. IGI Global, Hershey, pp 202–219. https://doi.org/10.4018/978-1-5225-4162-2.ch012

Ullah I, Khan K, Sohail M, Ullah K, Ullah A, Shaheen S (2017) Synthesis, structural characterization and catalytic application of citrate-stabilized monometallic and bimetallic palladium at copper nanoparticles in microbial anti-activities. Int J Nanomedicine 12:8735–8747. https://doi.org/10.2147/IJN.S145085

Vargas G, Cypriano J, Correa T, Leão P, Bazylinski D, Abreu F (2018) Applications of magnetotactic bacteria, magnetosomes and magnetosome crystals in biotechnology and nanotechnology: mini-review. Molecules 23(10):2438. https://doi.org/10.3390/molecules23102438

Vijayaraghavan K, Mahadevan A, Sathishkumar M, Pavagadhi S, Balasubramanian R (2011) Biosynthesis of Au(0) from Au(III) via biosorption and bioreduction using brown marine alga Turbinaria conoides. Chem Eng J 167(1):223–227. https://doi.org/10.1016/j.cej.2010.12.027

Wang G, Kennedy SP, Fasiludeen S, Rensing C, DasSarma S (2004) Arsenic resistance in Halobacterium sp. strain NRC-1 examined by using an improved gene knockout system. J Bacteriol 186(10):3187–3194. https://doi.org/10.1128/JB.186.10.3187-3194.2004

Xue X, Cheng R, Shi L, Ma Z, Zheng X (2017) Nanomaterials for water pollution monitoring and remediation. Environ Chem Lett 15(1):23–27. https://doi.org/10.1007/s10311-016-0595-x

Yadav A, Kon K, Kratosova G, Duran N, Ingle AP, Rai M (2015) Fungi as an efficient mycosystem for the synthesis of metal nanoparticles: progress and key aspects of research. Biotechnol Lett 37(11):2099–2120. https://doi.org/10.1007/s10529-015-1901-6

Yadav L, Tripathi RM, Prasad R, Pudake RN, Mittal J (2017) Antibacterial activity of Cu nanoparticles against *E. coli*, *Staphylococcus aureus* and *Pseudomonas aeruginosa*. Nano Biomed Eng 9(1):9–14. https://doi.org/10.5101/nbe.v9i1.p9-14

Younis NS, Mohamed ME, El Semary NA (2022) Green synthesis of silver nanoparticles by the cyanobacteria Synechocystis sp.: characterization, antimicrobial and diabetic wound-healing actions. Mar Drugs 20(1):56. https://doi.org/10.3390/md20010056

Zaimy MA, Saffarzadeh N, Mohammadi A, Pourghadamyari H, Izadi P, Sarli A, Moghaddam LK, Paschepari SR, Azizi H, Torkamandi S, Tavakkoly-Bazzaz J (2017) New methods in the diagnosis of cancer and gene therapy of cancer based on nanoparticles. Cancer Gene Ther 24(6):233–243. https://doi.org/10.1038/cgt.2017.16

Zafrilla B, Martínez-Espinosa RM, Alonso MA, Bonete MJ (2010) Biodiversity of Archaea and floral of two inland saltern ecosystems in the Alto Vinalopó Valley, Spain. Saline Syst 6(1):10. https://doi.org/10.1186/1746-1448-6-10

Zhang X, Yan S, Tyagi RD, Surampalli RY (2011) Synthesis of nanoparticles by microorganisms and their application in enhancing microbiological reaction rates. Chemosphere 82(4):489–494. https://doi.org/10.1016/j.chemosphere.2010.10.023

Part II

Biomedicinal and Biotechnological Applications

Synthesis and Studies of TTAHOT: Macro, Micro and Nano Crystalline Composite for Electronic and Bio-Medicinal Use

8

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Abstract

Tris [Triphenyl Antimony(V)] Hexa(μ-Oxido) Tellurium (VI)—TTAHOT chalcogenide is important in photoconductivity, here crystals with Tellurium are grown and analysed by single-crystal XRD as monoclinic with bond lengths as 47.7150 Å; 9.1178 Å; 22.9325 Å; with beta as 104.168°, confirmed by DFT; and also employed in frequency enhancers, phase matching. The electronic interactions by Hirshfeld analysis are reported. The hardness of TTAHOT is of reverse indentation size effect. The influxes of TTAHOT are in microns for filters. The anti-diabetic illustration with IC_{50} for macro, micro, and nano, the prediction of the −ve photoconductivity for macro TTAHT; in antioxidant utility as the best

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pharma tool from the chalcogenide family with ORTEP are reported for TTAHOT.

Keywords

Tellurium · Photoconductivity · Optical · Hardness · Anti-diabetic · Anti-oxidant

8.1 Introduction

Chalcogenides are group 16 elements of the periodic table that they are further normally standby for sulfides, selenides, tellurides, and polonides, rather than oxides. Many metallic ores occur by way of chalcogenides. Photoconductive chalcogenides are well and properly employed in xerographic use (Gunasekaran et al. 2013; Aarthi et al. 2018; Senthilkannan et al. 2013b; Kishore et al. 2017; Saravanan et al. 2020a, b; Gnanam et al. 2019; Krishnaveni et al. 2019). Organic materials are having enhanced activities in optical, electronic, and bio use based on their combinations (SenthilKannan 2018; SenthilKannan et al. 2013b, 2014; Malathi Rekha et al. 2018; Flora et al. 2020a, b, c; Senthilkumar et al. 2020). Due to the presence of delocalised electrons at the orbitals of $\pi-\pi^*$, organic NLO materials mixed with chalcogen are assumed to have comparatively strong nonlinearity behaviour (SenthilKannan et al. 2020a, b, c; Wilcox 2005; Yang et al. 2019; Tundis et al. 2010; Khadayat et al. 2020; Kumar et al. 2020; Farrugia 2012). This enhances the pursuit for improved NLO materials amongst the type of organic category of crystalline materials (Periyathambi et al. 2020; Selvaraj et al. 2020; Flora et al. 2020a, b; Senthilkannan et al. 2020d, e, f; Saravanan et al. 2020b; Baskaran et al. 2020a, b).

The materials can be adapted for optical modulations, optical expedients, and laser frequency modulations. Organic NLO materials are further superior than inorganic NLO materials (Jothibas et al. 2019; Kurtz and Perry 1968; Oyedemi et al. 2017; SenthilKannan and Gunasekaran 2013; SenthilKannan et al. 2013a) owing to their advanced command of optical alteration proficiency (Baskaran et al. 2020a, b; SenthilKannan et al. 2020g, h, i, j, k; Kalaipoonguzhali et al. 2020; Kolanjinathan et al. 2020). In recent decades, molecular crystalline specimens are having massive impressions on electronic and another sort of usage by theoretic and investigational examination (SenthilKannan et al. 2020l; Flora et al. 2020c; Krishnamurthy et al. 2014; Patel et al. 2021; Zhang et al. 2002; Von Hippel et al. 1953). Computational—density-functional theory (DFT) methods are playing the crucial part in forecasting the symmetrical, active molecular properties similar to the hyperpolarisabilities of order I and of NLO susceptibility hypothetically (Hrizi et al. 2012; Senthilkannan et al. 2013b; Dhieb et al. 2015; Tundis et al. 2010; Khadayat et al. 2020; Baskaran et al. 2020a, b; Williams et al. 2019). Our main focal point, as well as the intention, is to grow up the chalcogenide-based mixed crystals, especially TTAHOT (Burley et al. 2019; Dallakyan and Olson 2014; Halgren 1996; Momma and Izumi 2011) for the precise depiction using XRD, theoretical, and NLO to analyse its possessions and uses. The density-functional theory (DFT) is working to estimate the proper crystalline structure of the sample tribology is also premeditated (Spackman et al. 2021; Pek 2003; Senthilkumar et al. 2020).

8.2 Experimental

8.2.1 Synthesis and Crystallisation of TTAHOT Crystals

The initial substantial, $Ag_3H_3TeO_6$, is produced conferring by the methodology with that a solution containing of Ph_4SbBr and of acetonitrile is properly added. The mixture is properly and perfectly manner stirred for 3–4 h. Desertion of the solution harvested a colourless glass-like substantial by low-temperature growth method. Slow evaporation was enabled and TTAHOT crystals were obtained in 21 days with a size of $15 \times 12 \times 9$ mm^3.

8.3 Analyses/Results

8.3.1 XRD of TTAHOT Crystals

The single-XRD data of TTAHOT is showing the monoclinic nature with C2/c space group and a; b; c values are, respectively, as 47.7150 Å; 9.1178Å; 22.9325Å with molecular formula as $Sb_3Te(C_6H_5)_9O_6$ with beta as 104.168°.

8.3.2 DFT, Cell Parameters, Matrix, Atomic Data, and PLATON Plot by Theoretical Way

The bond length and bond angle of the TTAHOT are analysed in theoretical manner by software and reported for Sb- and Te-based major contributions and reported as in Table 8.1. The direct and reciprocal cell parameters of TTAHOT are portrayed in Tables 8.2a and 8.2b for better understanding and the tensors for direct and reciprocal case are mentioned in tables; matrix depiction for orthonormal mode and vice versa in Tables 8.2c and 8.2d, respectively. Atomic information on some major Tellurium, antimony, and oxygen atoms with *x*/*a*; *y*/*b*; *z*/*c* data is provided in Table 8.3. The Platon plot version of TTAHOT is shown in Fig. 8.1 for the proper atomic arrangement as well as six Te-O-Sb channels; and is the counter-verification of the structure depicted by XRD.

8.3.3 Hirshfeld Interactions, Molecular Model, Polyhedral, and Weak Interactions of TTAHOT Crystals

The electronic interactions by Hirshfeld such as d_{norms}, d_i, d_e, shape indexing, curvedness and fragmented patching and specifiy the electron-rich profile, interactions, optoelectronic effectiveness by the coloured shape index, patched work, curvedness by Fig. 8.2a–f and the fingerprint effect of TTAHOT is mentioned in Fig. 8.2g d_i vs d_e effect of standard all elements. The space-filled TTAHOT, polyhedral representation for the proper projections; coordination polyhedral for the proper arrangements; Voronoi polyhedral for the proper projections of the

Table 8.1 Significant geometric parameters (Å, °) of TTAHOT crystal

Atoms	Bond parameter	Atoms	Bond parameter
C1–C2	1.403	O3–Sb2–C25	118.63
C1–C6	1.388	O3–Sb2–O4	76.51
C21–H21	0.953	O4–Sb2–C31	87.75
C2–C3	1.379	O4–Sb2–C25	88.96
C2–H2	0.952	O3–Sb2–C31	119.84
O1–Sb1–O2	76.13	C31–Sb2–C19	97.8
O1–Te1–O3	94.47	O4–Sb2–C19	164.79
O1–Te1–O6	174.62	C1–Sb1–C13	114.52
O2–Te1–O1	81.65	O5–Sb3–C43	87.66
O2–Te1–O3	88.61	O1–Sb1–C7	85.37
O2–Te1–O4	166.72	O5–Sb3–C49	89.29
O2–Te1–O5	97.77	C25–Sb2–C31	119.07
O2–Te1–O6	94.15	O2–Sb1–C1	91.51
O4–Te1–O1	91.63	O1–Sb1–C1	119.66
O4–Te1–O3	80.52	O3–Sb2–C19	88.81
O4–Te1–O6	93.66	O2–Sb1–C13	91.61
O5–Te1–O1	95.96	C49–Sb3–C43	113.77
O5–Te1–O3	168.96	O2–Sb1–C7	161.24
O5–Te1–O4	94.81	O6–Sb3–C43	126.91
O5–Te1–O6	81.63	O1–Sb1–C13	124.86
O6–Sb3–C49	116.63	O6–Sb3–O5	76.57
O6–Te1–O3	88.91	C25–Sb2–C19	101.24
Sb1–C1	2.115	Te1–O2–Sb1	100.21
Sb1–C13	2.129	Sb2–O3–Te1	102.55
Sb1–C7	2.179	Te1–O4–Sb2	99.98
Sb1–O1	1.995	C43–Sb3–C37	98.76
Sb1–O2	2.095	Te1–O1–Sb1	102.21
Sb2–C19	2.176	C7–C8–C9	119.8
Sb2–C25	2.139	C8–C7–Sb1	121.9
Sb2–C31	2.152	C12–C7–Sb1	118.7
Sb2–O3	1.969	Te1–O5–Sb3	99.46
Sb2–O4	2.097	Te1–O6–Sb3	102.52
Sb3–C37	2.168	C13–Sb1–C7	97.67
Sb3–C43	2.127	C1–Sb1–C7	100.17
Sb3–C49	2.117	O5–Sb3–C37	165.59
Sb3–O5	2.115	O6–Sb3–C37	89.55
Sb3–O6	1.973	C24–C19–Sb2	121.11
Te1–O1	1.954	C44–C43–Sb3	120.4
Te1–O2	1.907	C20–C19–Sb2	118.13
Te1–O3	1.970	C49–Sb3–C37	100.65
Te1–O4	1.922	C26–C25–Sb2	120.11
Te1–O5	1.908	C30–C25–Sb2	119.8
Te1–O6	1.968	C48–C43–Sb3	119.9

Table 8.2a Direct cell parameters of TTAHOT crystals

a	47.7150 Å
b	9.1178 Å
c	22.9325 Å
Alpha	90°
Beta	104.168°
Gamma	90°

Table 8.2b Reciprocal cell parameters of TTAHOT crystals

a*	0.0209 $Å^{-1}$
b*	0.1096$Å^{-1}$
c*	0.0436 $Å^{-1}$
Alpha*	90°
Beta*	75.832°
Gamma*	90°

Table 8.2c Direct and reciprocal metric tensors of TTAHOT crystals

GD			GR		
2276.62	0.0000	−267.82	0.0004	0.0000	0.0002
0.0000	83.13	0.0000	0.0000	0.0120	0.0000
−267.82	0.0000	525.89	0.0002	0.0000	0.00202

Table 8.2d Matrix illustration of TTAHOT crystals

Crystal_to_orthonormal_matrix			Orthonormal_to_crystal matrix		
47.7140	0.0000	−5.6131	0.0209	−0.0000	0.0052
0.0000	9.1176	0.0000	0.0000	0.1096	0.0000
0.0000	0.0000	22.2348	0.0000	0.0000	0.0449

Table 8.3 Atomic information some specified major atoms of TTAHOT

Atom	Symbol	*x/a*	*y/b*	*z/c*
Te1	Te	0.1172	0.6814	0.0480
Te1	Te	0.1172	0.6814	0.0480
Sb1	Sb	0.0704	0.5747	−0.0605
Sb2	Sb	0.1800	0.6063	0.0494
Sb3	Sb	0.1128	0.8156	0.1679
O1	O	0.1026	0.7188	−0.0378
O2	O	0.0850	0.5513	0.0328
O3	O	0.1416	0.5152	0.0364
O4	O	0.1524	0.7840	0.0494

CPU-time: 0 min 0.375 s

coordination effect as in Fig. 8.3a–d. The molecular model of TTAHOT is represented in Fig. 8.4a; the 3D impact of TTAHOT is portrayed in Fig. 8.4b–d depicts the weak interactive way by Vander Waal's impactness of 50% and 75%

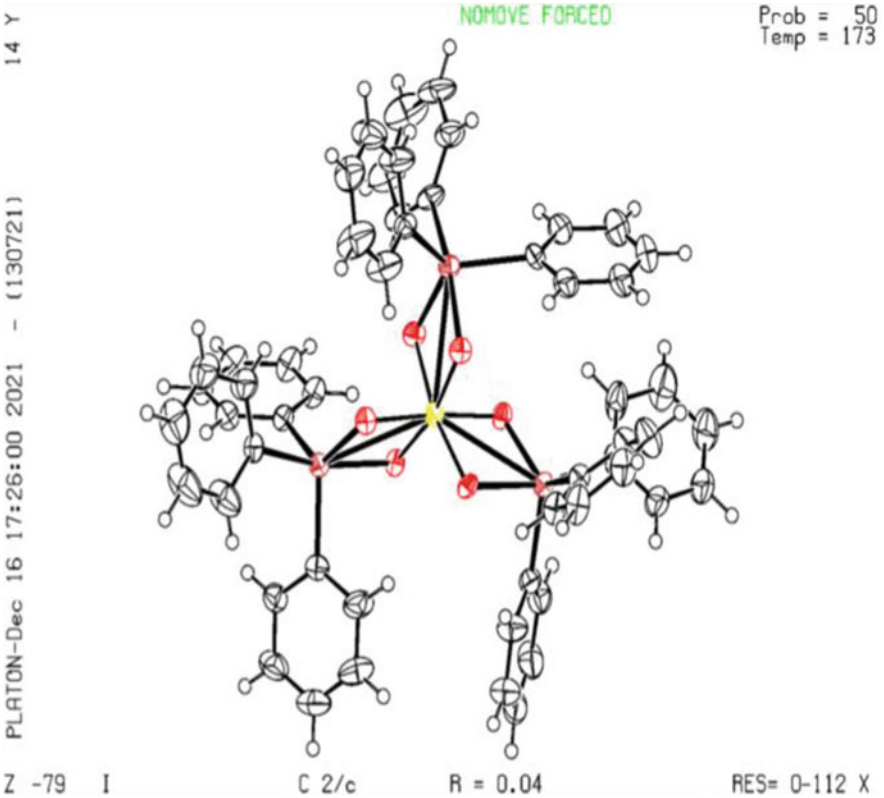

Fig. 8.1 Platon plot of TTAHOT crystals

effectiveness correspondingly (SenthilKannan et al. 2020m, n; Suganya et al. 2022; Sathiya et al. 2022; Vasanth Winston et al. 2022).

8.3.4 NLO, Phase Matching, and Frequency Enhancer of TTAHOT Crystals

The effective crystalline material is identified by the use of NLO applications and here TTAHOT is a used for phase matching 63.25 mV of SHG output related to KDP of 55 mV and it is varied and pronounced for less than 50; 50–100; 100–150; above 150 as particle size in micrometres; based on NLO-SHG value as mentioned in Fig. 8.5, the TTAHOT is used for frequency converters and formal normal diodes it is 2.1 times the input frequency and for macro TTAHOT coated diodes it is 2.28 times; for nano-TTAHOT coated diodes it is 2.31 times the input frequency and is enabled for frequency doubling circuit.

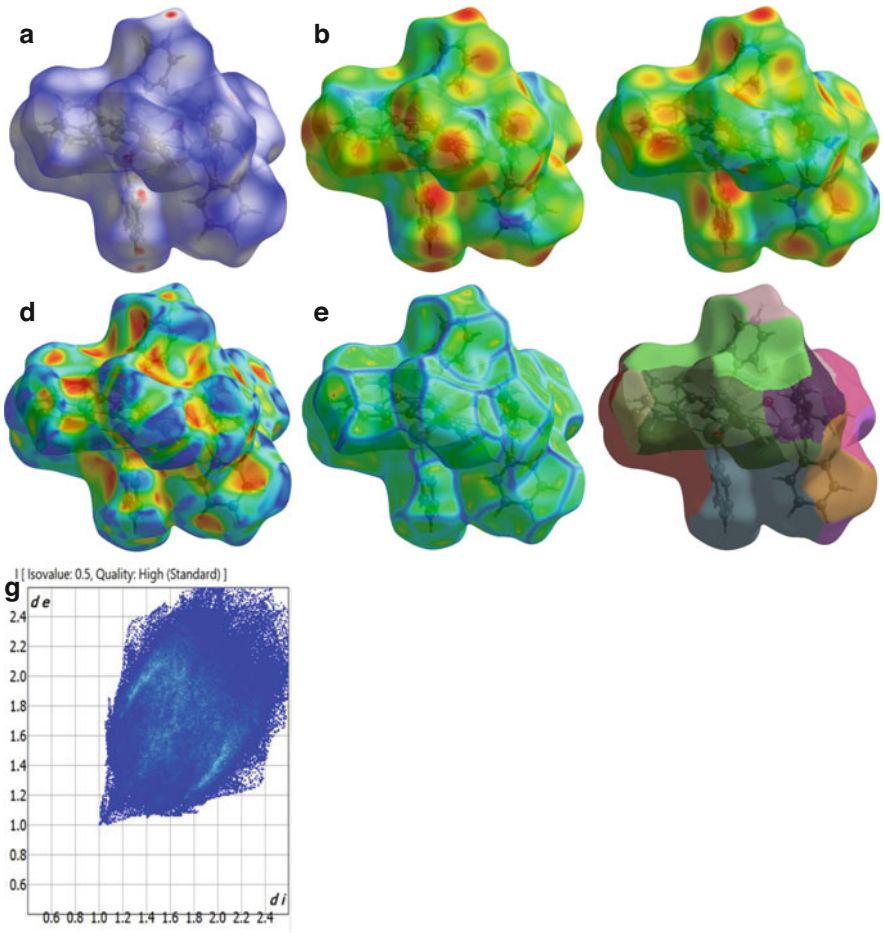

Fig. 8.2 (**a**) d_{norms} of TTAHOT crystals. (**b**) d_i of TTAHOT crystals. (**c**) d_e of TTAHOT crystals. (**d**) Shaped index outline of TTAHOT crystals. (**e**) Curvedness profile of TTAHOT crystals. (**f**) Fragmented patching profile of TTAHOT crystals. (**g**) Fingerprint profile of TTAHOT crystals

8.3.5 Hardness and Tribological Studies of TTAHOT Crystals

The hardness effectiveness of TTAHOT is analysed for load in grams and correspondingly the H_V in kg/mm^2 as mentioned in Fig. 8.6. The load increases and hardness too increase proportionally with n as 3.27 give rise to RISE—Reverse indentation size effect as n is more than 2. Based on this, it can proceed for tribological work. As the calculation of friction loss and revolutions; the load in 10 N, diameter of bearing 15 mm, thickness of film as 1 μm, viscous value of 0.02 Pa s; depth of channel as 8 μm, channel angle 15°, number of channels as 15 leads to an angular velocity as 3.6919 rad/s; rotational velocity as 35.2550 rpm; frictional coefficient as 0.0031; frictional torque as 0.0002 Nm; with power loss 0.0008 W

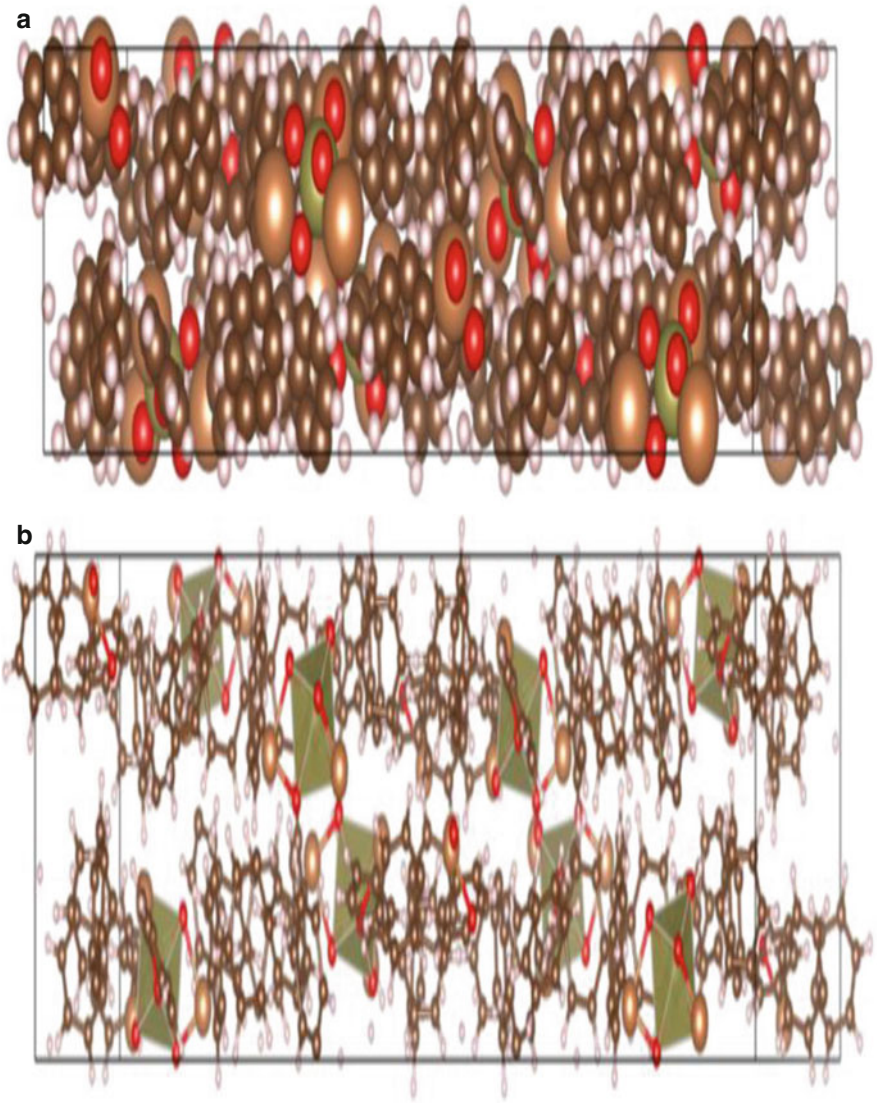

Fig. 8.3 (**a**) Space-filling model of TTAHOT crystals. (**b**) Polyhedral model of TTAHOT crystals. (**c**) Polyhedral-coordinated model of TTAHOT crystals. (**d**) Voronoi polyhedral model of TTAHOT crystals

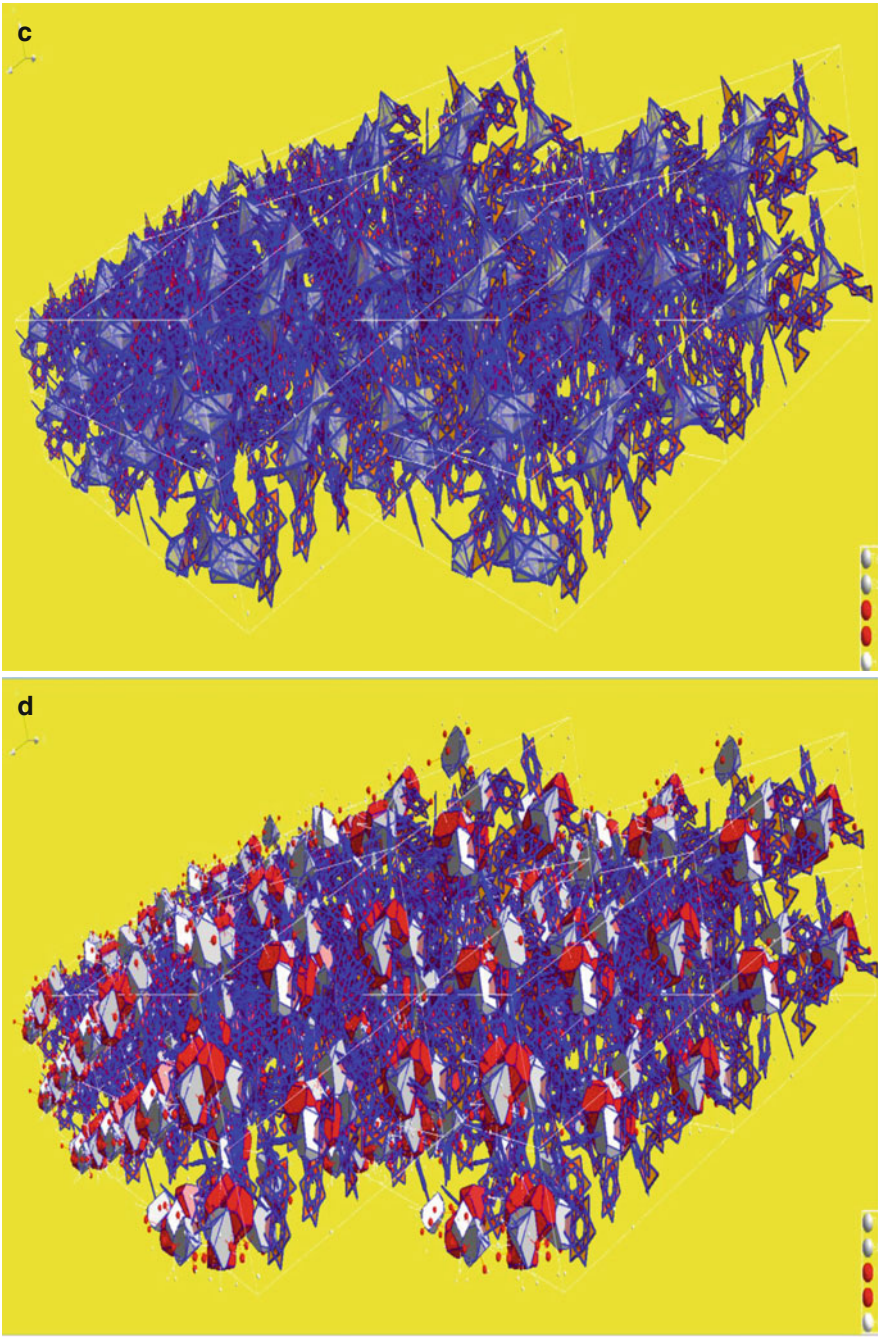

Fig. 8.3 (continued)

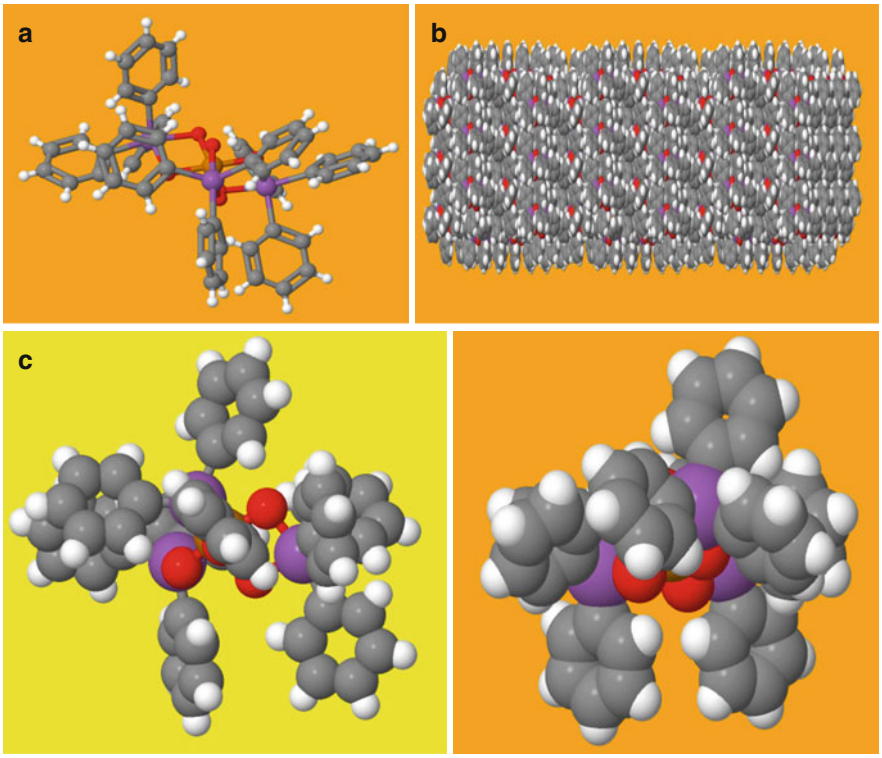

Fig. 8.4 (**a**) Molecular arrangement of TTAHOT crystals by computational way. (**b**) Molecular arrangement in 3D pattern of TTAHOT crystals - computational way. (**c**) Vander walls 50% effect of TTAHOT crystals by the computational way. (**d**) Vander walls 75% effect of TTAHOT crystals by computational way

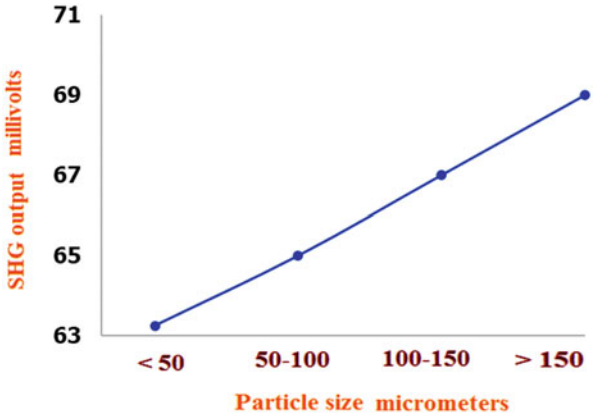

Fig. 8.5 Phase matching NLO effect of TTAHOT crystals

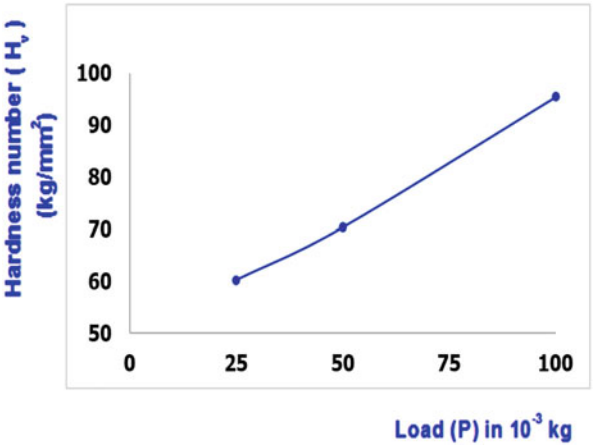

Fig. 8.6 Hardness impact of TTAHOT crystals

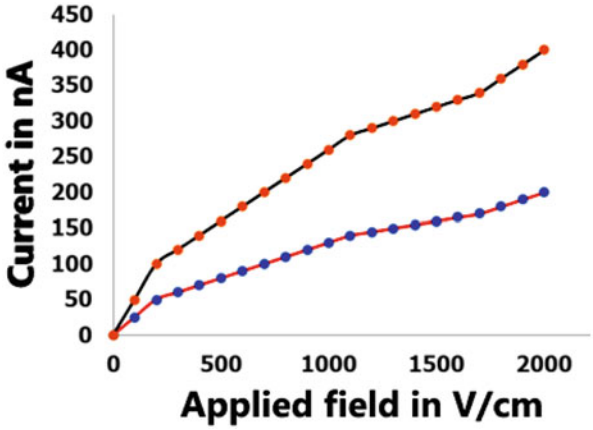

Fig. 8.7 Photoconductivity effect of TTAHOT crystals

for the TTAHOT macro coated tribology data and is better than uncoated one in loss factors and by frictional parameters.

8.3.6 Photoconductivity, Anti-diabetic, and Anti-oxidant, ORTEP Studies of TTAHOT Crystals

The photoconductivity nature of TTAHOT is measured for applied field in 30–2000 V/cm range and current in 25–400 nA and the black coloured line for dark current and red coloured line for photocurrent and predicts the −ve photoconductivity as dark current leads the photocurrent as portrayed in a better manner in Fig. 8.7. The alpha-amylase depiction of TTAHOT with IC_{50} as 49.76, 48.16 and 47.12 for macro, micro and nano-case as the titled specimen having phenyl and antimony for anti-diabetic usage; as customary one nano-TTAHOT is preferred for bio use than the

Table 8.4 AD of macro, micro, and nano-TTAHOT crystals

Plate level	Influx macro scaling	Influx micro scaling	Influx nano-scaling
Long wave	2.9976 microns	3.1216 microns	3.8765 microns

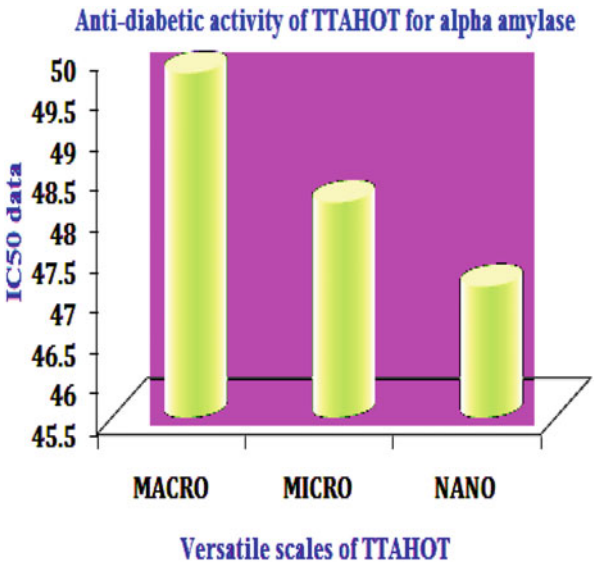

Fig. 8.8 AD of TTAHOT—macro, micro, and nano-scalings

Table 8.5 Influx of TTAHOT crystals

IC_{50} values of macro TTAHOT	IC_{50} values of micro TTAHOT	IC_{50} values of nano-TTAHOT
49.76	48.16	47.12

other case of specimen. The anti-diabetic (AD) characterisation of TTAHOT crystals is appropriately conceded out. The AD action of TTAHOT is primarily owed to the existence of Tellurium and not due to the antimony by the chemical structure and properties as by Table 8.4 and by column chart in Fig. 8.8. Influx value in microns of TTAHOT correspond to macro influx consigns that TTAHOT is superior NLO material and in microns in nano-scaling portrays with the purpose of its superior and enhanced viewpoints in filtering usefulness and in beam displacement as by Table 8.5. So, the TTAHOT crystals are properly and better manner employed in filtering purposes also the data correspond to the arrangement as in Table 8.5 and by column chart in Fig. 8.9. Free radical capability of the extorts is investigated by DPPH, FRAP, and total radical assay as described. A solution of DPPH in methanol is prepared and is mixed with extract in methanol at different concentrations. The test solution and DPPH solution are added with tris-Hcl buffer and the amount with purified water and the tube is protected in dark arrangement to be measured using spectrophotometer; The entire antioxidant action of the test is determined by means of the phosphor molybdenum process as in Table 8.6. The ORTEP—thermal plots of

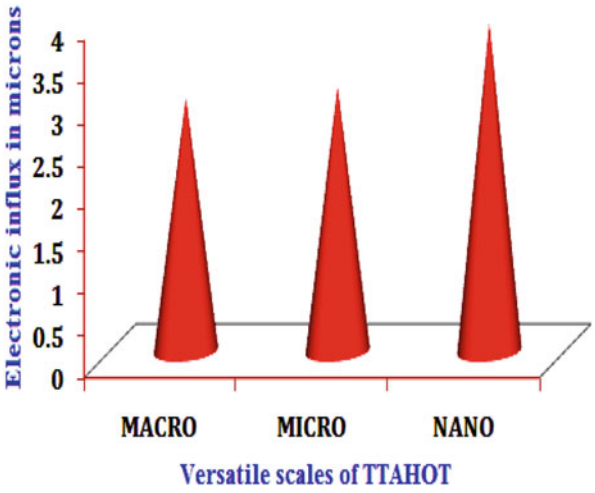

Fig. 8.9 Influx of TTAHOT—macro, micro, and nano-scales

Table 8.6 AO of macro, micro, and nano-TTAHOT crystals

% of DPPH for macro scale	% of DPPH for macro scale	% of DPPH for nano-scale
37.88	37.88	39.43
% of FRAP for macro scale	% of FRAP for macro scale	% of FRAP for nano-scale
19.7	19.7	19.9
Total anti-oxidant for macro scale	Total anti-oxidant for macro scale	Total anti-oxidant for nano-scale
46.0	46.0	47.7

TTAHOT are eventually represented in Figs. 8.10, 8.11, and 8.12 for molecular; unit cell; unit cell exposed approach for the crystalline specimen to identify the orientation as well as the details of the specimen.

8.4 Discussion

Chalcogenide-based crystals have excellent optical use; here TTAHOT is analysed for XRD for lattice parameters and proceeded for frequency doubling and phase matching by NLO data; analysed for the direct, reciprocal lattice, electronic interactions with polyhedral, 3D effect by software. The hardness data gives n as above 2 and can be preceded for tribological work with power loss measurement. The optoelectronic filters are measured for filter use; the −ve photoconduction as well as anti-diabetic and antioxidant pharma use for macro, micro, and nano-scaling is reported.

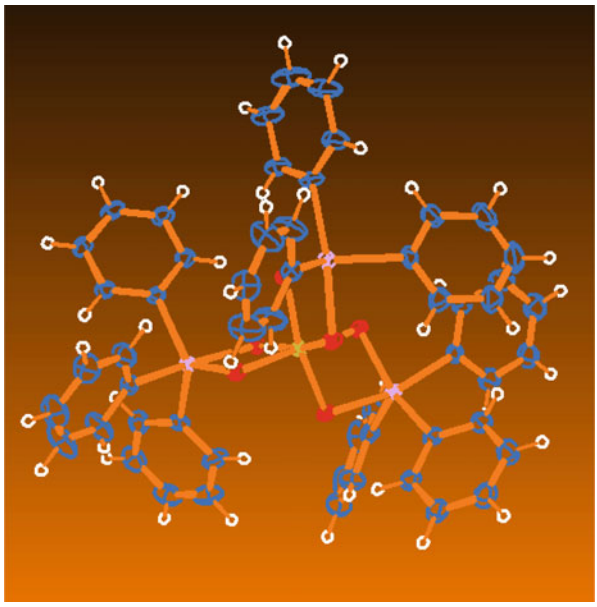

Fig. 8.10 ORTEP of TTAHOT crystals

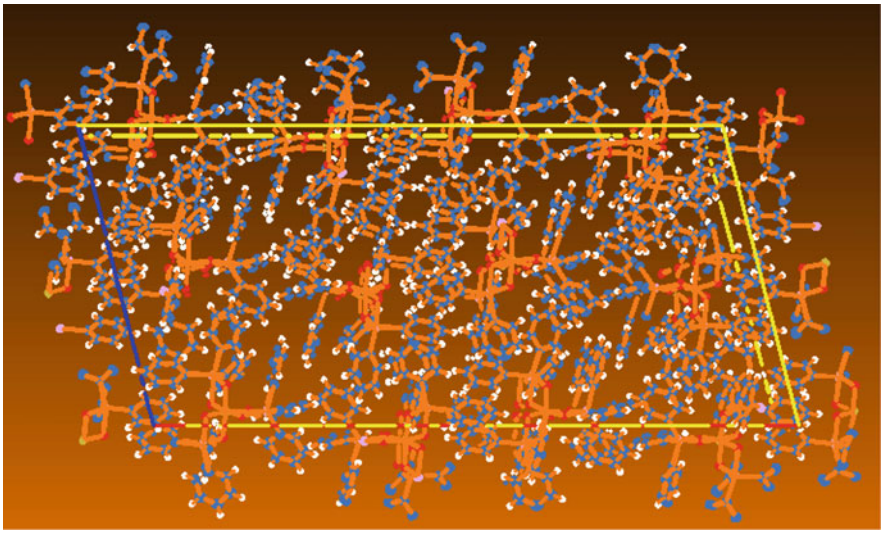

Fig. 8.11 ORTEP—unit cell of TTAHOT crystals

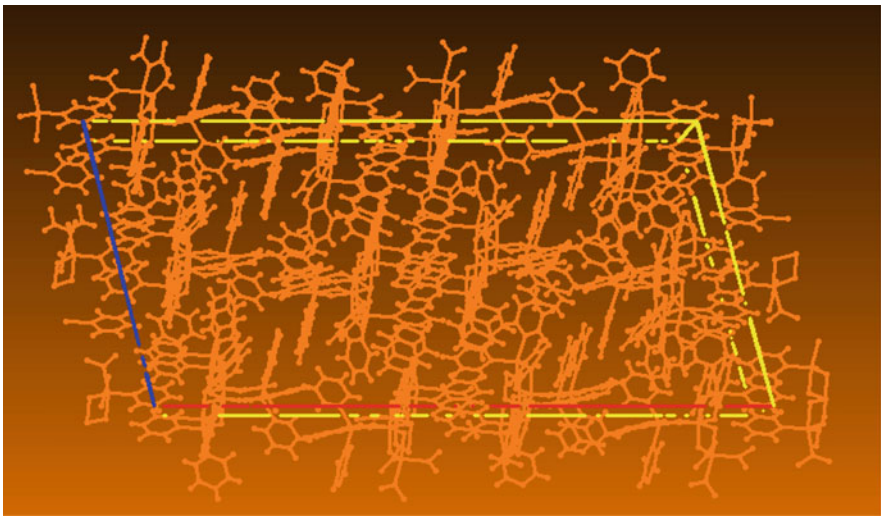

Fig. 8.12 ORTEP—unit cell—exposed effect of TTAHOT crystals

8.5 Conclusion

Chalcogenide crystals of TTAHOT with Tellurium are grown by and studied with single crystal XRD data as monoclinic nature of sample with bond lengths as 47.7150 Å; 9.1178 Å; 22.9325 Å with beta as 104.168°, confirmed by DFT calculations. The nonlinearity is employed for frequency doublers and in phase matching. The direct, reciprocal lattice with matrix parameters, and electronic interactions by Hirshfeld analysis are reported theoretically. The morphology of TTAHOT is performed using SEM analysis and found no major defects/flaws. The hardness of TTAHOT is of Reverse Indentation size effect—RISE and found *n* as above 2 and can be proceeded for tribological uses mainly here coated friction loss measurement. The macro, micro, and nano-influx of TTAHOT are in microns, respectively, for electronic filter usage. The anti-diabetic and anti-oxidant illustration of TTAHOT with IC_{50} for macro, micro, and nano-case by the presence of specimen, the prediction of the −ve photoconductivity is identified for TTAHOT.

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References

Aarthi R, Ramalingam S, Periandy S, SenthilKannan K (2018) Pharmaceutical property interpretation and biological property study on Benzoyl peroxide using quantum spectroscopic and computational tools. J Taibah Univ Sci 12(1):104–122

Baskaran P et al (2020a) Anti-diabetic activities of ZnO doped with Ce (3 at%) nano particles. Mater Today Proc 33:3051–3052. https://doi.org/10.1016/j.matpr.2020.03.268

Baskaran P et al (2020b) Anti-diabetic studies of barium paranitro phenolate macro and nano crystals. Mater Today Proc. https://doi.org/10.1016/j.matpr.2020.03.509

Burley SK, Berman HM, Bhikadiya C (2019) RCSB Protein Data Bank: biological macromolecular structures enabling research and education in fundamental biology, biomedicine, biotechnology and energy. Nucleic Acids Res 47:464–474. https://doi.org/10.1093/nar/gky1004

Dallakyan S, Olson AJ (2014) Small-molecule library screening by docking with PyRx. Methods Mol Biol 1263:243–250. https://doi.org/10.1007/978-1-4939-2269-7_19

Dhieb AC, Valkonen A, Rzaigui M, Smirani W (2015) Synthesis, crystal structure, physico-chemical characterization and dielectric properties of a new hybrid material, 1-Ethylpiperazine-1,4-diium tetrachlorocadmate. J Mol Struct 1102:50–56. https://doi.org/10.1016/j.molstruc.2015.08.044

Farrugia LJ (2012) J Appl Crystallogr 45:849–854

Flora G et al (2020a) Anti diabetic (AD), stiffness and hardness studies of 2-[4-(Trifluoromethyl) phenyl]-1H-benzimidazole crystals-(BAPTDHCPCN) macro and nano crystal. Mater Today Proc 33:4233–4236. https://doi.org/10.1016/j.matpr.2020.07.347

Flora G et al (2020b) Anti-diabetic (AD) and crystal stiffness characterizations of NaBr-added L-alanine (LANB)–a comparative analysis in macro and nano scale crystals. Mater Today Proc. https://doi.org/10.1016/j.matpr.2020.06.268

Flora G et al (2020c) Anti-inflammatory (AI) and crystalline hardness characterisations of 4-(4-chlorophenyl-7,7-dimethyl-7,8-dihydro-4h-1-benzopyran-2,5(3h,6h)-dione-CPDMDHHBPHHD)—comparative analysis of macro and nano scales crystals. Mater Today Proc. https://doi.org/10.1016/j.matpr.2020.05.656

Gnanam S et al (2019) Antimicrobial activity of the novel metal oxide nanoparticles against selected human pathogenic bacteria. IOP Conf Ser Mater Sci Eng 561:012086. https://doi.org/10.1088/1757-899X/561/1/012086

Gunasekaran S, SenthilKannan K, Loganathan S et al (2013) Structural studies on picolinium maleate crystal by density functional methods. Indian J Phys 87:1189–1197. https://doi.org/10.1007/s12648-013-0363-8

Halgren TA (1996) Merck molecular force field I basis, form, scope, parameterization, and performance of MMFF94. J Comput Chem 17:490–519. https://doi.org/10.1002/(SICI)1096-987X(199604)17:5/6<490::AID-JCC1>3.0.CO;2-P

Hrizi C, Chaari N, Abid Y, Chniba-Boudjada N, Chaabouni S (2012) Structural characterization, vibrational and optical properties of a novel one-dimensional organic–inorganic hybrid based-iodobismuthate(III) material [C10H7NH3]BiI4. Polyhedron 46:41–46. https://doi.org/10.1016/j.poly.2012.07.062

Jothibas M et al (2019) Structural, optical and photocatalytic activity of Ag doped ZnO nanoparticles obtained by sol-gel method. AIP Conf Proc 2162:020151. https://doi.org/10.1063/1.5130361

Kalaipoonguzhali V et al (2020) Comparison of adsorption energy, ionization potential and electron affinity of CuS-ACT and CuS-Nit nanostructures monowire for nano device fabrication by computational approach. Mater Today Proc. https://doi.org/10.1016/j.matpr.2020.01.579

Khadayat K, Marasini BP, Gautam H et al (2020) Evaluation of the alpha-amylase inhibitory activity of Nepalese medicinal plants used in the treatment of diabetes mellitus. Clin Phytosci 6:1–8

Kishore N, SenthilKannan K, Periyanayagi T et al (2017) CO and HCHO adsorption on FeO monowire devices: a DFT study. Appl Phys A Mater Sci Process 123:706. https://doi.org/10.1007/s00339-017-1330-6

Kolanjinathan M, Senthilkannan K, Paramasivam S, Baskaran P, Iyanar M (2020) Anti-diabetic studies of 4-(4-chlorophenyl)-7,7-dimethyl-7,8-dihydro-4H-1-benzopyran-2,5(3H,6H)-dione – (CPDMDHHBPHHD) nano crystals. Mater Today Proceed. https://doi.org/10.1016/j.matpr.2020.01.575

Krishnamurthy MS, Begum NS et al (2014) Crystal structure of 4-azido-methyl-6-isopropyl-2H-chromen-2-one. Acta Crystallogr E 70:760. https://doi.org/10.1107/S2056989015004387

Krishnaveni R et al (2019) Antimicrobial activity of medicinal plants such as green tea (Camellia sinensis), illavangam (Cinnamomum verum) and pomegranate (Punica granatum) used against UTI (urinary tract infection) causing pathogens. Int J Anal Exp Modal Anal 11:8

Kumar K, Senthilkannan K, Hariharasuthan R, Jothibas M, Vimalan M, Baskaran P, Iyanar M, Kolanjinathan M (2020) Growth of diethyl 3,30-[(2,4-dichlorophenyl) methylidene] bis (1H-indole-2-carboxylate)-(D32DMBC) organic NLO single crystal and its optical, thermal, mechanical, dielectric and computational studies. J Mater Sci Mater Electron 31(23):1–8. https://doi.org/10.1007/s10854-020-04594-y

Kurtz SK, Perry TT (1968) A powder technique for the evaluation of nonlinear optical materials. J Appl Phys 39:3798–3813. https://doi.org/10.1063/1.1656857

Malathi Rekha T et al (2018) Photoluminescence study of LaPO4 phosphor. Int Res J Nat Appl Sci 5(4):133–154

Momma K, Izumi F (2011) VESTA 3 for three-dimensional visualization of crystal, volumetric and morphology data. J Appl Crystallogr 44:1272–1276. https://doi.org/10.1107/S0021889811038970

Oyedemi SO, Oyedemi BO, Ijeh II (2017) Alpha-amylase inhibition and antioxidative capacity of some antidiabetic plants used by the traditional healers in Southeastern Nigeria. Sci World J 2017:3592491. https://doi.org/10.1155/2017/3592491

Patel RP, SenthilKannan K, Hariharasuthan R et al (2021) Growth and XRD, elemental, mechanical, dielectric, optical and photoconductivity, and surface morphological characterizations of 2-[4-(trifluoromethyl) phenyl]-1H-benzimidazole (TFMPHB) crystals for electronic, mechanical applications. Braz J Phys 51:339–350. https://doi.org/10.1007/s13538-021-00883-x

Pek AJS (2003) Single – crystal structure validation with the program PLATON. J Appl Crystallogr 36:7–11. https://doi.org/10.1107/S0021889802022112

Periyathambi P et al (2020) Fluorescence and filter characterizations of NaBr-added L-alanine (LANB)–A comparative analysis in macro and nano scaled crystals. Mater Today Proc. https://doi.org/10.1016/j.matpr.2020.06.208

Saravanan P, SenthilKannan K, Divya R et al (2020a) A perspective approach towards appreciable size and cost-effective solar cell fabrication by synthesizing ZnO nanoparticles from Azadirachta indica leaves extract using domestic microwave oven. J Mater Sci Mater Electron 31:4301–4309. https://doi.org/10.1007/s10854-020-02985-9

Saravanan P et al (2020b) Biofriendly and competent domestic microwave assisted method for the synthesis of ZnO nanoparticles from the extract of Azadirachta indica leaves. Mater Today Proc. https://doi.org/10.1016/j.matpr.2020.03.799

Sathiya V, Suganya K, SenthilKannan K et al (2022) J Mater Sci Mater Electron 33:19514. https://doi.org/10.1007/s10854-022-08787-5

Selvaraj L et al (2020) Anti-diabetic (AD) studies of bis glycine hydro bromide–BGHB macro crystals milled to nano scale of 219 nm as the preliminary fine particles. Mater Today Proc. https://doi.org/10.1016/j.matpr.2020.06.207

SenthilKannan K (2018) Growth and characterisation-XRD, NLO of bis 2 amino pyridinium maleate (B2APM) crystals. Int J Eng Sci Math 7:1–3

SenthilKannan K, Gunasekaran S (2013) Synthesis, growth and interpretation of (organic NLO) 4 bromo-4l chloro benzylidene aniline (BCBA) crystals. Int J Front Int Sci Technol 3(3):29–36

SenthilKannan K, Gunasekaran S, Seethalakshmi KA (2013a) Growth and spectroscopic studies of pure and L-proline doped ZTS crystal (with Taxol). Int J Sci Eng Res 4(2):1–5
Senthilkannan K et al (2013b) Spectroscopic (IR & Raman) studies of picolinium maleate (pm) single crystal. Sch Res Libr Arch Appl Sci Res 5(3):100–103
SenthilKannan K et al (2014) UV, SEM, powder XRD of AAC crystals. Int J ChemTech Res 6(5): 3187–3190
SenthilKannan K, Kaleemullah Khan B, Ali HAJ, Ponnusamy VK, Govindan NM (2020a) Mater Today Proc 33:2779. https://doi.org/10.1016/j.matpr.2020.02.133
SenthilKannan K, Krishnaveni R, Anbuvel D, Porselvi VM, Ali HAJ (2020b) Mater Today Proc 33: 2776. https://doi.org/10.1016/j.matpr.2020.02.132
Senthilkannan K et al (2020c) Tribological, filter studies of 3-Bromo-2-Hydroxy benzoic acid (BHBA) macro and nano crystals. Mater Today Proc. https://doi.org/10.1016/j.matpr.2020.06.582
Senthilkannan K et al (2020d) Fluorescence, filter, nano tribological studies of 12-(4-Chlorophenyl)-9, 9-Dimethyl-9, 10-Dihydro-8H-Benzo [A] Xanthen-11 (12H)-One–(CPDDHBXH) macro and nano crystals. Mater Today Proc. https://doi.org/10.1016/j.matpr.2020.06.593
Senthilkannan K et al (2020e) Tribological, filter, FTIR and fluorescence studies of L-Alaninium tartrate (LAT) Macro and nano crystals. Mater Today Proc. https://doi.org/10.1016/j.matpr.2020.06.585
Senthilkannan K et al (2020f) Anti diabetic (AD) studies of bis-glycine hydro bromide (45 nm) nano crystals. Mater Today Proc. https://doi.org/10.1016/j.matpr.2020.04.203
SenthilKannan K et al (2020g) Anti-diabetic (AD) activities of ZnO doped with Ce (7 at%) nano particles (NP). Mater Today Proc. https://doi.org/10.1016/j.matpr.2020.03.505
Senthilkannan K et al (2020h) Anti-diabetic activities of ZnO doped with Ce (5 at%) nano particles (NPs). Mater Today Proc. https://doi.org/10.1016/j.matpr.2020.03.506
SenthilKannan K et al (2020i) Anti diabetic (AD) studies of picolinium maleate nano crystals. Mater Today Proc. https://doi.org/10.1016/j.matpr.2020.03.076
SenthilKannan K et al (2020j) Effect of anti microbial and fluorescence on L-Alaninium maleate (LAM) macro and nano crystals. Mater Today Proc. https://doi.org/10.1016/j.matpr.2020.02.133
SenthilKannan K et al (2020k) Anti microbial and fluorescence activities of L-valinium picrate (LVP) macro and nano crystals. Mater Today Proc. https://doi.org/10.1016/j.matpr.2020.02.132
SenthilKannan K et al (2020l) Photo catalytic, anti bacterial activities of Ce doped zinc oxide nano particles. Mater Today Proc. https://doi.org/10.1016/j.matpr.2020.01.576
SenthilKannan K et al (2020m) Electronic transport, HOMO–LUMO and computational studies of CuS monowire for nano device fabrication by DFT approach. Mater Today Proc. https://doi.org/10.1016/j.matpr.2020.01.574
SenthilKannan K et al (2020n) Anti diabetic (AD) activities of L-valinium picrate (LVP) macro and nano crystals. Mater Today Proc. https://doi.org/10.1016/j.matpr.2020.01.550
Senthilkumar R et al (2020) Anti-diabetic (AD) and hardness profile of 12-(4-chlorophenyl)-9,9-dimethyl-9,10-Dihydro-8H-benzo [a] xanthen-11 (12H)-one–(CPDDHBXH)–comparative analysis of macro and nano crystals. Mater Today Proc 33:4167–4170. https://doi.org/10.1016/j.matpr.2020.06.594
Spackman PR, Turner MJ, McKinnon JJ, Wolff SK, Grimwood DJ, Jayatilaka D, Spackman MA (2021) J Appl Crystallogr 54:3. https://doi.org/10.1107/S1600576721002910
Suganya K, Maalmarugan J, Manikandan R et al (2022) J Mater Sci Mater Electron 33:19320. https://doi.org/10.1007/s10854-022-08770-0
Tundis R, Loizzo MR, Menichini F (2010) Natural products as alpha-amylase and alpha-glucosidase inhibitors and their hypoglycaemic potential in the treatment of diabetes: an update. Mini Rev Med Chem 10:315–331. https://doi.org/10.2174/138955710791331007
Vasanth Winston X, Sankar D, SenthilKannan K et al (2022) J Mater Sci Mater Electron. https://doi.org/10.1007/s10854-022-08873-8

Von Hippel A, Gross EP, Telstis FG, Geller A (1953) Photocurrent, space-charge buildup, and field emission in alkali halide crystals. Phys Rev 91:568–579. https://doi.org/10.1103/PhysRev.91.568

Wilcox G (2005) Insulin and insulin resistance. Clin Biochem Rev 26:19–39

Williams LK, Zhang X, Caner S (2019) The amylase inhibitor montbretin A reveals a new glycosidase inhibition motif. Nat Chem Biol 11:691–696. https://doi.org/10.1038/nchembio.1865

Yang CY, Yen YY, Hung KC et al (2019) Inhibitory effects of pu-erh tea on alpha glucosidase and alpha amylase: a systemic review. Nutr Diabetes 9:1–6. https://doi.org/10.1038/s41387-019-0092-y

Zhang ZY, Yong XY, Xiao M (2002) Lattice contraction in free-standing CdSe nanocrystals. Appl Phys Lett 81:2076–2078. https://doi.org/10.1063/1.1507613

Growth and Characterizations of Red Bromide: The Pleochroism Based Crystals for Bio-Medicinal, Electronic and Mechano Uses

9

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Abstract

The red bromide (N,N-dimethyl-p-phenylenediamine *bromide*) crystal is grown properly using methanol as solvent after successive recrystallization process and is a pleochroism-based crystal varying from dark to pale greenish colour while polarized. The lattice constants of red bromide crystals confirmed the orthorhombic type of system and the grown crystal is confirmed for elements by CHNSO method experimentally. The electronic property is confirmed by filter influx property in microns for macro, micro, thin-film, and nano scalings as 4.1836,

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4.2576, 4.5481, and 4.9186, respectively. The anti-diabetic property of the specimen for macro, micro, and nano scalings are analyzed for α amylase and α glucosidase as bio-medicinal use and amongst them nano is preferred; also analyzed for anti-bacterial and anti-fungal investigations against specimen. The crystalline hardness is found to have RISE effect based on n value.

Keywords

Red bromide · Pleochroism · Filters · Hardness · Anti-diabetic

9.1 Introduction

The organic type of crystals is so preferred based on their profound use in electronic as well as other zones; the interactions of organic specimen are more prevalent in industrial, manufacturing, and gadgets (Gunasekaran et al. 2013; Aarthi et al. 2018; SenthilKannan et al. 2013b; Kishore et al. 2017; Saravanan et al. 2020b; Jothibas et al. 2019; Gnanam et al. 2019). The organic nanocrystalline (Krishnaveni et al. 2019; SenthilKannan 2018; SenthilKannan et al. 2013a, b, 2014, 2020a, b, c; Malathi Rekha et al. 2018; Flora et al. 2020a, b, c; Senthilkumar et al. 2020b) specimen by the methodology of reprecipitation is of core credit in nano scales (SenthilKannan et al. 2020d, e; Wilcox 2005; Yang et al. 2019; Tundis et al. 2010; Khadayat et al. 2020; Kumar et al. 2020; Farrugia 2012). Low molecular weight aromatic compounds are so preferred due to their potential candidate profile in nano-medicinal and nano-electro approaches (Kolanjinathan et al. 2020a, b; Selvaraj et al. 2020; Flora et al. 2020a, b; SenthilKannan et al. 2020f). Red bromide is pleochroism-based crystalline materials of macro, micro, and nano-scale and thin-film based; for analyzing the XRD, elemental, absorbance, structural, 3D portfolio, axial, Laue's pattern, phase match, photoconductive nature, hardness, anti-diabetic with alpha amylase and alpha glucosidase cases and reported for bio-medicinal case nano is preferred (Saravanan et al. 2020b; SenthilKannan et al. 2020g, h, i, j, k).

9.2 Characterizations

9.2.1 XRD Data

The lattice parameters are measured using XRD method and are *a*, *b,* and *c* as 6.380 Å, 22.481 Å, 6.212 Å and the dimensions are 15 × 12 × 6 mm^3 with volume as 890.97 $Å^3$, the space group is $Cmc2_1$ and crystal is orthorhombic (Senthilkannan et al. 2020l, m; Kalaipoonguzhali et al. 2020).

9.2.2 CHNSO Data

The elemental part of red bromide macro scaled one is represented with C, H, and N as 44.44%, 5.60%, and 12.96% and Br is not detected in the specimen; but present in red bromide composite as in Table 9.1 (Kolanjinathan et al. 2020b; Senthilkannan et al. 2020m, n; Flora et al. 2020c; Krishnamurthy and Begum 2014; Patel et al. 2021; Zhang et al. 2002).

9.2.3 Computational Data

The molecular structure of red bromide by software is given in Fig. 9.1; the space-filled effective model of Zwitter ionic nature of red bromide is given in Fig. 9.2; the unit cell impact of the titled crystal is in Fig. 9.3; the 3D collection of the crystal is in Figs. 9.4, 9.5, and 9.6 portray the stereographic projection, and the Laue's interpretation of the red bromide crystal is shown in Figs. 9.7, 9.8, 9.9, and 9.10

Table 9.1 CHNSO analysis of red bromide crystals

C8H12N2Br/elements type	% of elements
C	44.44
H	5.60
N	12.96
Br	Not detected in CHNSO but present in the specimen
Total	63%

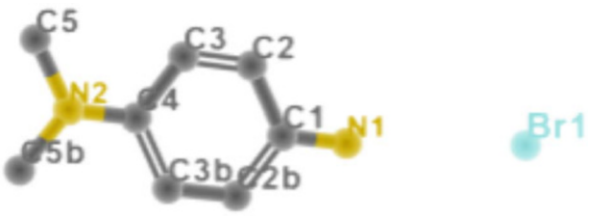

Fig. 9.1 Molecular impact by computational of red bromide

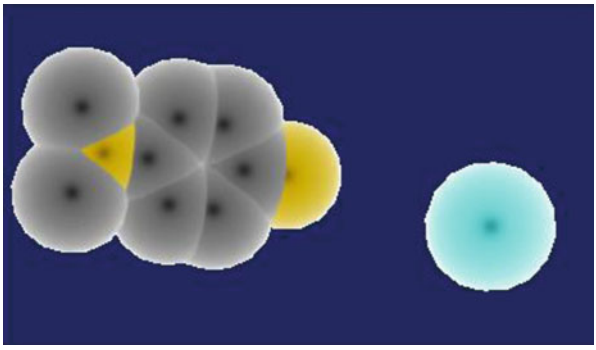

Fig. 9.2 Molecular impact by space-filled effect by computational of red bromide

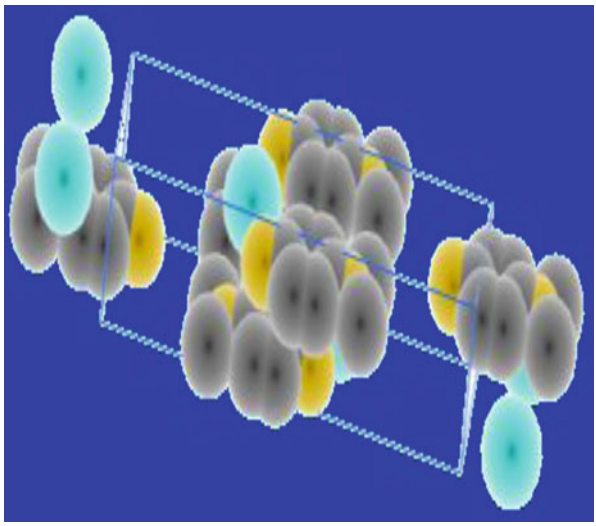

Fig. 9.3 Unit cell impact by computational of red bromide

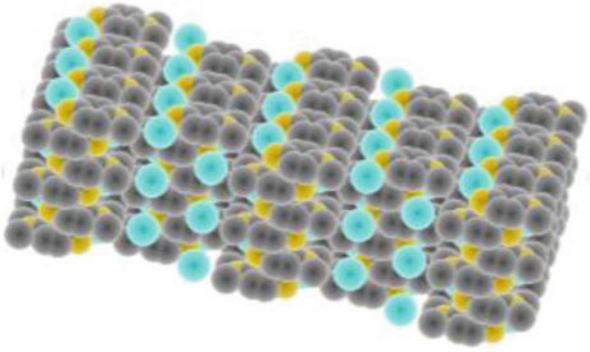

Fig. 9.4 3D impact by computational of red bromide

correspondingly for 1161 generated hkl parameter with d value min and max as 0.918Å; 3.489Å; h limit as 7; k limit as 25; l limit as 7; voltage value as 40 kV; wavelength min value as 0.309 Å (Kurtz and Perry 1968; Von Hippel et al. 1953; Hrizi et al. 2012; SenthilKannan et al. 2013b; Dhieb et al. 2015; Tundis et al. 2010; Oyedemi et al. 2017).

9.2.4 Absorbance, Phase Matching, Photoconductivity, and Influx of the Red Bromide Crystals

The absorbance data from Fig. 9.11 tells about the nano level cut-off of 272 nm; in the spectral range of 200–800 nm; and the line after 300 nm nearly low absorption and portrays the nonlinearity in specimen (Khadayat et al. 2020; Baskaran et al. 2020a, b; Burley et al. 2019; DeLano 2020; Dallakyan and Olson 2014). Figure 9.12

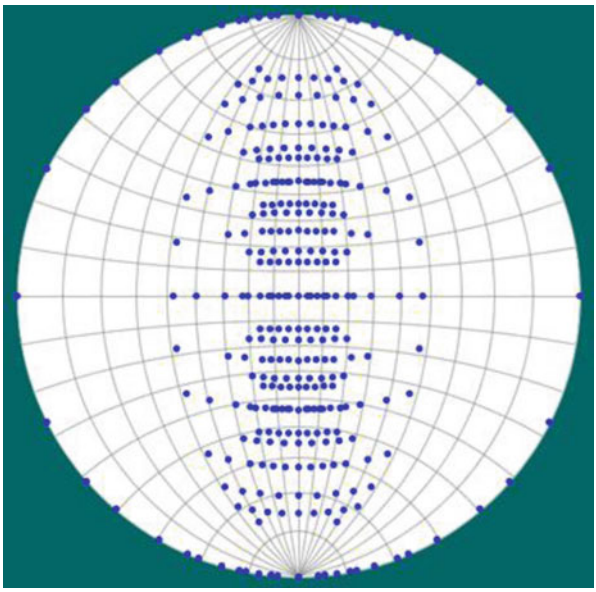

Fig. 9.5 Stereographic projection by computational of red bromide by mode I

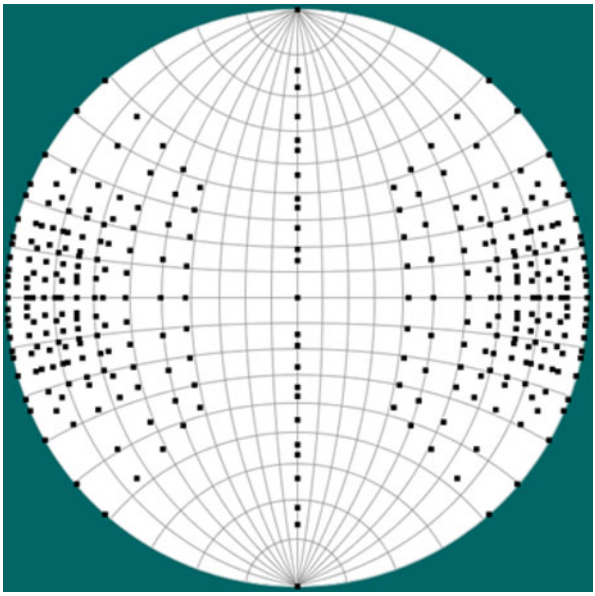

Fig. 9.6 Stereographic projection by computational of red bromide by mode II

explains the 94.05 mV for the phase matching proviso of red bromide for the related KDP sample; the versatile particle size is mentioned and is for the less than 50 μm scaling (Halgren 1996; Momma and Izumi 2011; Spackman et al. 2021; Pek 2003; Senthilkumar et al. 2020b; SenthilKannan et al. 2020c, d).

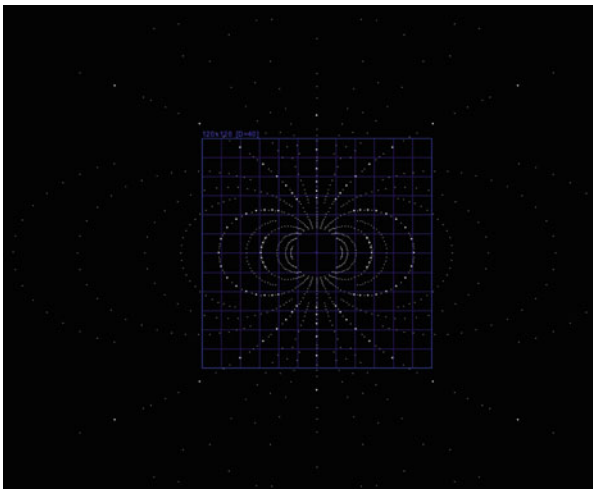

Fig. 9.7 Laue's impact by computational of red bromide by mode I with box

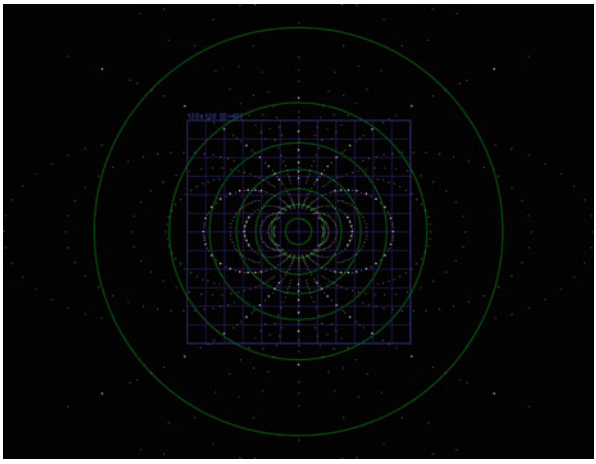

Fig. 9.8 Laue's impact by computational of red bromide by mode II with box, circle

The photoconductive nature of red bromide is measured in the 320 nA; 1250 V/cm range and specifies that the negative photo-conducting nature of the specimen as dark current leads to photocurrent as in Fig. 9.13 (Suganya et al. 2022; Sathiya et al. 2022; Vasanth Winston et al. 2022). The electronic property is long-established by filter influx belongings in the units of microns for macro, micro, thin-film and nano scalings—which is milled from macro scales one as 4.1836, 4.2576, 4.5481, and 4.9186, respectively, as the predominant factor for photovoltaic and opto-electronic property (Pek 2003; Senthilkumar et al. 2020b; SenthilKannan et al. 2020c, d; Suganya et al. 2022; Sathiya et al. 2022; Vasanth Winston et al. 2022).

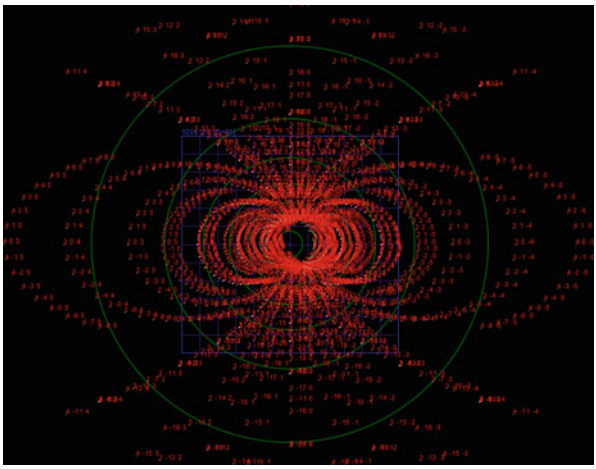

Fig. 9.9 Laue's impact by computational of red bromide by (100) mode with label

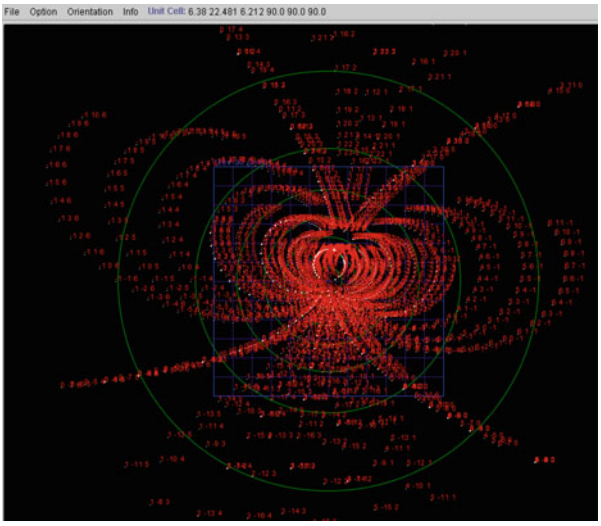

Fig. 9.10 Laue's impact by computational of red bromide by (111) mode with label

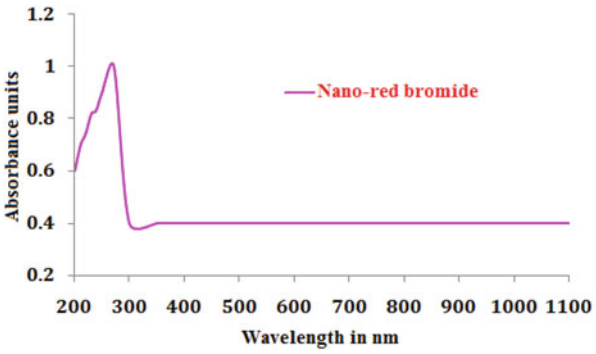

Fig. 9.11 Absorbance data red bromide of nano scale

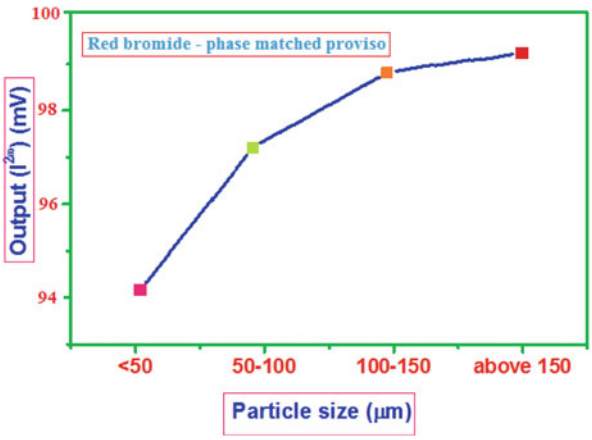

Fig. 9.12 Phase matching data for versatile particle sizes of red bromide

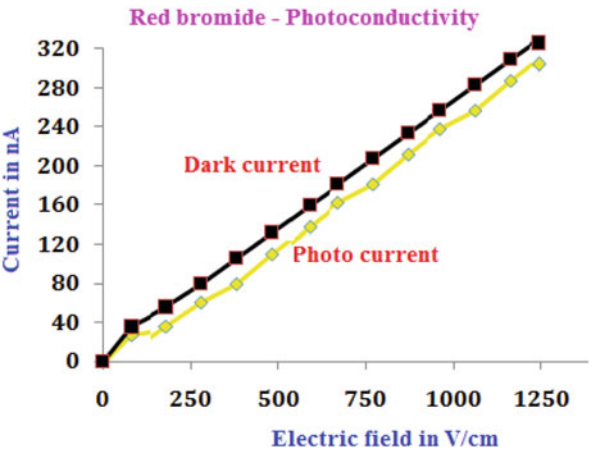

Fig. 9.13 Photoconductivity data for red bromide

Table 9.2 Antibacterial work of red bromide crystals

Specimen	50 μL	100 μL	Disc (CAZ) 10 mg	DMSO
E. coli	2 mm	3 mm	2 mm	Nil
B. subtilis	3 mm	4 mm	7 mm	Nil
S. aureus	2 mm	3 mm	9 mm	Nil

9.2.5 Hardness and Bio-medicinal Impact of Red Bromide Crystals

The red bromide crystal is analyzed for hardness by Vicker's profile for 25, 50, and 100 g and found the RISE—reverse ISE effect based on H_V data by the diagonal scalings for the different values and n is 3.52.

The antibacterial-AB, antifungal-AF as well as antidiabetic-AD for AA-alpha amylase and AG-alpha glucosidase are analyzed for red bromide crystals and reported as in Tables 9.2, 9.3, and 9.4 and bar chart (Figs. 9.14, 9.15, and 9.16)

Table 9.3 Antifungal work of red bromide crystals

Specimen	50 µL	100 µL	Standard
A. niger	Nil	Nil	Nil
A. flavus	Nil	Nil	Nil
A. terreus	2 mm	3 mm	Nil

Table 9.4 Antidiabetic work of red bromide crystals

Specimen	IC_{50}-AA	IC_{50}-AG
Macro	58.86	59.94
Micro	57.34	58.76
Nano	56.16	57.98

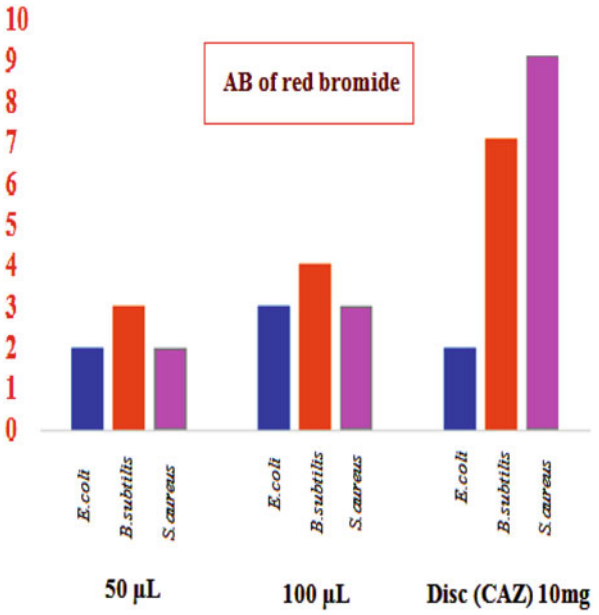

Fig. 9.14 Antibacterial column chart of three versatile species of red bromide

corresponding to AB; AF; AD and described that AB is active for all species for macro-scale and AF only for *A. terreus* for macro-scale and AD for all of macro, micro, and nano scalings and nano is preferred in AD and concluding that red bromide specimen is better against diabetic and bacterial and less of antifungal impact and is a better bio-medicinal tool for analyzing against diabetic and bacteria (Periyathambi et al. 2020; Saravanan et al. 2020a; SenthilKannan and Gunasekaran 2013; Senthilkumar et al. 2020a; Williams et al. 2019).

9.3 Discussions

The red bromide crystal is grown properly using methanol as solvent after successive recrystallization processes.

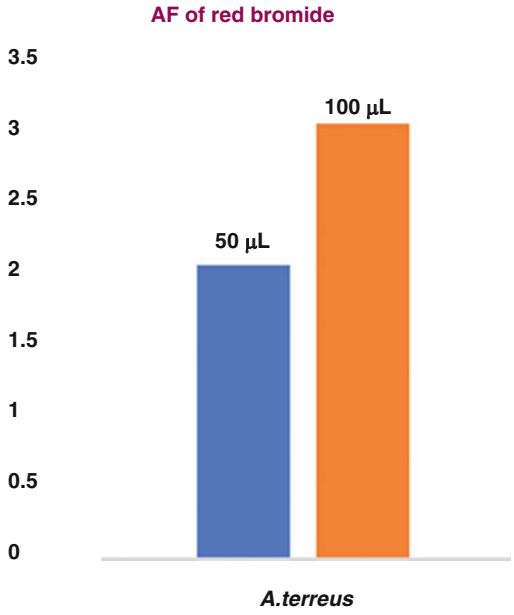

Fig. 9.15 Antifungal column chart of *A. terreus* species of red bromide

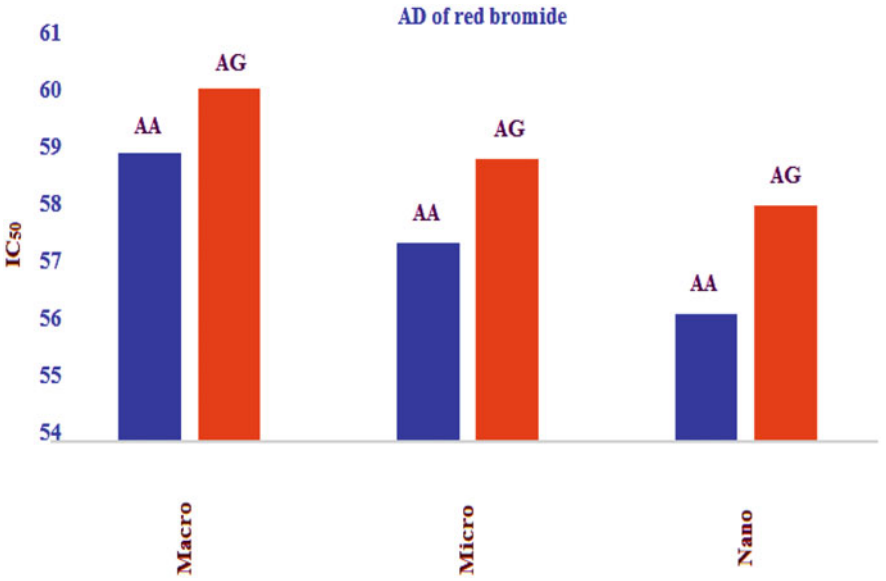

Fig. 9.16 Antidiabetic chart of AA and AG for versatile scalings of red bromide

It is a pleochroism-based crystal varying from dark to pale greenish colour while polarized.

The lattice constants of red bromide crystals confirmed the orthorhombic type of system

The grown crystal is confirmed for elements by CHNSO method experimentally. The electronic property is confirmed by filter influx property in microns for macro, micro, thin-film, and nano scalings as 4.1836, 4.2576, 4.5481, and 4.9186, respectively.

The anti-diabetic property for α amylase and α glucosidase and anti-bacterial and anti-fungal investigations against specimen are reported.

The crystalline hardness is found to have a RISE effect based on n value.

9.4 Conclusions

The red bromide crystal is grown subsequently with sequential recrystallization procedure and is a pleochroism-based crystal varying the colour while polarized. The lattice constants are confirming the orthorhombic type of system and the grown crystal is confirmed for elements by CHNSO method experimentally and made to nano form by milling of 51 nm. The electronic property is confirmed by filter influx property in microns for macro, micro, thin-film, and nano scalings, respectively. The anti-diabetic property of the specimen for macro, micro, and nano scalings are analyzed for α amylase and α glucosidase as bio-medicinal use and analyzed for anti-bacterial and anti-fungal investigations using the versatile scaling of the specimen. The crystalline hardness is found to have RISE effect based on *n* value the work hardening esteem.

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References

Aarthi R, Ramalingam S, Periandy S, SenthilKannan K (2018) Pharmaceutical property interpretation and biological property study on Benzoyl peroxide using quantum spectroscopic and computational tools. J Taibah Univ Sci 12:104–122

Baskaran P et al (2020a) Anti-diabetic studies of barium paranitro phenolate macro and nano crystals. Mater Today Proc. https://doi.org/10.1016/j.matpr.2020.03.509

Baskaran P et al (2020b) Anti-diabetic activities of ZnO doped with Ce (3 at%) nano particles. Mater Today Proc. https://doi.org/10.1016/j.matpr.2020.03.268

Burley SK, Berman HM, Bhikadiya C (2019) RCSB Protein Data Bank: biological macromolecular structures enabling research and education in fundamental biology, biomedicine, biotechnology and energy. Nucleic Acids Res 47:464–474. https://doi.org/10.1093/nar/gky1004

Dallakyan S, Olson AJ (2014) Small-molecule library screening by docking with PyRx. Methods Mol Biol 1263:243–250. https://doi.org/10.1007/978-1-4939-2269-7_19

DeLano WL (2020) The PyMOL molecular graphics system. http://www.pymol.org

Dhieb AC, Valkonen A, Rzaigui M, Smirani W (2015) Synthesis, crystal structure, physico-chemical characterization and dielectric properties of a new hybrid material, 1-Ethylpiperazine-1,4-diium tetrachlorocadmate. J Mol Struct 1102:50–56. https://doi.org/10.1016/j.molstruc.2015.08.044

Farrugia LJ (2012) J Appl Crystallogr 45:849–854

Flora G et al (2020a) Anti diabetic (AD), stiffness and hardness studies of 2-(4-(trifluoromethyl) phenyl)-1H-benzimidazole crystals-(BAPTDHCPCN) macro and nano crystal. Mater Today Proc. https://doi.org/10.1016/j.matpr.2020.07.347

Flora G et al (2020b) Anti-diabetic (AD) and crystal stiffness characterizations of NaBr-added L-alanine (LANB)–A comparative analysis in macro and nano scale crystals. Mater Today Proc. https://doi.org/10.1016/j.matpr.2020.06.268

Flora G et al (2020c) Anti-inflammatory (AI) and crystalline hardness characterisations of 4-(4-chlorophenyl)-7,7-dimethyl-7,8-dihydro-4h-1-benzopyran-2,5(3h,6h)-dione-CPDMDHHBPHHD–comparative analysis of macro and nano scales crystals. Mater Today Proc. https://doi.org/10.1016/j.matpr.2020.05.656

Gnanam S et al (2019) Antimicrobial activity of the novel metal oxide nanoparticles against selected human pathogenic bacteria. IOP Conf Ser Mater Sci Eng 561:012086. https://doi.org/10.1088/1757-899X/561/1/012086

Gunasekaran S, SenthilKannan K, Loganathan S et al (2013) Structural studies on picolinium maleate crystal by density functional methods. Indian J Phys 87:1189–1197. https://doi.org/10.1007/s12648-013-0363-8

Halgren TA (1996) Merck molecular force field I basis, form, scope, parameterization, and performance of MMFF94. J Comput Chem 17:490–519. https://doi.org/10.1002/(SICI)1096-987X(199604)17:5/6<490::AID-JCC1>3.0.CO;2-P

Hrizi C, Chaari N, Abid Y, Chniba-Boudjada N, Chaabouni S (2012) Structural characterization, vibrational and optical properties of a novel one-dimensional organic–inorganic hybrid based-iodobismuthate(III) material, (C10H7NH3)BiI4. Polyhedron 46:41–46. https://doi.org/10.1016/j.poly.2012.07.062

Jothibas M et al (2019) Structural, optical and photocatatic activity of Ag doped ZnO nanoparticles obtained by sol-gel method. AIP Conf Proc 2162:020151. https://doi.org/10.1063/1.5130361

Kalaipoonguzhali V et al (2020) Comparison of adsorption energy, ionization potential and electron affinity of CuS-ACT and CuS-Nit nanostructures monowire for nano device fabrication by computational approach. Mater Today Proc. https://doi.org/10.1016/j.matpr.2020.01.579

Khadayat K, Marasini BP, Gautam H et al (2020) Evaluation of the alpha-amylase inhibitory activity of Nepalese medicinal plants used in the treatment of diabetes mellitus. Clin Phytosci 6:1–8

Kishore N, SenthilKannan K, Periyanayagi T et al (2017) CO and HCHO adsorption on FeO monowire devices: a DFT study. Appl Phys A Mater Sci Process 123:706. https://doi.org/10.1007/s00339-017-1330-6

Kolanjinathan M, Senthilkannan K, Paramasivam S, Baskaran P, Iyanar M (2020a) Anti-diabetic studies of 4-(4-chlorophenyl)-7,7-dimethyl-7,8-dihydro-4H-1-benzopyran-2,5(3H,6H)-dione –(CPDMDHHBPHHD) nano crystals. Mater Today Proc. https://doi.org/10.1016/j.matpr.2020.01.575

Kolanjinathan M et al (2020b) Anti-diabetic studies of 4-(4-chlorophenyl)-7,7-dimethyl-7,8-dihydro-4H-1-benzopyran-2,5(3H,6H)-dione-(CPDMDHHBPHHD) nano crystals. Mater Today Proc. https://doi.org/10.1016/j.matpr.2020.01.575

Krishnamurthy MS, Begum NS (2014) Crystal structure of 4-azido-methyl-6-isopropyl-2H-chromen-2-one. Acta Crystallogr E 70:760. https://doi.org/10.1107/S2056989015004387

Krishnaveni R et al (2019) Antimicrobial activity of medicinal plants such as green tea (Camellia sinensis), illavangam (Cinnamomum verum) and pomegranate (Punica granatum) used against UTI (urinary tract infection) causing pathogens. Int J Anal Exp Modal Anal 11:8

Kumar K, Senthilkannan K, Hariharasuthan R, Jothibas M, Vimalan M, Baskaran P, Iyanar M, Kolanjinathan M (2020) Growth of diethyl 3,30-((2,4-dichlorophenyl) methylidene) bis (1H-indole-2-carboxylate)-(D32DMBC) organic NLO single crystal and its optical, thermal, mechanical, dielectric and computational studies. J Mater Sci Mater Electron 31(23):1–8. https://doi.org/10.1007/s10854-020-04594-y

Kurtz SK, Perry TT (1968) A powder technique for the evaluation of nonlinear optical materials. J Appl Phys 39:3798–3813. https://doi.org/10.1063/1.1656857

Malathi Rekha T et al (2018) Photoluminescence study of LaPO4 phosphor. Int Res J Nat Appl Sci 5(4):133–154

Momma K, Izumi F (2011) VESTA 3 for three-dimensional visualization of crystal, volumetric and morphology data. J Appl Crystallogr 44:1272–1276. https://doi.org/10.1107/S0021889811038970

Oyedemi SO, Oyedemi BO, Ijeh II et al (2017) Alpha-amylase inhibition and antioxidative capacity of some antidiabetic plants used by the traditional healers in Southeastern Nigeria. Sci World J 2017:1–12. https://doi.org/10.1155/2017/3592491

Patel RP, SenthilKannan K, Hariharasuthan R et al (2021) Growth and XRD, elemental, mechanical, dielectric, optical and photoconductivity, and surface morphological characterizations of 2-(4-(trifluoromethyl) phenyl)-1H-benzimidazole (TFMPHB) crystals for electronic, mechanical applications. Braz J Phys 51:339–350. https://doi.org/10.1007/s13538-021-00883-x

Pek AJS (2003) Single – crystal structure validation with the program PLATON. J Appl Crystallogr 36:7–11. https://doi.org/10.1107/S0021889802022112

Periyathambi P et al (2020) Fluorescence and filter characterizations of NaBr-added L-alanine (LANB)–a comparative analysis in macro and nano scaled crystals. Mater Today Proc. https://doi.org/10.1016/j.matpr.2020.06.208

Saravanan P, SenthilKannan K, Divya R et al (2020a) A perspective approach towards appreciable size and cost-effective solar cell fabrication by synthesizing ZnO nanoparticles from Azadirachta indica leaves extract using domestic microwave oven. J Mater Sci Mater Electron 31:4301–4309. https://doi.org/10.1007/s10854-020-02985-9

Saravanan P et al (2020b) Biofriendly and competent domestic microwave assisted method for the synthesis of ZnO nanoparticles from the extract of Azadirachta indica leaves. Mater Today Proc. https://doi.org/10.1016/j.matpr.2020.03.799

Sathiya V, Suganya K, SenthilKannan K et al (2022) J Mater Sci Mater Electron 33:19514. https://doi.org/10.1007/s10854-022-08787-5

Selvaraj L et al (2020) Anti-diabetic (AD) studies of bis glycine hydro bromide–BGHB macro crystals milled to nano scale of 219 nm as the preliminary fine particles. Mater Today Proc. https://doi.org/10.1016/j.matpr.2020.06.207

SenthilKannan K (2018) Growth and characterisation-XRD, NLO of bis 2 amino pyridinium maleate (B2APM) crystals. Int J Eng Sci Math 7:1–3

SenthilKannan K, Gunasekaran S (2013) Synthesis, growth and interpretation of (organic NLO) 4 bromo-4l chloro benzylidene aniline (BCBA) crystals. Int J Front Int Sci Technol 3(3):29–36

SenthilKannan K, Gunasekaran S, Seethalakshmi KA (2013a) Growth and spectroscopic studies of pure and L-proline doped ZTS crystal (with taxol). Int J Sci Eng Res 4:2

Senthilkannan K et al (2013b) Spectroscopic (IR & Raman) studies of picolinium maleate (pm) single crystal. Sch Res Libr Arch Appl Sci Res 5(3):100–103

SenthilKannan K et al (2014) UV, SEM, powder XRD of AAC crystals. Int J ChemTech Res 6(5): 3187–3190

SenthilKannan K, KaleemullahKhan B, Abdul JaffarAli H, Ponnusamy VK, Govindan NM (2020a) Mater Today Proc 33:2779. https://doi.org/10.1016/j.matpr.2020.02.133

SenthilKannan K, Krishnaveni R, Anbuvel D, Porselvi VM, Ali HAJ (2020b) Mater Today Proc 33: 2776. https://doi.org/10.1016/j.matpr.2020.02.132

SenthilKannan K et al (2020c) Anti diabetic (AD) activities of L-valinium picrate (LVP) macro and nano crystals. Mater Today Proc. https://doi.org/10.1016/j.matpr.2020.01.550

SenthilKannan K et al (2020d) Anti diabetic (AD) studies of bis-glycine hydro bromide (45 nm) nano crystals. Mater Today Proc. https://doi.org/10.1016/j.matpr.2020.04.203
SenthilKannan K et al (2020e) Anti diabetic (AD) studies of picolinium maleate nano crystals. Mater Today Proc. https://doi.org/10.1016/j.matpr.2020.03.076
SenthilKannan K et al (2020f) Anti microbial and fluorescence activities of L-valinium picrate (LVP) macro and nano crystals. Mater Today Proc. https://doi.org/10.1016/j.matpr.2020.02.132
SenthilKannan K et al (2020g) Anti-diabetic (AD) activities of ZnO doped with Ce (7 at%) nano particles (NP). Mater Today Proc. https://doi.org/10.1016/j.matpr.2020.03.505
SenthilKannan K et al (2020h) Anti-diabetic activities of ZnO doped with Ce (5 at%) nano particles (NPs). Mater Today Proc. https://doi.org/10.1016/j.matpr.2020.03.506
SenthilKannan K et al (2020i) Effect of anti microbial and fluorescence on L-Alaninium maleate (LAM) macro and nano crystals. Mater Today Proc. https://doi.org/10.1016/j.matpr.2020.02.133
SenthilKannan K et al (2020j) Electronic transport, HOMO–LUMO and computational studies of CuSmonowire for nano device fabrication by DFT approach. Mater Today Proc. https://doi.org/10.1016/j.matpr.2020.01.574
SenthilKannan K et al (2020k) Photo catalytic, anti bacterial activities of Ce doped zinc oxide nano particles. Mater Today Proc. https://doi.org/10.1016/j.matpr.2020.01.576
Senthilkannan K et al (2020l) Tribological, filter studies of 3-bromo-2-hydroxy benzoic acid (BHBA) macro and nano crystals. Mater Today Proc. https://doi.org/10.1016/j.matpr.2020.06.582
Senthilkannan K et al (2020m) Tribological, filter, FTIR and fluorescence studies of L-Alaninium tartrate (LAT) macro and nano crystals. Mater Today Proc. https://doi.org/10.1016/j.matpr.2020.06.585
Senthilkannan K et al (2020n) Fluorescence, filter, nano tribological studies of 12-(4-chlorophenyl)-9, 9-dimethyl-9,10-dihydro-8H-benzo (A) xanthen-11 (12H)-one–(CPDDHBXH) macro and nano crystals. Mater Today Proc. https://doi.org/10.1016/j.matpr.2020.06.593
Senthilkumar R, Senthilkannan K, Udhayakumar S, AadithyaNarayanan ST (2020a) Mater Today Proc 33:4167. https://doi.org/10.1016/j.matpr.2020.06.594
Senthilkumar R et al (2020b) Anti-diabetic (AD) and hardness profile of 12-(4-chlorophenyl)-9, 9-dimethyl-9, 10-dihydro-8H-benzo (a) xanthen-11 (12H)-one–(CPDDHBXH)–comparative analysis of macro and nano crystals. Mater Today Proc. https://doi.org/10.1016/j.matpr.2020.06.594
Spackman PR, Turner MJ, McKinnon JJ, Wolff SK, Grimwood DJ, Jayatilaka D, Spackman MA (2021) J Appl Crystallogr 54:3. https://doi.org/10.1107/S1600576721002910
Suganya K, Maalmarugan J, Manikandan R et al (2022) J Mater Sci Mater Electron 33:19320. https://doi.org/10.1007/s10854-022-08770-0
Tundis R, Loizzo MR, Menichini F (2010) Natural products as alpha-amylase and alpha-glucosidase inhibitors and their hypoglycaemic potential in the treatment of diabetes: an update. Mini Rev Med Chem 10:315–331. https://doi.org/10.2174/138955710791331007
Vasanth Winston X, Sankar D, SenthilKannan K et al (2022) J Mater Sci Mater Electron. https://doi.org/10.1007/s10854-022-08873-8
Von Hippel A, Gross EP, Telstis FG, Geller A (1953) Photocurrent, space-charge buildup, and field emission in alkali halide crystals. Phys Rev 91:568–579. https://doi.org/10.1103/PhysRev.91.568
Wilcox G (2005) Insulin and insulin resistance. Clin Biochem Rev 26:19–39
Williams LK, Zhang X, Caner S (2019) The amylase inhibitor montbretin A reveals a new glycosidase inhibition motif. Nat Chem Biol 11:691–696. https://doi.org/10.1038/nchembio.1865
Yang CY, Yen YY, Hung KC et al (2019) Inhibitory effects of pu-erh tea on alpha glucosidase and alpha amylase: a systemic review. Nutr Diabetes 9:1–6. https://doi.org/10.1038/s41387-019-0092-y
Zhang ZY, Yong XY, Xiao M (2002) Lattice contraction in free-standing CdSe nanocrystals. Appl Phys Lett 81:2076–2078. https://doi.org/10.1063/1.1507613

Nanodiagnostics for Rapid and Accurate Detection of Infectious Diseases

10

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Abstract

The emerging field of nanotechnology addresses the current limitations in science particularly in diagnostics as well as in treatment processes. Nanotechnology plays an important role in the study of toxic effects and intensity modules in the detection of infectious diseases. Where they are more prevalent and common source of the morbidity and mortality across the world and facing a great demand to combat with infections. Due to the emergence of new pathogens, invariability in prognosis, emergence of drug resistance, and the type of microbes limit the use of therapeutics as well as perfect diagnosis. More over any failure regarding the control, invariable spread of the infectious disease would also represent a threat; nevertheless, most of the infectious diseases are in dire need of diagnostic tools. In view of the fact that, since from so many years, the technology upgradation is not up to the level and in order to uplift the analysis where the skilled paramedical/workers number is in scanty. Hence, there is a threshold inability and number to detect multiple pathogens during severity.

Accurate identification of causative pathogens is very essential to prevent the spread of infections and to deliver appropriate and timely therapeutics as well. Various parameters deliberately looking based on the range from cost-effective and lengthy yield of current diagnostic modalities are highlighted to the need for new approaches. But nanotechnology has been employing the several materials at nanoscale, which possess a cutting edge kind of technology for new research with eco-friendly, highly sensitive with rapidity in community level of screening has a

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wide range of applications. It represents innovative directions offering many advantages for pathogen detection and identification through surface modifications of nanoparticles in particular which allows binding microbial surface-tailed markers, nucleic acids, and toxins has led to the scope for development of quicker, more sensitive, and more economical diagnostic perspectives. Recent advances in nanotechnology encompass to address issues at two levels, i.e., diagnosis and treatment, prevention of pathogen spread requires a rapid, and reliable identification of the infectious agents in order to develop for a proper treatment. The present book chapter provides an overview of current developments in the diagnostics of infectious diseases enabled us by nanotechnology with suitable and representative examples. Furthermore, we highlighted that how best the nanotechnology could aid in improving existing diagnostic methodologies and treatment modalities. We summarize the progress for outline potentials of future directions in nanotechnology to empower the impact of new technology in the field of worldwide medicine.

Keywords

Nanodiagnosis · Pathogens · COVID-19 · Mycobacterium · Nanostructures

Abbreviations

ALP	Alkaline phosphatase
AuNP	Gold nanoparticles
$CdSeO_3$	Cadmium selenite
CNS	Central nervous system
CT scan	Computed tomography scan
Ds DNA	Double-stranded DNA
E. coli	*Escherichia coli*
ELISA	Enzyme-linked immunosorbent assay
EMBL	European molecular biology laboratory
Fe_2O_3	Iron oxide
FITC	Fluorescein isothiocyanate
HBV	Hepatitis B virus
HCV	Hepatitis C virus
HIV	Human immuno virus
ICT	Immune chromatographic test
IgG	Immunoglobulin G
IgM	Immunoglobulin M
LCR	Ligase chain reaction
MALDI	Matrix-assisted laser desorption/ionization
MNPs	Manganese nanoparticles
MTB	Mycobacterium tuberculosis
NASBA	Nucleic acid sequence-based amplification

NB	Negative barcode
NMR	Nuclear magnetic resonance
PCR	Polymarase chain reaction
PDB	Protein database
PPE	Paraphenylene ethynylene
RAPD	Rapid amplification of polymorphic DNA
RdRP	RNA-dependent RNA polymasase
RFLP	Restriction fragment length polymaorphism
RIA	Radial immuno assay
RSF	Raman spectroscopic fingerprint
Rt PCR	Real-time polymarase chain reaction
SEM	Scanning electron microscopy
SiO_2NP	Silicon oxide nanoparticles
SSDNA	Single-stranded DNA
TB	Tuberculosis
TEM	Transmission electron microscopy

10.1 Introduction

Nanomedicine is an emerging scientific approach toward the implementation of nanotechnological systems to detect amongst various infectious diseases, because of probable projections of the future suspicious of mortality rate and discomfortness (Saglam et al. 2021). There are many useful tools in scientific decisions, on prioritizing to the health care investment and more patterns of ill health determined factors such as progress in education, socio-economic status, and technological improvement among populations. Mostly the chief causative agents of infections are Bacteria, Fungi, Viruses, and Parasites and have a threshold impact on vertebrates including mankind, because of the exclusive characteristics of pathogens such as rapid generation time, unpredictability, as well as co-evolutionary advantages. Every year more than 57 million (25%) annual death are reported worldwide by general infectious diseases. But not with post-infectious problems and their consequences, instead, variety of complications united with chronic illness, like carcinoma, renal problems, and liver failure. The load of morbidity and mortality composed with infectious diseases which fall most seriously on public health, particularly on infants and children are marked highest rate in developing countries, where the lack of resources and poor health care including insufficient vaccines. Unfortunately, differing that situation in the clinical trials for infectious diseases are very scanty compared to other chronic complications, i.e., cancer and cardiovascular diseases. There is an urgent need to identify practical problems and impactful strategies that require better diagnosis for infectious diseases.

10.2 Existing Diagnostic Methods and Their Limitations

Up-to-date and experimentally possible diagnostic procedures are usually required to facilitate an effective treatment and optimal prevention of infectious diseases. In addition, the efficacy of treatment should be monitored during therapy by pathogen detection as well. Most popularly existing conservative diagnostics techniques of various infections such as microscopy, ICT assays, tissue culture, enzyme-linked immunosorbent assays (ELISAs), RIA (Radio immune assays) compliment fixations, Neutralization and biochemical tests, and their limitations are listed in Table 10.1. In the recent past, various molecular diagnostic techniques are very popular in use and mostly depend on nucleic acid sequence-based amplification are LCR, PCR (polymerase chain reaction), and real-time PCR, NASBA have been adapted widely to test and monitor infections because of their higher specificity and sensitivity at genetic level rather than that of antigen-antibody-based diagnostics. However, because of owing drawbacks of these procedures, i.e., pre-sample processing, high cost, and time consuming, they are commonly used in urbanized countries, but not suited for growing nations, where communicable illnesses are foremost causes of severe deaths, in conjunction with less trained clinical staff and specific laboratory facilities available. Henceforth, there is a huge demand for the development of new diagnostic rapid procedures and Point of Care facilities.

A prominent diagnostic device required for developing countries would be able to detect pathogens with high intensity, low-cost, handy, and presumed source

Table 10.1 Current available diagnostic methods and their limitations

S. No	Name of the diagnostic test	Technique	Target	Limitations
1.	Microscopy	Fluorescence microscopy TEM SEM	Direct observation of pathogen	Microscopy requires well trained and supervised technologist Low parasite count
2.	Immunological methods	ELIA ICT Agglutination Western blot Immuno fluorescence	Antigen or antibody	Cross reactivity and falls positives
3.	Molecular methods	PCR Typing Hybridization RFLP, RAPD LCR, NASBA	DNA or RNA	Cannot be used during incubation period. techniques are expensive and may produce many false-positive reactions due to contaminations. Required costly equipments and trained persons
4.	Culture and sensitivity	Inoculating on special medium	Cultivation of pathogens	Time intensive and costly and results oriented and dependent on stringent transport mechanisms to maintain specimens Not available in rural areas

detection system with accurate, highly reliable, and sensitive. In spite of the above, DNA microarray is one of the latest diagnostic technologies for rapid identification of various infections. Each microarray/chip holds a numerous oligo-nucleotide sequences that recognize the target sequences from a clinical sample by the detection of oligo-nucleotides which can be hybridized to pathogen genes. For instance, there are many difficulties in the identification of pathogen-prime target genes and in the design of primers for multiplex PCR. The first and foremost difficulty lies with gene analogs which are more similar and unique to particular genes of a pathogen. Therefore, to overcome such problems, we thought to select the pathogens and their 16S rRNA could be an alternative to replace these problems. However, some of the organisms belongs to the same species used to share a large number of nucleotides in the 16S rDNA, which requires further identification of microorganisms at species level is highly solicited for prompt phylogenetic analysis. There is another challenge ahead to design selective primers, which will amplify genes of desired pathogens without any false amplifications. But in general, quick reports and several rounds of reaction would be considered to cover the complete and potential probes which specifically identify infectious organisms on time with single test procedure.

If a perfect diagnostic tool is to be considered for infectious diseases, it should possess the capability to overcome all these technical problems raised in terms of rapidity, sensitivity, specificity, accurate, robust, cost-effective as well as user-friendly. Since from past half-century, many improvements have been developed and approved in the scientific field especially in diagnostic microbiology. Therefore, several molecular procedures have significantly played a vital role in the diagnosis of various diseases, but it is not a patient friendly due to owing more expensive, delay in results, inaccurate, and require skilled technicians.

The current available diagnostic methods are having some drawbacks, i.e., delay of sample preparations, narrow identification and lengthy procedures, etc. are the key problems. Therefore, novel and new diagnostic methods are required to develop the easy detection used to cure infectious diseases to meet medical challenges with low cost, extremely sensitive, and selective for many point-of-care tests at a time among families in public health sectors across the globe (Singh et al. 2020).

10.3 Nanodiagnostics

Nanodiagnostics are termed as, the use of nanomaterials in medical diagnosis to detect several acute to chronic infections with suitable applications. Emerging of these nanoscience-based methods have recently popularized, attracted, and paved the interest as an easiest approach. Hence, indigenously conquer the problems of present diagnostics through precise mode of exploitations and uniqueness in their physical properties. Huge surface to more volume ratio property among nanostructures is extremely essential and appropriate to attach lots of molecules which enhances the authenticity of components. Similarly other unique properties (rapid and real-time detection) of nonmaterial confer the suitable nature to develop

nanodiagnostics for various infectious diseases by using very minute quantity of clinical samples. These techniques may be applied in order to develop rapid, accurate, safe, reliable, cost-efficient, specific, and easily available methods for the detection of pathogens at any point of time. At present, the majority of nanodiagnostic materials have a wider range of applicability for the detection and confirmation of variety of infections (Jackson et al. 2017). Present trendy reliable techniques possessing different projections and numerous options for quantification diagnostic perspectives, which are easily accessible for the preparations of suspensions, emulsions, and niosomes with nanomaterials. Therefore nanotechnology-based techniques have a great potential to minimize the cost and increase the accuracy (Wang et al. 2017; Maddela et al. 2021). In view of these limitations, the sensitive nanodiagnostics platforms are very intensive to be affordable, and reproducible. It could also be appropriate to develop diagnostic tools for numerous infectious diseases, particularly in resource-poor environment. In the present book chapter, the authors coated several examples in order to communicate the importance of nanotechnology and its applications by using different nanomaterials

10.4 Nanodiagnostics for *Mycobacterium* Tuberculosis

Gold nanoparticles (AuNPs) are one among the prominent materials that showed distinctive optical, biological, and physiochemical characteristics making use of a suitable nanomaterial for diagnosis of *M. tuberculosis*. The opacity of AuNPs along with detectable (antibody or antigen) enables their usefulness in the diagnostics. Moreover, these particles do not disturb the functional properties of an antigen after binding has clearly explained by Sonawane and Nimse (2016). The antigen and antibody interaction are improved by fiction atom of gold nanoparticles, thus the signals have been increased at the time of immunoassay, which intern promote the test quality and made it effective too (Kim et al. 2018). Colorimetric detection of pathogen also offers to target the genes from the clinical samples through ssDNA, linked either with SH group or modified probes with gold particles (Cordeiro et al. 2016). This assay has been enlightened to be very specific and fabricate the predominant results with precise quantity of pathogen DNA. Similarly, Baptista et al. (2008) have emphasized the DNA probes coupled with AuNPs in order to detect *M. tuberculosis* by colorimetric method at 526 nm, in which the results can be read at simple color change in the test sample (Pink color is positive, whereas purple is negative). Furthermore, it has been strongly accepted method when compared with other diagnostic procedures. For example, InnoLiPA-Rif-TB has 100% concordance than other techniques which has been proven to be highly reliable than traditional techniques. The major benefits of this process are that the less contamination and speedy results (Baptista et al. 2008).

Subsequently, the accuracy of these nanomethods was compared with semi-nested PCR and automated liquid culture system, which showed reliability, sensitivity, and specificity during the detection of group-specific pathogens (*M. tuberculosis*

complex) (Cordeiro et al. 2016). Later SPR (Surface Plasmon Resonance) technique has attracted and paid a great deal of attention for the use of novel gold particles (Au), that produce red color with colloidal AuNPs, that depend on concurrent monitoring of modifications, surface refractive index of sensors (Khan et al. 2019). The optical sensor sensitivity of this test remains capable of sensing very small amount of the analyte without any crucial modifications. Later Yang et al. (2015) developed a SPR-dependent CFP-10 system for the detection of specific antigens to monitor stages of tuberculosis in clinical samples, which showed reputable usefulness in clinical diagnosis. Zhu and his co-workers had developed a different electrode system for the detection of TB bacterium from the clinical samples by using genomic DNA without any special treatment. In this technique they had been used two different probes, i.e., capture and Au probes are paired with an ALP enzyme as single detection probe. For instance, the ITO probe is activated by combining with capture probe, then it is dipped in the sample to form dsDNA. Finally, the signals are then observed and noted by voltmeter (Zhu et al. 2017).

Gold nanoparticle-mediated dipstick assay enthusiastically developed as an alternate and easiest method where AuNPs coated antigens act as detector system with colloidal gold particles coated with antigens of *M. tuberculosis* using derivatives of alkane thiols. The anti-MTB rabbit antibodies collected from rabbit serum and immobilized on the NC membrane bind to the MTB antigen coated on AuNPs, binding could be visualized directly by the formation of red color (Stephen et al. 2015).

The mesoporous SiO_2NPs are used in biological sciences as biosensors, drug designing and delivery as well as in imaging techniques. The IIFM method has been developed by coupling fluorescent dyes with nanoparticles for the detection of *M. tuberculosis*. The intensity of fluorescent signal is fivefold superior to conventional fluorescence detection method (FITC). Results recorded within 2 h and further considered as a potential technique for the rapid and quick detection of *M. tuberculosis* (Qin et al. 2007).

The magnetic nanoparticles (MNPs) are also used in nano-biomedicine, for the favorable results in imaging therapy. The surface of these particles thus easily be modified with detectable moieties, like antibodies/antibiotics that enable us to apply for the bacterial identification. Paramagnetic Iron oxide (IO) nanoparticles are associated with magnetite (Fe_3O_4) or para magnemite (γ-Fe_2O_3 NP) and are commonly used in drug therapy. For instance, the cell signaling and drug delivery by MRI systems are well-popularized in the field of biology (Sabale et al. 2017). At the same time, IONPs integrated along with IgG have significantly improved the detection limit of bacterial cells in nano-MALDI workplaces. Although a variety of scientific studies have been noticed that nanodiagnostic methods use magnetic resonance with IO (iron oxide) nanoparticles to detect DNA of *M. tuberculosis* (Vallabani and Singh 2018). Interestingly, Engström et al. (2013) build a novel strategy by means of magnetic nanobeads coupled with streptavidin-labeled biotin used for the detection of rifampicin mutations in the *rpoB* gene. This system consists of 11 probes that are targeting for 23S internal transition gene sequence region of *M. tuberculosis,* from which one probe is for MTBC detection and another probe for

natural Mycobacterium type and the remaining 9 probes are made to detect a common platform for the detection of various mutations in the RRDR-*rpoB* gene.

According to Sabale et al. (2017), they tried different capacities of superparamagnetic IO nanomaterials to increase the specificity and sensitivity of MRI technique during mycobacterium detection at the molecular level and also offer a valuable tool for the ag/ab interaction to investigate the host-parasite interactions. This is one of the generalized methods which is highly specific and extensively recommended for the detection of various types of CNS TB, musculoskeletal TB, and abdominal TB (Skoura et al. 2015).

Apart from the use of above nanoparticles, it is high time to use quantum dots, more suitable tool for diagnostics, which ensure exclusive optical and physical features (Kairdolf et al. 2013). The wide absorption of thin emission spectra slowed down the decay rates at excited state, therefore the absorption of cross sections would be the main benefit of quantum dots when compared with FITC-dependent methods. The finding system of quantum dots and magnetic beads are used to detect specific probes for *M. tuberculosis* which in turn 1st probe binds to the *rRNA* gene (*23S*) and the 2nd probe recognizes the conserved sequence (IS900). In addition, there is an alternative method to improve quantum-based dot-magnetic conjugates exposed to UV light, which emits red fluorescence from the clinical sample. It provides a rapid diagnosis rather than other techniques (Gazouli et al. 2012). Thereafter a parallel study was conducted by Liandris et al. (2009) who described that quantum dots of $CdSeO_3$ attached to streptavidin used to detect Mycobacterium species, as it consists of two probes that would distinguish the target DNA at its optimum level.

The principle mechanism of magnetic barcode (MB) assays is similar to that of quantum dots in which a specific cDNA of *M. tuberculosis* is used as detection system for TB monitoring. In parallel that reaction omits the DNA extraction and PCR amplification layer and then therefore captures the probe by a specific mechanism. After capturing the DNA by probes, the target gene is then labeled by matching or suitable magnetic nanoparticle probes, and further analysis carried out by NMR system (Chen et al. 2017).

10.5 Nanodiagnostics for *Streptococcus pneumoniae*

Shi et al. (2014) presented their work on applications of nanoparticles in the diagnosis of *S. pneumoniae*, rolling cycle model of DNA replication by surface Plasmon resonance sensors. These probes carry the boundary sequences that are complementary to the adjacent sequences and coupled with gold nanoparticles and are specific for 16S rRNA sequences. Hybridization of the target probes brings the two ends in contact, while resulting in circularization, which has tremendous flexibility toward the development of a potential test to know the diversity of many pathogens at a time such as *E. coli*, *S. epidermidis*, *S. dysenteriae*, *A. aureus,* and *E. faecalis*. Furthermore, the present test has a tremendous efficacy

in line of analysis to detect typical pneumonia in clinical samples collected from ventilated patients, and the accuracy was improved from 91.89 to 99% ($N = 74$).

10.6 Nanodiagnostics for *Salmonella typhi*

Similarly, Das et al. (2014) have published recently an article that explored the information regarding DNA sensors to detect *S. typhi* Vi gene in clinical samples. A self-assembled DNA sensor contains a layer of organosilane 3-mercaptopropyltrimethoxysilane (MPTS) on top screen-printed electrodes were used to deposit gold nanoparticles augmented with modified DNA probes with thiol groups attached to detect target DNA of *S. typhi*.

10.7 Nanodiagnostics for *Escherichia coli*

Cheng et al. (2014) developed a novel detection system to detect *E. coli* (O157:H7) using amperometric immune sensor based on four-layer magnetic nanoparticles. The core consists of magnetic Fe_3O_4, Prussian blue; N-(2-aminoethyl)-3-aminopropyl trimethoxyl silane, and the last coating is with the gold (Au) nanoparticle shell. The conjugation of nanomaterial will ensure to permit the target and quantify the pathogens in different samples. There is an evident that drug-resistant bacteria could also be differentiated from nonresistant bacteria alternatively by using nanoparticles with RSF method. Gold nanoparticles mixed with poly paraphenylene ethynylene (PPE) could be applied to monitor bacterial DNA by fluorescence method.

10.8 Nanodiagnostics for Viral Infections

Nanoparticles may also be used to diagnose several viral diseases. HCV and HBV diagnostic assays using immune gold silver staining with Au-NPs are under investigation (Pedrosa and Baptista 2015; Qasim et al. 2014). It is presumed that nanotechnology played a vital role in the detection of current pandemic COVID-19. Currently, COVID-19 is detected by RT-PCR method in clinical samples including swabs from nasopharyngeal, oropharyngeal, sputum, lower respiratory tract secretions, stool, and blood. The main drawbacks of this technique are high cost, time taking and required a special trained persons and not available in rural areas. CT scan is also an alternate imaging method for COVID-19 detection. New diagnostic methods for detection of COVID-19 have also been developed; for example, Abbott developed a rapid test based on nucleic acid amplification at single temperature. According to Carter et al. (2020), this kit identifies the RNA-dependent RNA polymerase (RdRP) in clinical samples. Also, IgM and IgG antibodies from the patient serum are used to confirm COVID-19 by a serological test, which can detect after 10–30 days of infection which is not advised for early detection. These

conventional diagnostic methods are cross-reactive with other similar viral strains. Therefore the timely diagnosis required and can lead to more competent quarantine or distancing practices lowers the burden of socioeconomic status, and further it prevents the exacerbation of cases. Providentially, the present nanotechnology provides to detect even very low amounts of viral load in infected samples. Hence employing nanomaterials in the medical diagnosis field will enhance the accuracy and rapidity in low-volume samples, at an affordable cost, which helps for early detection (Eslami and Jalili 2020). Many of the nanomaterials include QD, carbon tubes, silica, metal nanoparticles, and graphene oxide, extensively used as biosensors to diagnose pathogenic viruses like HTNV virus, RVFV virus, hepatitis A, B, E virus, herpes virus including Kaposi's sarcoma, influenza virus A, human immunodeficiency virus (HIV), and human papillomavirus (H) (Nikaeen et al. 2020).

10.9 Safety Evaluation of Nanomaterials

According to US regulatory agencies, unambiguous risk assessment techniques would be used for the evaluation of nanomaterials. However, Walker and Bucher (2009) proved and displayed four critics why these materials to be assessed for their toxicity, differently:

(a) Because of many new exposure and emerging routes, when a nanomaterials are small enough to enter into cellular portals.
(b) Nanomaterials of similar size and shape have different surface properties, dosimeter, and alter toxic kinetics.
(c) So many commercial applications are in lime light that may direct to new interactions and unexpected development of toxicity.
(d) Evaluation of risk factors using dose expressed relatively in terms of mass may lead to false outcomes. Because some nanomaterials' dose can measure with a size-dependent property of its surface area and few physical properties of nanomaterials are relevant to the first three steps (a, b, and c).

Since much of the nanomaterial is required to complete information, i.e., physical characteristics of nanomaterials (surface area, composition, shape, and agglomeration state) are unavailable. At the same time there is a necessity to depend on reproducibility exposure and toxicity data persists in the scientific field matters regarding nanoparticles. Although significant research is progressed in nanotoxicology and nanomedicine has been made us to extend much more work remains to be done. But unfortunately, there is no abundant, reputed, and internationally accepted standard protocol available for toxicity testing with nanomaterials. Since, here are few of internationally accepted and well-characterized–positive controls available so far to intend more and more nanomaterial studies. Thus, the high-throughput monitoring of nanomaterials appear to be promising and might be probable mechanism of adoptability in future science. The nature of complex

nanomaterials makes the development of security assessment challenging. Hence, with these limitations, the application of the nanotechnology in science and medicine enhances the future prospects and emerges to be bright.

10.10 Future Challenges for Point-of-Care Diagnostics

We selected major bacterial and few viral infections for the explanation of the medical significance and their prognosis promotes concisely to discuss the methods available for current diagnosis of infectious diseases. Then, we proceed to progress and to adopt novel improvements for the above said infections based on microfluidic and nanodiagnostic strategies. In general, the number of available microfluidic tools for point-of-care detection is very less, because, the specific reasons for development comprise the genetic or immunological and clinical complexity in regulating the diseases. In this view, the developments and opportunities for the new diagnostic devices include:

(a) Improving current clinical standards by simple diagnosis in a resource less environment.
(b) The newly introduced devices are successfully utilized for a specific disease can be expanded its applicability in clinical diagnosis.
(c) Multi-parametric testing is essential in order to target many infections at a time with single slot, of course these test tool will contribute to a quick and exact diagnosis.
(d) Novel design concepts are highly recommended to detect various bacterial, viral, and parasitic specific antibodies (IgM) and antigens to perform the test by nanomaterials.

Since, there are other major and suitable fast-developing scientific fields in use in silico analysis, molecular modeling methods by bioinformatics tools, i.e., biological database (gene bank, PDB, EMBL, etc.) enables the prediction of the structure, function, and the optimization of target material by novel devices. That ultimately promotes the basic scientific understanding and molecular behavior in nanofluidics and/or nano confinement with a practicality that leads to improving the point-of-care devices. In addition, variety of computer-aided tools and programs made by the professionals might also be used for the characterization of new molecular targets.

10.11 Conclusions

The emerging field of nanotechnology addresses the current limitations of conventional diagnostic and treatment perspectives and also provides new dimensions for the advancement of diagnostics. Furthermore, it ensures the fast, easy to available, affordable rate, and safe and potable use of products that may develop from traditional testing methods and will help us to control variety of infectious diseases

to improve public health concerns. We hope and believe that in order to facilitate an advance research approach with nanoparticle-based diagnostics and necessary to develop systematic and rational design practice of nanoparticles. In the present book chapter, we summarized a variety of clinically applicable nanoparticles and their specific selectivity in order to make the diagnostic methodology as easy as possible.

References

Baptista P, Pereira E, Eaton P, Doria G, Miranda A, Gomes I, Quaresma P, Franco R (2008) Gold nanoparticles for the development of clinical diagnosis methods. Anal Bioanal Chem 391(3): 943–950

Carter LJ, Garner LV, Smoot JW, Li Y, Zhou Q, Saveson CJ, Sasso JM, Gregg AC, Soares DJ, Beskid TR, Jervey SR, Liu C (2020) Assay techniques and test development for COVID-19 diagnosis. ACS Cent Sci 6(5):591–605

Chen YT, Kolhatkar AG, Zenasni O, Xu S, Lee TR (2017) Biosensing using magnetic particle detection techniques. Sensors 17(10):2300

Cheng P, Huang ZG, Zhuang Y, Fang LC, Huang H, Deng J, Jiang LL, Yu KK, Li Y, Zheng JS (2014) A novel regeneration-free E. coli O157: H7 amperometric immunosensor based on functionalised four-layer magnetic nanoparticles. Sensors Actuators B Chem 204:561–567

Cordeiro M, Ferreira Carlos F, Pedrosa P, Lopez A, Baptista PV (2016) Gold nanoparticles for diagnostics: advances towards points of care. Diagnostics 6(4):43

Das R, Sharma MK, Rao VK, Bhattacharya BK, Garg I, Venkatesh V, Upadhyay S (2014) An electrochemical genosensor for Salmonella typhi on gold nanoparticles-mercaptosilane modified screen printed electrode. J Biotechnol 188:9–16

Engström A, de la Torre TZG, Strømme M, Nilsson M, Herthnek D (2013) Detection of rifampicin resistance in Mycobacterium tuberculosis by padlock probes and magnetic nanobead-based readout. PLoS One 8(4):62015

Eslami H, Jalili M (2020) The role of environmental factors to transmission of SARS-CoV-2 (COVID-19). AMB Express 10:1–8

Gazouli M, Lyberopoulou A, Pericleous P, Rizos S, Aravantinos G, Nikiteas N, Anagnou NP, Efstathopoulos EP (2012) Development of a quantum-dot-labelled magnetic immunoassay method for circulating colorectal cancer cell detection. World J Gastroenterol 18(32):4419

Jackson TC, Patani BO, Ekpa DE (2017) Nanotechnology in diagnosis: a review. Adv Nanoparticles 6:93–102

Kairdolf BA, Smith AM, Stokes TH, Wang MD, Young AN, Nie S (2013) Semiconductor quantum dots for bioimaging and biodiagnostic applications. Annu Rev Anal Chem (Palo Alto, Calif) 6: 143–162

Khan I, Saeed K, Khan I (2019) Nanoparticles: properties, applications and toxicities. Arab J Chem 12(7):908–931

Kim J, Oh SY, Shukla S, Hong SB, Heo NS, Bajpai VK, Chun HS, Jo CH, Choi BG, Huh YS, Han YK (2018) Heteroassembled gold nanoparticles with sandwich-immunoassay LSPR chip format for rapid and sensitive detection of hepatitis B virus surface antigen (HBsAg). Biosens Bioelectron 107:118–122

Liandris E, Gazouli M, Andreadou M, Comor M, Abazovic N, Sechi LA, Ikonomopoulos J (2009) Direct detection of unamplified DNA from pathogenic mycobacteria using DNA-derivatized gold nanoparticles. J Microbiol Methods 78(3):260–264

Maddela NR, Chakraborty S, Prasad R (2021) Nanotechnology for advances in medical microbiology. Springer Singapore. (ISBN 978-981-15-9915-6) https://www.springer.com/gp/book/9789811599156

Nikaeen G, Abbaszadeh S, Yousefinejad S (2020) Application of nanomaterials in treatment, anti-infection and detection of coronaviruses. Nanomedicine 15(15):1501–1512

Pedrosa P, Baptista PV (2015) Gold and silver nanoparticles for diagnostics of infection. In: Nanotechnology in diagnosis, treatment and prophylaxis of infectious diseases. Academic, New York, pp 1–18

Qasim M, Lim DJ, Park H, Na D (2014) Nanotechnology for diagnosis and treatment of infectious diseases. J Nanosci Nanotechnol 14(10):7374–7387

Qin D, He X, Wang K, Zhao XJ, Tan W, Chen J (2007) Fluorescent nanoparticle-based indirect immunofluorescence microscopy for detection of Mycobacterium tuberculosis. J Biomed Biotechnol 2007:89364

Sabale S, Kandesar P, Jadhav V, Komorek R, Motkuri RK, Yu XY (2017) Recent developments in the synthesis, properties, and biomedical applications of core/shell superparamagnetic iron oxide nanoparticles with gold. Biomater Sci 5(11):2212–2225

Saglam N, Korkusuz F, Prasad R (2021) Nanotechnology applications in health and environmental sciences. Springer International Publishing. (ISBN: 978-3-030-64410-9) https://www.springer.com/gp/book/9783030644093

Shi D, Huang J, Chuai Z, Chen D, Zhu X, Wang H, Peng J, Wu H, Huang Q, Fu W (2014) Isothermal and rapid detection of pathogenic microorganisms using a nano-rolling circle amplification-surface plasmon resonance biosensor. Biosens Bioelectron 62:280–287

Singh S, Kumar V, Dhanjal DS, Datta S, Prasad R, Singh J (2020) Biological biosensors for monitoring and diagnosis. In: Singh J, Vyas A, Wang S, Prasad R (eds) Microbial biotechnology: basic research and applications. Springer Nature Singapore, pp 317–336

Skoura E, Zumla A, Bomanji J (2015) Imaging in tuberculosis. Int J Infect Dis 32:87–93

Sonawane MD, Nimse SB (2016) Surface modification chemistries of materials used in diagnostic platforms with biomolecules. J Chem 19:1–20

Stephen BJ, Singh SV, Datta M, Jain N, Jayaraman S, Chaubey KK, Gupta S, Singh M, Aseri GK, Khare N (2015) Nanotechnological approaches for the detection of mycobacteria with special references to Mycobacterium avium subspecies paratuberculosis (MAP). Asian J Anim Vet Adv 10:518–526

Vallabani NS, Singh S (2018) Recent advances and future prospects of iron oxide nanoparticles in biomedicine and diagnostics. 3 Biotech 8(6):1–23

Walker NJ, Bucher JR (2009) A 21st century paradigm for evaluating the health hazards of nanoscale materials? Toxicol Sci 110(2):251–254

Wang Y, Yu L, Kong X, Sun L (2017) Application of nanodiagnostics in point-of-care tests for infectious diseases. Int J Nanomedicine 12:4789

Yang H, Qin L, Wang Y, Zhang B, Liu Z, Ma H, Lu J, Huang X, Shi D, Hu Z (2015) Detection of Mycobacterium tuberculosis based on H37Rv binding peptides using surface functionalized magnetic microspheres coupled with quantum dots–a nano detection method for Mycobacterium tuberculosis. Int J Nanomedicine 10:77

Zhu G, Song Q, Liu W, Yan X, Xiao J, Chen C (2017) A gold nanoparticle-modified indium tin oxide microelectrode for in-channel amperometric detection in dual-channel microchip electrophoresis. Anal Methods 9(29):4319–4326

Smart Drug Nanoparticles from Microorganisms and Drug Delivery

11

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Abstract

Smart drug nanoparticles are a type of drug delivery system that uses nanomaterials, typically made of biocompatible materials such as lipids or polymers, to deliver drugs to specific parts of the body. These nanoparticles can be designed to target specific cells or tissues and can be engineered to release drugs in response to certain triggers, such as changes in pH or temperature, etc. Microorganisms, such as bacteria or fungi, can be used to produce these nanoparticles, either through genetic engineering or using naturally occurring nanoparticles produced by the microorganisms. The use of smart drug nanoparticles has the potential to improve the efficacy and safety of many different types of drugs and is an active area of research in the field of drug delivery.

Keywords

Biogenic · Drug delivery · Microbicidal · Surface modifications · Smart nanomaterials

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Abbreviations

BMS	Magnetosomes
CK	Chemokines
CQDs	Carbon quantum dots
DDS	Drug delivery system
EPR	Enhanced permeability and retention
EVS	Extracellular vehicles
GIT	Gastrointestinal tract
IL	Interleukins
MPS	Mononuclear phagocyte system
MRI	Magnetic resonance imaging
MSNS	Mesoporous silica nanoparticles
MTB	Magnetotactic bacteria
PEG	Polyethylene glycol
TNF	Tumour necrotic factor
TNT	Titanium nanotubes
TTIS	Time-temperature indicators
UV	Ultraviolet

11.1 Introduction

Smart drug delivery systems are a type of drug delivery technology that utilizes specific triggers, such as changes in pH or temperature, to release drugs at the desired location in the body (Mahfuz et al. 2022). These systems can be designed to target specific cells or tissues and can be made from a variety of biocompatible materials, such as lipids or polymers. One example of a smart drug delivery system is targeted nanoparticles, which are engineered to specifically target cancer cells and release drugs at the site of the tumour (Siddiqui et al. 2022; Prasad et al. 2017a). Another example is pH-sensitive systems, which can be designed to release drugs at a specific pH level found in diseased tissue, such as tumours, but not in healthy tissue (Manivasagan et al. 2022). Smart drug delivery systems have the potential to improve the efficacy and safety of many different types of drugs by targeting the delivery of drugs to specific cells or tissues, while reducing side effects (Alvarez-Lorenzo and Concheiro 2019). Additionally, they can also help to increase the solubility and stability of drugs, making them more effective. The use of smart drug delivery systems is an active area of research in the field of drug delivery, and many different types of smart drug delivery systems are under development and testing (Sun et al. 2017; Maddela et al. 2021).

In the modern world, nanotechnology has become one of the most significant science technologies. The process relies on nanoparticle production and

management, requiring substantial changes to the material's properties (Shi et al. 2010). It has been known for thousands of years that nanoparticles have been employed inadvertently for various purposes. For example, gold nanoparticles, long used to colour drinking glasses, now have medicinal properties. Innovative techniques are increasingly used to identify nanoparticles' shape- and size-dependent physiochemical properties. Several metal nanoparticle applications have been explored in biology, agriculture, the environment, and physiochemistry in recent years (Rather et al. 2011; Prasad et al. 2017b, c; 2018). Paclitaxel, methotrexate, and doxorubicin have been precisely distributed through gold nanoparticles. Angiogenesis, tumour detection, hereditary diseases, genetic disorders, photoimaging, and photothermal therapy have all been performed utilizing gold nanoparticles (Bhagat et al. 2015). Medical procedures involving iron oxide nanoparticles include cancer therapy, magnetic resonance imaging, hyperthermia, medication administration, tissue repair, cell labelling, targeting, and immunoassays. In addition to their many antimicrobial properties, silver nanoparticles have been used to treat wounds, cancer, and inflammation (Li et al. 2018).

In addition to their biocompatibility, nontoxicity, self-cleansing, skin-compatible, antibacterial, and dermatological properties, zinc and titanium nanoparticles have been used in several innovative applications, including biomedical, cosmetic, ultraviolet (UV)-blocking, and UV-blocking agents (Haldar and Nath 2020; Jassal et al. 2022; Kavitha et al. 2023). Various materials, such as copper and palladium nanoparticles, have been used to make batteries, polymers, plasmonic waveguides, and optical limit devices. Furthermore, they possess antibacterial properties that protect against many deadly infections. Several biomolecules have also been spatially analysed to improve spatial resolution and sensitivity utilizing nanoparticles (Herrmann et al. 2021). Among the molecules observed are several metabolites, peptides, nucleic acids, lipids, fatty acids, glycosphingolipids, and pharmaceutical substances. Additionally, nanoparticles are suitable for creating electrochemical sensors and biosensors due to their unique properties. Nanosensors have detected many contaminants in drinking water, such as mycobacteria, mercury, and algal toxins. In addition to testing soil nutrient levels and stress factors, nanosensors have also been developed using nanomaterials (Jia et al. 2021). These nanosensors can regulate hormone levels, identify agricultural pests, monitor viruses, and identify agricultural pests. As an example, nanosensors can detect oxygen and auxin distribution (Harish et al. 2022).

The scientific community has spent considerable time and effort developing suitable methods for producing nanoparticles due to the physiochemical properties and wide range of uses of nanoparticles (Ozalp et al. 2011). Physiochemical techniques are the most effective way to produce metal nanoparticles but are constrained by environmental pollution caused by heavy metals. Since, the biological synthesis of nanoparticles is nontoxic, repeatable, easy to scale up, and well-defined in morphology, it has become an increasingly popular method for nanoparticle production (Singh et al. 2016a). The ability of microorganisms and plants to synthesize nanoparticles has been demonstrated as a novel source with significant promise. Various microorganisms, including bacteria, fungi, and yeast,

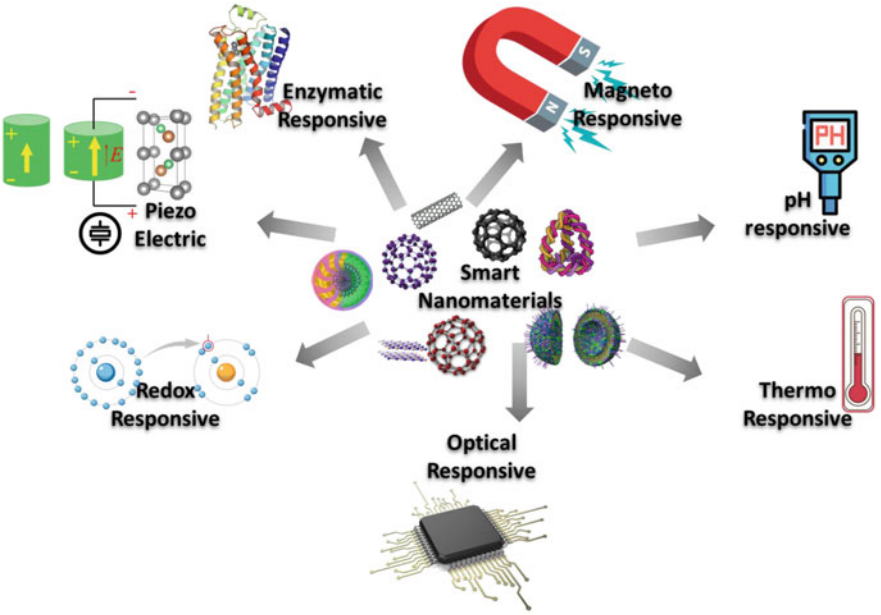

Fig. 11.1 Some significant smart nanomaterial applications based on the physical properties

have been studied to create metal nanoparticles (Prasad 2014; Prasad et al. 2016; 2018; Srivastava et al. 2021; Koch et al. 2023). Despite the extensive study that has already been done in other areas regarding the synthesis of nanoparticles, we give you an overview of the current applications of microbial-derived smart nanomaterials illustrated in Fig. 11.1.

11.2 Drug Delivery Systems (DDS)

A drug delivery system (DDS) is designed to deliver drugs easily and effectively despite physiological obstacles. DDS, which includes devices and formulations, was created to address the physiological properties of diseases to improve the pharmacokinetics and pharmacodynamics of medications (Wei et al. 2008). A broad range of articles spanning many academic disciplines has been produced over the years due to extensive research into DDSs. It is possible to categorize DDSs roughly into three generations based on their changes over the past 60 years. Transdermal patches and oral formulations were early methods of delaying medication release dating back to the 1950s (Shi et al. 2010).

These concepts led to significant developments in drug release, such as diffusion, dissolution, osmosis, or ion exchange. The concept of second-generation controlled

release has been developed since the 1980s to keep a constant drug concentration in the blood (Ozalp et al. 2011). During this period, bio-responsive polymers were introduced, leading to more regulated DDSs. There were a few second-generation DDSs on the market. A third generation of nanomaterial-based DDSs has made it possible to practice "precision medicine" by tailoring drug administration and enhancing pharmacokinetics based on personalized genetic data since 2010 (Alvarez-Lorenzo et al. 2012).

Pharmaceutical treatments must deliver the active substance to the target at a concentration sufficient to provide therapeutic results for the duration necessary (Alvarez-Lorenzo and Concheiro 2014). A medicine should ideally be exposed only to tissues containing the pharmacological target to maximize its effectiveness and minimize side effects. It has been traditional, however, for drug administration to aim at getting the drug into the bloodstream instead of relying on tissue irrigation and drug affinities (Kumar et al. 2014). Rather than measuring bioavailability in target environments, medications are still measured in the bloodstream. Besides enzyme attacks, low tissue permeability, and difficulty reaching target cells once the medication reaches the target cell, medication faces many obstacles (Oh et al. 2014). To reach specific tissues or cells, therapy usually involves the administration of high doses of medication. When biotechnologically created active substances including peptides, enzymes, DNA, etc. cannot pass through the blood circulation, their complex structures and unstable properties exacerbate the problem. An active compound's ability to penetrate the target site greatly determines the effectiveness of therapy. Medical demands regarding delivery sites and release rates are becoming more stringent daily (Lee et al. 2015).

Many commercially available sustained-release medications release measured amounts of drugs into the bloodstream. By doing this, the drug is prevented from entering the body's tissues through blood circulation (Wang et al. 2016b). In the case of so-called first-generation controlled release systems, drug release could be programmed at a rate that limits the amount of active drug released. Introducing excipients, mostly polymers, has resulted in researchers studying them extensively (Hosseinidoust et al. 2016). These are mostly polymers and allow dosage forms to be controlled through various methods, including osmotic, dissolving, and diffusion. Patients are more likely to comply with therapies involving short-half-lived medications when drug levels are therapeutically appropriate at smaller daily doses. The likelihood of adverse reactions is also reduced, in addition to minimizing unwanted effects. Added ingredients that allow the release process to occur within the gastrointestinal tract (GIT) at a preferred location have resulted in another milestone for oral sustained-release formulations. In particular, they can now be released in a GIT region more likely to be stable or absorbed (Dhanasekaran and Chopra 2016).

For activation-modulated drug release, excipients interact with specific biochemical, physical, or biophysical phenomena in the gastrointestinal tract, such as pH gradients or enzyme activity (Xu et al. 2017). With advanced dosage forms, the third generation aims to achieve feedback-regulated drug release, which can deliver the

drug like a courier to the target site as quickly as possible and also feedback-regulate drug release, ideally in response to the progression of specific disease markers, as well as the physio/pathological conditions of the body. Modern medication is also called a DDS to distinguish them from dosage forms that control the release of the medication before absorption and distribution. Sambi et al., research group provided the detailed mechanisms in an illustration behind the three generations of controlled release systems in their research discussions.

11.3 Nanoparticles from Microorganisms

A microorganism can operate as an environmentally friendly, safe, and affordable nanofactory, enabling the synthesis of physiologically active substances without the need for harsh, toxic chemicals (Singh et al. 2016a; Prasad et al. 2016). In microorganisms, the ability to accumulate and detoxify heavy metals is facilitated by numerous reductase enzymes that can transform metal salts into metal nanoparticles (Ding et al. 2022; Koch et al. 2023). There has been extensive research into the creation of metal nanoparticles by bacteria (such as actinomycetes), fungi, and yeast in recent years. Biomass, supernatants, and derived components of bacterial cells have been used for the synthesis of nanoparticles in a wide variety of biological processes (Hosseinidoust et al. 2016). In intracellular methodologies, several downstream steps are required to recover nanoparticles. Extracellular synthesis has drawn considerable attention because it eliminates these steps (Chifiriuc et al. 2016). For nanoparticle purification, several centrifugation and washing steps are required after sonication to break down the cell wall. Additionally, metal-resistant organic compounds, reducing cofactors, enzymes, proteins, peptides, and genes, contribute to reducing abilities. Furthermore, they aid in maintaining the long-term stability of nanoparticles by acting as natural capping during nanoparticle synthesis by preventing aggregation (Qu et al. 2018).

Bacillus methylotrophicus (Wang et al. 2016a), *Brevibacterium frigoritolerans* (Yaqoob et al. 2020), *Pseudomonas deceptionensis* (Chaudhry et al. 2018; Vyshnava et al. 2016), and *Bhargavaea indica* (Singh et al. 2015) are among the bacteria that have been tested for nanoparticle production. *Bacillus licheniformis* (Muras et al. 2021), *Bacillus amyloliquefaciens* (Ashengroph and Hosseini 2021), *Rhodobacter sphaeroides* (Dolly et al. 2015), *Listeria monocytogenes* (Kim and Song 2018), *Bacillus subtilis* (Srinath et al. 2018), and *Streptomyces anulatus* (Singh et al. 2021) have also produced nanoparticles with similar properties (Singh et al. 2016a). Numerous microorganism genera have been reported to synthesize metal nanoparticles, including *Bacillus* (Hsueh et al. 2015; Ashengroph and Hosseini 2021), *Pseudomonas* (Abdo et al. 2021; Kalaimurugan et al. 2019), *Klebsiella* (Baldi et al. 2016; Dolatabadi et al. 2021), *Escherichia* (Dolly et al. 2015; Li et al. 2020; Deb et al. 2022), *Enterobacter* (Konar et al. 2019; Qin et al. 2021), *Aeromonas* (Jayaseelan et al. 2012; Mohammed and Attia 2022; Iswarya et al. 2022), *Corynebacterium* (Santos et al. 2019; Zhao et al. 2021), *Lactobacillus* (Rajesh et al. 2015; Prema et al. 2022), *Weissella* (Singh et al. 2016b), *Rhodobacter* (Borghese et al.

Table 11.1 Examples of microbial synthesis of nanomaterials

Microorganism	Types of nanoparticle	Shapes	Size (nm)	References
Bacteria				
Pseudomonas deceptionensis	Silver	Spherical	10–30	Kalaimurugan et al. (2019), Abdo et al. (2021)
Weissella oryzae	Silver	Spherical	10–30	Singh et al. (2016b)
Bacillus methylotrophicus	Silver	Spherical	10–30	Wang et al. (2016a)
Brevibacterium frigoritolerans	Silver	Spherical	10–30	Jin et al. (2020)
Bhargavaea indica	Silver and gold	Silver anisotropic, gold, flower	30–100	Singh et al. (2015)
Bacillus amyloliquefaciens	Cadmium sulphide	Cubic/ hexagonal	3–4	Ashengroph and Hosseini (2021)
Bacillus pumilus, *Bacillus persicus*, and *Bacillus licheniformis*	Silver	Triangular, hexagonal, and spherical	77–92	Muras et al. (2021), Jouzani et al. (2017)
Listeria monocytogenes, *Bacillus subtilis*, and *Streptomyces anulatus*	Silver	Anisotropic	Vary	Srinath et al. (2018), Pallavi et al. (2022)
Fungus				
Neurospora crassa	Silver, gold, bimetallic, silver and gold	Quasi-spherical	>100	David et al. (2022)
Phoma sp.	Silver	Cubic	70	Soltani Nejad et al. (2022)
Fusarium oxysporum	Gold	Spherical	20–40	Ahmed et al. (2018)
Verticillium sp.	Copper	Spherical	25	Lalitha et al. (2020)
Aspergillus fumigatus	Silver	Oval	5–25	Szalewski et al. (2018), Elshafei et al. (2021)
Trichoderma asperellum	Silver	Cubic	134–18	Abdel-Ghany et al. (2018), Shanmugam et al. (2020)
Phanerochaete chrysosporium	Silver	Cubic	50–200	Tarver et al. (2019), Huang et al. (2020)
Actinomycetes				
Streptomyces sp. *LK3*	Silver	Spherical	5	Al-Dhabi et al. (2018b), Edison and Pradeep (2020)
Yeast				
Yarrowia lipolytica NCYC 789	Silver	Spherical	15	Chourabi et al. (2021)
Rhodosporidium diobovatum	Lead	–	2–5	Chaudhry et al. (2018), Patil and Kim (2018)

(continued)

Table 11.1 (continued)

Microorganism	Types of nanoparticle	Shapes	Size (nm)	References
Extremophilic yeast	Silver and gold	Irregular	Silver, 20 Gold, 30–100	Roychoudhury (2020), Romano et al. (2022)
Candida utilis NCIM 3469	Silver	Spherical	20–80	Bolbanabad et al. (2020), Gahlawat and Choudhury (2019)

2017; Veeramalini et al. 2022), *Rhodococcus* (Bardania et al. 2013; Kuyukina et al. 2022), *Brevibacterium* (Kiran et al. 2010; Jin et al. 2020), *Streptomyces* (Al-Dhabi et al. 2018a; Weeranantanapan et al. 2022), *Trichoderma* (Saravanakumar and Wang 2018; Shanmugam et al. 2020; Alghuthaymi et al. 2022), and *Desulfovibrio* (Gong et al. 2018; Wang et al. 2022). It has been shown that bacteria produce nanoparticles primarily through enzymes. Among other things, it has been discovered that the nitrate reductase enzyme is responsible for generating the silver nanoparticles in *B. licheniformis* (Yeh et al. 2020; Ding et al. 2022) which are mentioned in Table 11.1.

Biological nanoparticles can be synthesized through "mycosynthesis" without the use of bacteria. It is easy to culture fungi for effective, affordable nanoparticle synthesis due to their considerable metabolites that have a high bioaccumulation potential and straightforward downstream processing (Lee et al. 2015). A significant benefit of fungi is that they are more capable of tolerating and consuming metals than bacteria. This is especially true in terms of the high yield of nanoparticles that can be generated from metal salts bound to fungal biomass. It has been proposed that there are three possible explanations for the mycosynthesis of metal nanoparticles: electron shuttle quinones, nitrate reductase activity, or both (Boroumand Moghaddam et al. 2015; Ameen et al. 2021).

Researchers found that fungi manufacture nanoparticles using a mechanism like that of bacteria. These fungi include *Penicillium* sp. (Fouda et al. 2021; Gupta et al. 2022) and *Fusarium oxysporum* (Ahmed et al. 2018; Ilahi et al. 2022; Fonseca et al. 2022). The creation of nanoparticles using actinomycetes has not been explored thoroughly, despite their monodispersity, stability, and biocidal activity. *Streptomyces* sp. reductase enzyme is essential for reducing metal salts, as evidenced by the creation of silver, copper, and zinc nanoparticles (Weeranantanapan et al. 2022; Pallavi et al. 2022). The large-scale extracellular manufacture of nanoparticles with simple downstream processing has also been extensively studied in yeasts, as well as other microorganisms (Boroumand Moghaddam et al. 2015; Duarte et al. 2019; Rozene et al. 2021). It is also feasible for nanoparticles to be created using viruses (Khezerlou et al. 2018; Park et al. 2020). A complex set of procedures is also involved in the production of microorganism-based nanoparticles, such as the

analysis of microbial samples, their isolation, culture, and maintenance (Prasad et al. 2016; Gahlawat and Choudhury 2019) which are mentioned in the Table 11.1.

Globally, microbial cultures and plant-based extracts have been used to create NPs in a more sustainable way. A microbial cell can be used to synthesize nonpolar organic compounds due to its rapid growth rate, low cultivation cost, and ability to survive at ambient temperatures, pressures, and pH levels. Since they can survive in a toxic metallic environment, they are innately capable of generating inorganic NPs by reducing inorganic materials via intracellular and extracellular channels utilizing reduction mechanisms. As a result of enzymatic activity, bacteria take metallic ions from the environment and convert them into their elemental forms (Yang et al. 2018).

The production of nanomaterials based on fungi is growing in popularity around the world. NPs are produced more efficiently by fungal strains because their biomass is higher than that of bacteria (Prasad 2016, 2017; Prasad et al. 2018). There were numerous species of fungi used to create NPs, including *Fusarium oxysporum* (Ilahi et al. 2022), *Verticillium luteoalbum* (Chhipa 2019), *Trichothecium* sp. (Sundaramanickam and Maharani 2021), *Colletotrichum* sp. (Ajaz et al. 2021), *Alternaria alternate* (Salem et al. 2022), *Aspergillus oryzae* (Elshafei et al. 2021), and *Trichoderma viride* (Kaur et al. 2022). NPs of various shapes and sizes were created using these species. Biotechnology and pharmaceutical components can be made more environmentally friendly and safer by using eco-friendly, green chemicals and microorganisms (Edison and Pradeep 2020).

Bacteria such as *Saccharomyces cerevisiae* (Giese et al. 2020) and *Bacillus* sp. (Hsueh et al. 2015) produce manganese oxide, copper oxide, iron oxide, and titania oxide nanoparticles in an environmentally friendly way. In due course, metallic ions were significantly reduced in their effects due to the bacterial ability to synthesize NPs. Researchers have found that bacteria precipitate metals at the nanometre scale by reducing metallic ions. There is evidence that fungal species produce monodispersed NPs with clearly defined shapes and sizes using different enzymes both intracellular and extracellular. The researchers used titanium dioxide nanoparticles to biosynthesize antibacterial NPs for the treatment of *Klebsiella planticola* (Hussein et al. 2019), *Bacillus subtilis* (Srinath et al. 2018), and *Aspergillus* niger (Szalewski et al. 2018).

A mushroom with antibacterial properties has been used to produce iron nanoparticles (NPs) that can inhibit *E. coli* (Baldi et al. 2016), *Staphylococcus* sp. (Hussein et al. 2019), and *Bacillus* sp. (Srinath et al. 2018). Based on the concentration of substrates, iron nanoparticles inhibited bacterial respiration by limiting the oxygen supply. All three variables contributed to the size, monodispersion, and development of NPs formed in the incubated medium. According to Sharma et al., the capping agent and the incubation period directly regulate the stability and size of formed NPs. The synergistic effects of carbenicillin, ciprofloxacin, and nitrofurantoin were observed when silver nanoparticles were prepared from *Rhizopus stolonifer* using an environmentally safe technique (Ventura-Aguilar et al. 2021).

The most common cause of death for women is breast cancer. According to published reports, microorganism-based metallic nanoparticles have significant anticancer effects (Sambi et al. 2017). Using *Saccharomyces boulardii* nanoparticles, platinum nanoparticles were tested against cancerous A-431 and MCF-7 cell lines (Guerra et al. 2020). *Cryptococcus laurentii*-derived silver nanoparticles exhibit a superior anticancer effect when applied to malignant cell lines, particularly breast cancer cells (Hamidi et al. 2022). It has been found that greener-produced silver nanoparticles stimulate apoptosis in tumour cells and improve endocytic activity. It was discovered that the efficiency of silver NPs was equivalent to the endocytic activity of tumour cells. The biologically active selenium nanorods were prepared using *Streptomyces bikiniensis* and demonstrated antitumor activity against MCF-7 and Hep-G2 cancer cells. Anticancer properties are associated with selenium, a trace element (Marathe et al. 2021).

Copper nanorods reduce Hep-G2 and MCF-7 cells by linking to chromatin and triggering an oxidative response. MCF-7 breast cancer cells and HEPG-2 human liver cells were treated in vitro with gold nanoparticles made from *Streptomyces cyaneus* (El-Batal et al. 2018). Nanoparticles of gold stimulate mitochondrial apoptosis and delay cytokinesis, causing DNA impairment. Gold nanoparticles made with *Candida albicans* bind to liver cancer cell surface-specific antibodies, making them useful for analysing liver cancer cells (Ashrafi et al. 2020). The antibodies bound to NPs were firmly attached to the surface antigen of the cancerous cells, and they were able to distinguish cancerous cells from healthy cells. Further research is needed to provide a more realistic picture of how microbially produced nanomaterials can be used in diagnostics (Park et al. 2020).

An extracellular silver nitrate reduction mechanism induces *Fusarium oxysporum* to release a bioactive compound. In addition to having excellent anti-inflammatory and antibacterial properties, silver nanoparticles can speed wound healing. By stabilizing silver nanoparticles and decreasing metallic ions, the nitrate-dependent reductase enzyme, the quinine shuttle, and secreted proteins of the fungus work together (Hermida-Montero et al. 2019; Aziz et al. 2016, 2019). The antibacterial activity of silver nanoparticles made using the aforementioned technique was tested on silk and cotton fabrics against *Staphylococcus aureus* (Hussein et al. 2019). A similar protein was secreted by algae that inhibited not only silver ions but also silver nanoparticles. *Chlorella vulgaris* also produced a protein that regulated the shape and synthesis of nanoparticles in addition to reducing silver ions (Rajkumar et al. 2021).

A bioengineered bacterium could be used as a vector to deliver anticancer drugs to tumours in these early experiments. Microorganisms that target tumours are genetically enhanced to be less immunogenic and toxic. Infection-mediated oncolysis (defined as the killing of tumour cells) was frequently associated with acute toxic effects, septic shock, and mortality, which has led to genetic modifications of toxin-targeting strains to lower their immunogenicity. Bacteria that target cancer can be transformed through genetic modification into vectors that deliver therapeutic proteins to tumours, thus enabling the same technique to be used against cancer (Mahfuz et al. 2022). A variety of pathologies have been

treated with genetically altered bacteria, including GIT disease, diabetes, cancer, and viral infections, with many cases making it to the clinical trials stage. Genetically altered bacteria have been used to deliver proteins, medications, enzymes, and genes for decades (Khan et al. 2022).

Biological activities can be added or changed in already-existing organisms thanks to recent technological advancements. Despite the paradigm shift caused by synthetic biology and enhanced by revolutionary DNA synthesis and gene editing technologies, bacteria are beginning to play a new role as microbial "physicians" as we move beyond their role as therapeutic drug delivery vehicles (Chaudhry et al. 2018). In addition to moving independently, sensing their immediate environment, responding to external signals, and being detectable externally, bacterial cells are well suited to serve as miniature doctors. Using these abilities, bacteria can determine the severity of a disease and the effectiveness of treatment while controlling the spatiotemporal timing of therapeutic action.

Due to cutting-edge gene editing techniques and cutting-edge design principles such as biohybrid microsystem designs, it is now possible to design therapeutic systems that go beyond wild-type organisms' natural propensities (Dolatabadi et al. 2021). The next generation of bacterial cell therapy systems will be autonomous microrobots capable of diagnosing human disease, selecting a course of action, performing the action, and then self-eradicating from the human host upon resolution. As well as explaining the key characteristics of bacterial cells that can be used in the creation of such bacterium-based bioengineered and biohybrid therapeutic systems, this paper also highlights some of the remaining challenges (Veeramalini et al. 2022; Chaudhry et al. 2018; Khezerlou et al. 2018).

11.4 Important Properties of Microbes Made Suitable for Smart Drug Delivery Agents

Many stimuli can stimulate bacteria, including chemicals, temperature, light, osmolarity, and pH. When the environment changes, bacteria sensitive to stimuli change their behaviour dramatically. By taking advantage of this capability to detect physical stimuli and environmental cues, bioengineered bacteria can be used to target or sense illness biomarkers. When designing drug delivery systems, it is pertinent to consider bacterial stimulus response some examples are detailed in the Table 11.2.

11.4.1 Transcriptional Control by Light-Induced Optogenetics

Ion channels are membrane proteins that produce pores and govern ion flow and cell volume by regulating the flow of ions across the cell membrane (Velea et al. 2019). Bacterial cells can be genetically altered to express light-sensitive ion channels, enabling transcriptional control that is significantly more extensive than is possible with conventional inducible promoter systems. An altered form of EL222, a bacterial light-oxygen-voltage protein that binds DNA when irradiated with blue light, was

Table 11.2 Examples of microbial-based smart nanomaterials

Microbes	Applications	Administration	References
Lactococcus lactis LL-THY12	Crohn's disease	Oral	Mohd Yusof et al. (2020)
Lactococcus lactis AG03	Oral mucositis	Mucosal	Prema et al. (2022)
Salmonella enterica ser. Typhimurium	Neoplasm metastasis, advanced unspecified solid tumours, advanced unspecified solid tumours	Intravenous, intratumoral injection	Arshad et al. (2021)
S. typhimurium	Hepatic metastasis from a solid tumour cancer	Oral	Bolbanabad et al. (2020), Arshad et al. (2021)
Clostridium novyi-NT spores	Treatment-refractory solid tumour malignancies	Intratumoral injection	Janku et al. (2021)
Listeria monocytogenes ADXS11-001	Anal and rectal cancer, cervical cancer carcinoma, non-small-cell lung cancer, cervical, head and neck, human papilloma virus-related cervical cancer, and related oropharyngeal cancer	Intravenous	Li et al. (2022)
Listeria monocytogenes JNJ-64041757	Non-small cell lung cancer	Intravenous	Li et al. (2022), Gao et al. (2020)
Listeria monocytogenes CRS-207	Metastatic prostate cancer advanced solid tumours; malignant pleural mesothelioma; previously treated metastatic adenocarcinoma of the pancreas; platinum-resistant ovarian, fallopian, or peritoneal cancer; metastatic pancreatic; adenocarcinoma; previously treated metastatic adenocarcinoma of the pancreas	Intravenous	Kim and Song (2018)
Bacillus calmette-guerin	Bladder cancer	Intravesical	Juvet et al. (2020)

developed to demonstrate the feasibility of creating light-dependent or optogenetic drug delivery systems utilizing bioengineered bacteria (Spagnuolo et al. 2019). This method displayed quick activation and deactivation rates in vitro and a broad dynamic range for protein expression (Gheorghiu et al. 2021). Bioengineered bacteria were also employed to stimulate transcription in various eukaryotic systems with low-intensity blue light. To further investigate the relationships between bacteria and tumours, optogenetic methods can be applied to build bacterial switches. For this reason, strategies like using LACE (light-activated CRISPR/Cas9 effector systems) could be effective. LACE can be used to locate epigenetic markers caused by dynamic patterns of gene activation in cancers. It can also be used to find new

diagnostic markers in uncommon tumours and to examine the stability of feedback loops to create and administer therapies (Reshetnikov et al. 2022).

11.4.2 Microbes Are Responsive to Magnetic Fields

Due to their method of administration, bacterial taxis typically operate closer together than medication delivery systems. To achieve such long-range targeting, magnetically sensitive systems can be guided to their target locations with long-range, distant magnetic fields without requiring local input. Theranostics may also benefit from electromagnetic targeting because it can be utilized for diagnosis (such as magnetic resonance imaging) and therapy (Bardania et al. 2013). Magnetotactic bacteria contain ferromagnetic nanocrystals and can align with the Earth's magnetic field (25–65 T). Magnetic resonance imaging (MRI) machines can provide an external magnetic field capable of actively regulating the movement of magnetotactic bacteria; this method opens new possibilities for developing therapeutic systems that are more effective in addressing tumours and infections (Lemos et al. 2021; Anik et al. 2021).

Magnetotactic bacteria are also highly mobile, which makes them ideal for delivering medications. Magnetotactic bacteria doped with medicines were used in this study to target the angiogenic network in tumours. Even though bacterium-based magnetically directed medication delivery relies on magnetotactic bacteria, research in this area has changed its focus due to concerns about the viability of these cells in clinical settings (Lee et al. 2015). Recently, magnetotactic steering control was used to deliver drugs to bacteria that are not magnetically tethered to magnetic particles. Researchers have also worked to develop magneto-responsive systems utilizing bacterial species that may be commensal and have been conjugated with magnetic particles to achieve a better sense of safety. The concept of biohybrid microsystems was implemented to achieve the study's objectives (Li et al. 2020).

11.4.3 An Oxygen-Driven Approach to Targeting

Oxygen levels in the environment affect bacteria, as previously stated. Anaerobic bacteria are attracted to areas with low oxygen levels, whereas aerobic bacteria seek oxygen (Banerjee et al. 2020). As a result of their widespread distribution in the hypoxic core of solid tumours, *Clostridium* and *Streptococcus* were the first to discover bacteria that target cancers. The organism is sensitive to oxygen. In addition, *Clostridium* species are found in the environment. Through the induction of immunomodulatory proteins (such as TNF-α), these molecules are used to signal tumour cell death and improve IL-2β mediated antitumor immunity (Bhattacharjee et al. 2022). In addition to developing hypoxia-inducible switches for the expression of anticancer proteins, peptides, and genetic fragments in anaerobic bacteria, hypoxia-inducible switches are also being used to address a significant safety issue with bacterial drug delivery systems. *Salmonella* and *E. coli* are facultative

anaerobes that are not restricted to the tumour core but can multiply at the boundary between living and dead tissue. A notable instance is a genetically altered strain of the facultative anaerobe *E. coli* that expresses the *Yersinia* invasin protein to enable absorption into mammalian cells (Karthikeyan et al. 2021).

A hypoxia-responsive promoter with the lux quorum sensing circuit of *Vibrio fischeri* was used to ensure that cellular invasion only occurs in low-oxygen tumour settings. Cancer cells were bactofected with DNA encoding tumour-targeting toxins, which were then targeted and bound with this method by bacterial infection with *E. coli* (Komiyama et al. 2022). The delivery of siRNAs to silence genes promoting tumour cell growth in the cancer cells was carried out using *E. coli*. This strain also has the *Yersinia* invasin gene, which facilitates absorption into cells, and the *Listeria* listeriolysin protein, which facilitates endosomal escape. The same strategy has been successfully used to deliver particular genes via autofiction using *S. typhimurium* for gene silencing, stimulating a spectrum of immunomodulatory cytokines (IL-2, IL-18, and LIGHT protein) and chemokines (CCL21), or inducing natural killer cell-mediated inhibition of metastases (Mahfuz et al. 2022).

11.4.4 pH- and Thermoresponsive Drug Delivery Mechanisms for Bacteria

Many diseases are associated with changes in pH and temperature due to thermal and pH taxis. The metabolism of cancer cells (hypoxia) and inadequate blood perfusion lead to acidic and hot tumour masses (Ozalp et al. 2011). Anaerobic fermentation of infected tissues and changes in pH caused by the immune system also contribute to bacterial infections. As a result of the body's immune response, infections may also be caused by temperature changes. pH and temperature sensory mechanisms may aid in the locomotion and localization of bacteria at the disease site (Yang et al. 2018). In a recent study, we demonstrated that *Serratia marcescens* cells are pH-responsive by demonstrating unidirectional and bidirectional pH taxis with microbeads. Using this approach, we can tailor pH, temperature, or secreted biomolecules to fit the needs of a particular disease based on our understanding of the bacterial taxis pathway. The taxi pathway can also be linked to other bacterial signalling pathways to maintain confinement within a particular body niche (Li et al. 2019).

11.5 Smart Component Properties

It is not enough to have inert objects that do not participate in performance during release but rather active components that are part of an intelligent DDS. With the transition from conventional dosage forms to sophisticated DDSs, active excipients are created along with the evolution of biomaterials. Excipients can be thought of as a special sort of biomaterial. This is because excipients can be defined as any material that interfaces with biological systems to evaluate, treat, augment, or replace any tissue, organ, or function of the body (Shi et al. 2010). The primary role of

excipients in the manufacturing of medicines is to ease some technological stages and to maintain stability during storage.

Despite the complexity of the performance demanded advanced nano-DDS couldn't be sold without repeatable fabrication, so it's essential not to overlook these two fundamental tasks. A paradigm shift occurred in the first generation of biomaterials, when materials were no longer regarded as independent entities to be investigated as a function of their nature (Colililaa 2013). Rather, they were viewed as entities to be rated according to their interrelationships between processing, structure, and properties. In the field of biomaterials, traditional excipients are considered the first generation; their only contribution to drug release from solid medications is to facilitate the disintegration of dosage forms when they come in contact with physiological fluids. As a result, an array of uses such as quick oral release can still be achieved using this characteristic (Hosseinidoust et al. 2016).

It was in the latter third of the twentieth century that materials science and engineering principles were integrated with biology and biomedical criteria to develop the second generation of biomaterials, which induce favourable physiological responses to enhance tissue interaction during permanent or temporary contact biodegradation (Alvarez-Lorenzo and Concheiro 2014). Changing attitudes towards biocompatibility and, consequently, how we design and use biomaterials have gradually changed due to significant improvements in understanding the body's components as engineering structures. This has resulted in a fresh perspective on biological systems as engineering structures. Through direct interaction with the patient's biological components, a third-generation biomaterial is expected to assist the medical process. Pharmacokinetics and release of medications can be tuned with third-generation excipients by removing obstacles that keep the medicine from reaching its destination (Hosseinidoust et al. 2016).

The inherent organization and adaptability of natural materials make them appropriate models for how to build things. Consequently, lipids and polymers, which can be created using a variety of less-expensive techniques, are designed using knowledge of the conformation and usefulness of natural biomacromolecules. These biomimetic implantable biomaterials are also known as smart or fourth-generation materials, and they are expected to activate cellular responses on a cellular level to assist in tissue regeneration. Among the cutting-edge generation of stimuli-responsive excipients are smart DDS and theranostic systems, which integrate diagnosis and medication delivery capabilities within one entity (Unsoy and Gunduz 2018).

In the same way that natural materials modify their conformation and performance in response to conditions (stimuli) of the surrounding environment, high-performance DDS components should be able to tailor their release based on the physiological/pathological condition of the body. Consequently, they must be able to recognize signals from the body, process them, and alter their behaviour and functionality accordingly. Since smart DDSs are equipped to change their characteristics in response to environmental stimuli and challenging biological conditions, they can be referred to as "adaptive" medications. In addition to stimulus responsiveness, safety and excretion/elimination analyses must be considered when

designing materials that penetrate deeply into tissues and cell structures. To be considered a suitable medical component material, smart materials must meet a long list of conditions (Sanchez-Moreno et al. 2018; Kong et al. 2019).

11.6 Phase Transition Determinants

It is essential to have a balanced ratio and configuration of sensitive components in smart DDS. The most employed materials are polymers. This is because they have an unmatched variety of structural and functional groups that can significantly alter their properties. These groups can undergo continuous and reversible phase changes depending on the stimulus of interest. Thermal transitions govern phase transitions, which is the mechanical basis for smartness. In fact, D. W. Grainger recognized smart DDSs as an example of reasonable attempts to respect thermodynamics (Kim et al. 2021).

Currently, there are ten different types of phase transitions, with over half exclusive to polymers. It is common for phase changes to occur in the first or second order. As a function of the intensive thermodynamic quantities of pressure, temperature, or chemical potential, among others, the extensive thermodynamic quantities of volume, energy, entropy, or number of macromolecular moles exhibit discontinuities in the first-order transitions (Abdo et al. 2021). When the derivatives of the large thermodynamic quantities are shown, there is no discontinuity in the second-order example. To be effective as a stimulus-sensitive component for drug delivery, the polymer must be primarily responsive to the appearance or disappearance of a stimulus that is undergoing a first-order phase transition, which must be accompanied by an increase in the polymer's specific volume (Soliman et al. 2019).

There is no restriction on how many molecules can move through the transition. As monomers are sequentially connected to one another in a polymer chain, transitions within a single macromolecule can occur, unlike their comparable behaviour while free in solution. This type of transition is characterized by the transition of a helix to a random coil and the transition of a helix to a collapse. Transitions between helixes and coils are common in polypeptide chains, double-stranded DNA, and triple-stranded collagen (Deb et al. 2022). Both diffusely and first-order, these transitions are triggered by temperature changes or chemical potentials, altering intrastrand and interstrand hydrogen bonds. It is imperative to note that naked DNA undergoes first-order transitions with other molecules to undergo first-order transitions and to be more packed. This would result in a random coil conformation with dimensions larger than those of the cells. During a collapse transition, the monomers in a polymer try to expand due to their entropy rubber elasticity and the attractive interactions between them. At close range, monomers are repelled because each occupies a specific volume in the polymer and cannot pass through another (Komiyama et al. 2022).

Biological systems and water solutions undergo four primary intermolecular interactions: hydrogen bonds, van der Waals contacts, hydrophobic interactions, and Coulomb interactions (Kumar et al. 2014). As monomers are linked together into

flexible long chains, the volume phase transition has a significant impact on the diffusion of solutes, such as pharmaceuticals. This also impacts the fluid flow in the network. This results in significant changes to the polymer's conformation even when minor variations in key thermodynamic factors are introduced including temperature, pressure, and chemical potential.

Smart drugs are most often administered by forming membranes, micelles, or vesicles within groups of molecules. As a result of immobilizing one another, incompatible polymers are joined in blocks. It causes microphase separation, with each microdomain mainly containing one of the blocks and separated by thin interphase areas. Although incompatibility continues, it causes microphase separation. It depends on the length of each block relative to the others and whether each microdomain will form a lamellar, cylindrical, or spherical phase. It is possible for membranes, micelles, or vesicles to form free-standing in media with sufficient solvent. A substance may rapidly change its chemical make-up (such as hydrolysis or oxidation/reduction processes) and become a new substance with distinct chemical groups under certain conditions. Transitions in thermodynamics can accompany such transformations. Additionally, macromolecules regularly undergo linked transitions in nature, meaning that one transition does not preclude another (Uddin 2019).

11.7 Smart Nanoparticles and Drug Delivery Systems

A review elaboration from Shi et al. (2010) enlisted that, even though three targeted nanoparticle systems are currently in phase I/II clinical trials, the clinical translation of targeted delivery is not as straightforward as we anticipate. There is a potential impediment in the production of effective nanoparticles targeted at specific targets. It is possible for batch-to-batch variations and quality issues to occur during targeted nanoparticle production due to multiple processes including biomaterial assembly, ligand coupling and insertion, and purification. Using self-assembling prefunctionalized biomaterials to synthesize targeted nanoparticles, we can now produce them in a straightforward and scalable manner. Considering target ligands is another crucial consideration. Biocompatibility, cell specificity, binding affinity, mass manufacturing, and purity are some factors that need to be considered (Shi et al. 2010).

One of the notable discussions from Singh et al. (2016a, b) detailed that during the past few years, bacteria (such as actinomycetes), fungi, and yeasts have been studied for their ability to create metal nanoparticles extracellularly and intracellularly. Biological nanoparticles can be synthesized using mycosynthesis, an indirect method that does not require the use of bacteria. It is simple to cultivate and affordably synthesize nanoparticles from fungi since they produce metabolites with high bioaccumulation potential. Metal salts bind strongly to fungal biomass for the creation of nanoparticles in fungal biomass, which makes them more suitable for consumption by fungi than bacteria. It has been proposed that the mycosynthesis of metal nanoparticles may be caused by nitrate reductase activity, electron shuttle

quinones, or both. There is evidence that fungal enzymes, such as nitrate reductase and/-NADPH-dependent reductases, play an extremely significant role in creating nanoparticles (Singh et al. 2016a).

Wang et al. (2016a, b) discussed the applications of titanium nanotubes (TNT)as smart nanodevices, where TNT implants are utilized in the medical field for localized drug delivery, including bone therapies, dentistry, cardiovascular stents, localized cancer treatment, and other therapies that require an implantable device. By regulating drug release with optimal concentration for various time scales, these multimodal localized drug delivery systems based on TNTs will facilitate a smoother integration into clinical practice (Wang et al. 2016b).

Sambi et al. (2017) review discussion presented that the primary advance in the use of nanoparticles in medicine has been focused on developing effective targets for drug delivery. A synthetic drug delivery system primarily uses polymeric nanoparticles. Producing polymers is simple, thanks to the precise functionalization that can be applied to the chains. Despite their biocompatibility, polymers are particularly advantageous for drug administration because of their ability to self-assemble into a variety of forms. Spiral micelles, gyroids, and lamella with hydrophobic or hydrophilic cores can be constructed from polymers by self-assembling. For the oral administration of various medications, these nanoparticles can be customized for specific use. Nanoparticle size and shape can have a significant impact on treatment effectiveness, as demonstrated in this paper. Nanoparticles' surface area is enormous, which allows them to interact with the gastrointestinal tract more effectively than traditional oral delivery systems (Sambi et al. 2017).

Polymeric carriers have been used since polymerization was the earliest means of delivering medicine to rapidly replicating cells due to their vasculature. These carriers' efficacy varied greatly depending on their molecular weights and release mechanisms. As a second targeting strategy, polymers were functionalized for specific reactions based on their environment, such as pH, ionic strength, magnetic field, and heat. Physically distinct and environmentally responsive characteristics can result from a polymer's particular functionalization. In general, functionalization can improve the photocatalytic properties of a material. Furthermore, biodegradable polymers can be functionalized effectively for the purpose of tissue engineering to control their optical and magnetic properties. Nanostructures can be functionalized for direct drug delivery in the field of drug delivery. Changing microenvironments might lead to polymer-drug bond cleaving, releasing the drug. Covalent bonds between drugs and polymers are common (Iswarya et al. 2022).

The discussion from Yang et al. (2018) review, over the past three decades, presented that extracellular vesicles have attracted considerable attention due to their physiological significance and biomedical applications. The release of bilayered vesicles by eukaryotic cells into the extracellular environment in 1983 resulted in extracellular vehicles (EVs) being dismissed as cellular garbage disposals. Prokaryotes, eukaryotes, and archaea, to varying degrees, produce EVs, according to a wealth of research over the past few decades. The data indicate that cells have secreted EVs throughout evolution as a means of surviving. In the process of EV biogenesis, receptors specific to each cell type are activated, which is a very closely

controlled process. Several signalling molecules are involved in this process. Even though bacterial EV biogenesis has just recently begun to be clarified, eukaryotic EV biogenesis is well understood. We will discuss the synthesis of exosomes and the release of apoptotic bodies by bacteria in this section, which are also known as shed vesicles. More research is needed to better understand the mechanism behind the synthesis of bacterial EVs, particularly in Gram-positive bacteria and in bacteria undergoing apoptosis. The use of EVs in medicine, as biomarkers and pharmabiotics, is a developing field. Microbiota-derived EVs have potential applications in biomedicine, including vaccine adjuvants, medication delivery methods for amino acids and miRNAs, and biological markers for disease detection. By understanding how bacteria produce EVs and their physiological effects on humans, their therapeutic potential can be fully tapped (Yang et al. 2018).

Singh et al. (2018) discussions mentioned the surfactant proteins are produced by a wide array of microorganisms for many biological purposes, including the sporulation of fungi and bacteria. Surfactant proteins have received the most attention from researchers as small (<100 amino acids), cysteine-rich, amphiphilic globular proteins with remarkably surface-active properties, the ability to self-assemble monolayers on hydrophobic materials, and a low molecular mass (20 kDa). As a result of their amphipathic structures, hydrophobins are essential proteins for fungal development and growth, allowing them to escape aqueous environments and enter the atmosphere. It has been discovered that filamentous fungi including *Ascomycetes* and *Basidiomycetes* use these proteins to lower interfacial tension (Singh et al. 2018).

Hydropathy patterns and biophysical characteristics differentiate MHs into Classes I and II. It is easy to dissolve Class II MHs in aqueous solutions, even at quite high concentrations, but Class I MHs must be treated with powerful acids to separate. Hydrophobins self-assemble in a variety of industries, such as cosmetics, healthcare, agriculture, personal care products, separation technologies, and biosensors. Furthermore, MHs are harmless substances that can be used as multifunctional coatings for smart medication nanoparticles since they increase spore dispersion in the air by coating them (Singh et al. 2016b).

Yao et al. (2018) mentioned that the nanocarrier, also known as a nanoparticle-based delivery system, is typically smaller than 200 nm in size and has a variable shape and size. The nanocarriers can be loaded with cargo-like medications and imaging agents that help the investigator obtain data on diseases such as tumour locations and treatment effectiveness by covalent or noncovalent interactions. Many clinical medicinal applications have been developed using these nanocarriers. Due to their nanoscale size, nanoparticles are superior to carrier-free pharmaceuticals or free medications in terms of their physicochemical and biological characteristics. A key technique for modifying nanoparticles is PEGylation, which involves the addition of polyethylene glycol (PEG). As a result of PEGylation, the mononuclear phagocyte system (MPS) is unable to catch nanoparticles. Tumours are well known for their increased endothelial fenestrations and impaired lymphatic outflow, a phenomenon known as enhanced permeability and retention (EPR). By enhancing the EPR effect's "passive" tumour targeting, the drug becomes persistent in the bloodstream

because of PEGylation of the drug-loaded nanoparticle. For more precise and effective drug delivery, nanoparticles must be modified for "active" targeting, stimulation-responsive delivery, and intracellular delivery (Yao et al. 2018).

Li et al. (2019) studies show the development of a smart nanosystem; researchers succeeded in delivering drugs to cervical tumours by grafting CQDs with PEGs and FAs (Li et al. 2019; Vyshnava et al. 2020). The fact that CQDs are biocompatible, homogeneous in size, and small that makes them an ideal replacement for MTNs is undeniable. It was also found to dramatically increase the stability of CQDs by adding NH2-PEG-NH2 to their surfaces (Vyshnava et al. 2022a, b). This prevented nanodrugs from aggregating. As a consequence of covalent modifications with PEG and FA, the surface potential of the cGQDs similarly should also be effectively adjusted to meet drug delivery requirements. In addition to reducing cGQD quantities, MTN concentrations, and uptake times, these changes helped reduce the antitumor efficacy of MTN. Prior research has also demonstrated that cancer cells, particularly HeLa cells, overexpress FA receptors. A drug delivery system may be more effective at targeting tumours if it has this capability. Tračuma and Loca (2020) discussed that biomaterials are promising because they combine poly-L-lysine with hyaluronic acid. A similar strategy can be used to create "green" hyaluronic acid and poly-L-lysine hydrogels for local drug delivery in various biomedical applications using nontoxic cross-linkers, since hyaluronic acid and poly-L-lysine can be used to create multilayer films and polyelectrolyte complexes without chemical cross-linkers (Li et al. 2019).

Li et al. (2019) developed a drug delivery system using folic acid-poly (ethylene glycol)-cGQDs capturing 97.5% of their cargo and loading 40.1% of their cargo. An image of the human cell indicated that the nanosystem had invaded the cell. Macropinocytosis is primarily involved in the process of killing cervical cancer cells. Low systemic toxicity and a high anticancer capacity of this nanodrug delivery system have been demonstrated in vivo (Oliveira et al. 2019; Li et al. 2020).

Kuzajewska et al. (2020) mentioned in their review article, which provided that using standard treatments is frequently impossible or difficult, contributing to the rising cancer rate in modern medicine. Innovative research trajectories for enhancing cancer treatment effectiveness include developing efficient distribution systems for medicinal chemicals. Magnetotactic bacteria (MTB) have many applications in this field thanks to their magnetosomes (BMs) that contain ferromagnetic crystals. BMs and MTBs can be used to deliver chemotherapy precisely to the cancer cell's target site using biocompatible nanocarriers. The conjugation of MTBs and BMs with conventional anticancer medications, siRNA, DNA, antibodies, and liposomes is simple and straightforward. Their ferromagnetic characteristics enable these microbes to be manipulated inside a magnetic field. The creation of constructs that can be used in targeted cancer therapy opens up a wide range of possibilities (Kuzajewska et al. 2020).

The review discussion by Yeh et al. (2020) provided that various applications use mesoporous silica nanoparticles (MSNs) owing to their physicochemical stability, consistent porosity, large surface area, and biocompatibility. Drug delivery vehicles made from MSNs are excellent since they can be customized in terms of pore size,

shape, and capacity. This porous matrix is effective at protecting antibacterial compounds from enzyme degradation. MSNs may have their surface chemistry altered to facilitate passage through biomembranes. Several recent studies have focused on nanoparticles coated with natural cell membranes. This method can achieve a therapeutic benefit because native cell activity is maximized. Targeting specific immune cells with nanoparticles that mimic the immune system and cells is possible. Nanoparticles that can circulate widely can target specific immune cells. In addition to using cancer cells, erythrocytes, neutrophils, macrophages, or platelets, the nanoparticles can also be tested on the membranes of these cells to demonstrate their ability to bind with the source cells. In addition to simulating platelet interactions with bacteria, nanoparticles coated with platelets are also useful for developing antibiotics targeted at specific bacteria (Yeh et al. 2020).

Siddiqui et al. (2022) reviewed that pH sensors are one of a variety of noninvasive sensors that can monitor food quality and safety; they are able to detect changes in food composition as well as chemical and biological interactions. To detect changes in food composition, time-temperature indicators (TTIs) are crucial indicators because temperature affects whether and to what extent chemical reactions occur. pH is known to be influenced by the concentration of hydrogen ions or hydroxide ions, as well as the influence of temperature on chemical processes. By measuring the pH level, the pH sensors will provide information about the meal's chemical composition and how it varies. With TTIs and pH sensors working together, we can see how temperature alters the rate of chemical reactions and how it affects the pH of foods. TTIs and pH sensors work together to detect how temperature and pH affect the rotting process of food (Siddiqui et al. 2022).

Liu et al. (2021) mentioned that an extensive analysis of biotechnological manufacturing methods and bacterial nanocellulose, nanocrystals, and nanofibers has been conducted on nanocellulose, which consists of three different compounds: bacterial nanocellulose, nanocrystals, and nanofibers. Several publications have been published lately exploring the development of nanocellulose aerogels, responsive hydrogels, injectable hydrogels/implants, and magnetic nanocellulose. Furthermore, possible cross-linkers were discussed for enhancing the desirable properties of hydrogels. There are several factors that determine the release kinetics of nanocellulosic gels and hydrogels, ranging from minutes to weeks. These systems are referred to as "smart" systems due to their sustained drug release characteristics. Therapeutic pharmaceuticals can be delivered more efficiently to target sites using controlled drug delivery systems than other methods in recent years (Liu et al. 2021).

11.8 Current Challenges in the Development of Microbial-Based Smart Drug Delivery Systems

A significant barrier to using bacterial drug delivery systems is the dose-limiting toxicity of bacterial cells, which may limit efficacy; consequently, several clinical trials have been stopped. When the immune system responds to high bacterial concentrations, rapid bacterial clearance or even autoimmune responses may

occur. It is possible to decrease toxicity and immunogenicity through genetic alteration, but it is imperative to exercise caution when using molecular alteration. Molecular tampering may also limit the applicability of antibacterial therapeutics, such as their invasiveness essential for gene delivery, reducing their efficacy and scope. Additionally, residual toxicity has been reported even after the toxin genes have been removed. Regulatory approval for bacterial toxicity management in patients with immune compromise is the biggest challenge. Patients with immune compromise may experience problems from any residual virulence (Ozalp et al. 2011).

A good archetypal bacterium must not trigger a strong host immune response and be susceptible to conventional antibiotics. This is to be efficiently eliminated after treatment or in the event of a negative host reaction in such applications. As previously mentioned, communal bacteria have a distinct advantage. Nevertheless, even bacteria that are native to a niche can disrupt the delicate balance of the microbiota if used carelessly, which could worsen the condition. A holistic and individual examination of each vehicle and disease is necessary to prevent difficulties caused by unintentional dysbiosis (Colililaa 2013).

An antibiotic's safety threshold is largely determining the way it is administration. Considering how safe they are to use as medicine delivery systems, commensal bacteria have attracted attention. Even though research in this area has mostly focused on food-grade LAB, the findings cannot be generalized to human commensal bacteria. However, it is crucial to keep in mind that many commensal bacterial species may cause trouble elsewhere. This is even though they are beneficial in their particular niches in the human body. Even using genetically engineered strains for medication delivery to their natural body niche may be problematic. This is because genetically engineered strains have altered fitness features and pose a threat to delicate microbiota. This type of dysbiosis, or microbial imbalance, has been linked to a range of physical and mental illnesses and must be prevented. In addition, the ability of the bacterial cell to tune its drug production needs to be carefully managed. This is so that the medication is expressed or transported at levels significant enough to have therapeutic advantages without posing a health risk (Unsoy and Gunduz 2018).

Another significant concern in relation to bacterial therapy is the loss of engineered behaviour and functionalities of genetically modified bacteria, especially if an environmental selection is not used, a crucial aspect of plasmid-based genetic engineering. It may be possible to accomplish this by moving beyond using plasmid-based genetic engineering, which has become the standard method in this area due to its simplicity and programming of the desired function into the bacterial chromosome. Considering that potential difficulties are highly context-specific, it is also necessary to consider chromosomal alterations and/or horizontal gene transfer in each case individually. It is essential for bacteria to be designed in a way that ensures reliable performance in an environment that is complex and cyclical, such as the human body. This is because bacteria are living and evolving creatures. Using bacteria as tiny propellers to transport therapeutics contained in microparticles to the target site may alleviate concerns about stable performance. This is because most

of the therapeutic action can be separated from the bacterial cell, leaving it with the simple task of carrying the cargo (Alvarez-Lorenzo and Concheiro 2019).

Regulation approvals and market resistance are challenges faced by bioengineered bacteria. Even though effective containment strategies have been proposed, such as choosing auxotrophs that depend on nutrients or developing programmed eliminations, numerous reports in the literature provide a more nuanced picture of bacterial behaviour in complex environments that necessitate additional safety measures. Physicochemical characteristics of a target site influence the communication between bacterial communities, which can lead to a nonuniform distribution profile since bacteria cluster around specific geometrical features (Rao et al. 2019).

Further, it has been shown that bacteria segregate colloidal particles found in the environment. This causes them to gather around specific geometric characteristics. This suggests that bacteria may alter the microenvironment of target organs after they are introduced. To ensure efficient containment within the body and to address potential germ release into the environment, biophysical studies and randomized clinical trials are needed (Rao et al. 2019; Zhang et al. 2020).

11.9 Prospectus Applications and Studies

The biohybrid microrobotic system design idea offers a novel paradigm in the field of cell therapy. This is because it addresses all the elements of the perfect drug delivery system in a single bacterium. A synthetic material with enhanced, customized characteristics may be able to solve some of the problems associated with bacterium-based medication delivery systems. Encasing bacterial cells in microgels, for example, can enhance their immune defences and enable active long-range control. Magnets or photo-responsive materials can also be integrated with drug delivery systems for effective long-range control. It is nevertheless fundamentally difficult to build biohybrid systems that function when biological function is managed upon material contact. For bacteria to respond to outside stimuli and remain able to float, they must remain free-floating.

Biological/nonbiological interfaces may need to be carefully engineered due to bacterial inability to survive on specific surfaces. Several obstacles stand in the way of the widespread adoption of bacterium-based medicines, yet the potential is enormous. Because of safety concerns raised in the preceding paragraphs, future research in this area will tend towards investigating commensal bacteria and using bacterial communities as a group of strains to accomplish a common goal rather than one strain alone. Using entire bacterial communities directly from the human microbiota in the context of microbiota ecosystem therapy is a new paradigm in medicine that combines both concepts.

A thriving field of science has developed due to the trillions of microorganisms contained inside the human body, as well as a burgeoning business. We rely on these microbes for our health, so using them for medical therapy would represent a significant advancement both scientifically and economically. There is a degree of

interconnectedness between commensal bacterial physiology and host behaviour, which has not been fully explored in terms of the underlying biochemical interactions. Disruptions to the human microbiota must be treated with the utmost caution. For this reason, the most significant prerequisite for developing effective bacterium-based treatments will be a mechanistic understanding of how information flows between the host and the microbiome.

The development of tailored treatments based on the context-specific aspects of human disease requires using the commensal bacteria of patients. Methods of synthetic biology can be employed to develop bacterium-based drug delivery systems, e.g. precise gene editing and rational genetic engineering. By using these techniques, we can create tailored bacterial populations and cells that are easy to control and adapted to specific diseases. To realize this potential, however, we need to better understand the ecology of bacteria as well as the underlying biological causes of disease in humans.

By developing a fundamental understanding of the system biology that underlies both pathological and normal biological processes, we can gain this insight into how tumours and infections interact with the immune response and the tissue microenvironment. Finally, bacterial therapeutics cannot be expected to be a panacea for all medical conditions. Several treatments are required to completely eradicate most human diseases, like cancer, since they are multifactorial in nature. To maximize the efficiency of bacterium-based medicines, it is advisable to research how to combine them with other relevant treatment methods.

11.10 Conclusions

Molecular therapeutic agents derived from microbial cells are relatively recently developed. An unintentional infection of cancer patients more than 20 years ago led to the development of a platform technology that could open up novel therapeutic horizons in the future. Medications can be delivered to the patient using microbial cells because of their unique properties. By manipulating the molecular machinery of these cancer cells chemically, physically, and biologically, we can tailor the therapeutic action and fine-tune its spatiotemporal control, allowing the development of new therapeutic functions that cannot be achieved with delivery systems. It remains crucial to overcome several significant obstacles, even though preliminary results have been encouraging. A biohybrid design introduces a fresh new approach to bacterium-based drug delivery that explores both benefits and drawbacks of bioengineered bacteria.

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References

Abdel-Ghany TM, Ganash M, Bakri MM, Al-Rajhi AM (2018) Molecular characterization of Trichoderma asperellum and lignocellulolytic activity on barley straw treated with silver nanoparticles. Bioresources 13(1):1729–1744

Abdo AM, Fouda A, Eid AM, Fahmy NM, Elsayed AM, Khalil AMA, Alzahrani OM, Ahmed AF, Soliman AM (2021) Green synthesis of zinc oxide nanoparticles (ZnO-NPs) by Pseudomonas aeruginosa and their activity against pathogenic microbes and common house mosquito, Culex pipiens. Materials 14(22):6983

Ahmed A-A, Hamzah H, Maaroof M (2018) Analyzing formation of silver nanoparticles from the filamentous fungus Fusarium oxysporum and their antimicrobial activity. Turk J Biol 42(1): 54–62

Ajaz S, Ahmed T, Shahid M, Noman M, Shah AA, Mehmood MA, Abbas A, Cheema AI, Iqbal MZ, Li B (2021) Bioinspired green synthesis of silver nanoparticles by using a native Bacillus sp. strain AW1-2: characterization and antifungal activity against Colletotrichum falcatum Went. Enzym Microb Technol 144:109745

Al-Dhabi NA, Ghilan A-KM, Arasu MV, Duraipandiyan V (2018a) Green biosynthesis of silver nanoparticles produced from marine Streptomyces sp. Al-Dhabi-89 and their potential applications against wound infection and drug resistant clinical pathogens. J Photochem Photobiol B Biol 189:176–184

Al-Dhabi NA, Mohammed Ghilan A-K, Arasu MV (2018b) Characterization of silver nanomaterials derived from marine Streptomyces sp. al-dhabi-87 and its in vitro application against multidrug resistant and extended-spectrum beta-lactamase clinical pathogens. Nanomaterials 8(5):279

Alghuthaymi MA, Abd-Elsalam KA, AboDalam HM, Ahmed FK, Ravichandran M, Kalia A, Rai M (2022) Trichoderma: An eco-friendly source of nanomaterials for sustainable agroecosystems. J Fungi 8(4):367

Alvarez-Lorenzo C, Concheiro A (2014) Smart drug delivery systems: from fundamentals to the clinic. Chem Commun 50(58):7743–7765

Alvarez-Lorenzo C, Concheiro A (2019) Smart drug release from medical devices. J Pharmacol Exp Ther 370(3):544–554

Alvarez-Lorenzo C, Puga AM, Concheiro A (2012) Nanostructures and nanostructured networks for smart drug delivery. Biomimetic Approach Biomater Dev 14:417–458

Ameen F, Alsamhary K, Alabdullatif JA, Al Nadhari S (2021) A review on metal-based nanoparticles and their toxicity to beneficial soil bacteria and fungi. Ecotoxicol Environ Saf 213:112027

Anik MI, Hossain MK, Hossain I, Mahfuz A, Rahman MT, Ahmed I (2021) Recent progress of magnetic nanoparticles in biomedical applications: a review. Nano Select 2(6):1146–1186

Arshad R, Pal K, Sabir F, Rahdar A, Bilal M, Shahnaz G, Kyzas GZ (2021) A review of the nanomaterials use for the diagnosis and therapy of salmonella typhi. J Mol Struct 1230:129928

Ashengroph M, Hosseini S-R (2021) A newly isolated Bacillus amyloliquefaciens SRB04 for the synthesis of selenium nanoparticles with potential antibacterial properties. Int Microbiol 24: 103–114

Ashrafi M, Bayat M, Mortazavi P, Hashemi SJ, Meimandipour A (2020) Antimicrobial effect of chitosan–silver–copper nanocomposite on Candida albicans. J Nanostruct Chem 10:87–95

Aziz N, Pandey R, Barman I, Prasad R (2016) Leveraging the attributes of *Mucor hiemalis*-derived silver nanoparticles for a synergistic broad-spectrum antimicrobial platform. Front Microbiol 7:1984. https://doi.org/10.3389/fmicb.2016.01984

Aziz N, Faraz M, Sherwani MA, Fatma T, Prasad R (2019) Illuminating the anticancerous efficacy of a new fungal chassis for silver nanoparticle synthesis. Front Chem 7:65. https://doi.org/10.3389/fchem.2019.00065

Baldi F, Daniele S, Gallo M, Paganelli S, Battistel D, Piccolo O, Faleri C, Puglia AM, Gallo G (2016) Polysaccharide-based silver nanoparticles synthesized by Klebsiella oxytoca DSM 29614 cause DNA fragmentation in E. coli cells. BioMetals 29:321–331

Banerjee D, Shivapriya P, Gautam PK, Misra K, Sahoo AK, Samanta SK (2020) A review on basic biology of bacterial biofilm infections and their treatments by nanotechnology-based approaches. Proc Natl Acad Sci Biol Sci 90:243–259

Bardania H, Raheb J, Mohammad-Beigi H, Rasekh B, Arpanaei A (2013) Desulfurization activity and reusability of magnetite nanoparticle–coated Rhodococcus erythropolis FMF and R. erythropolis IGTS8 bacterial cells. Biotechnol Appl Biochem 60(3):323–329

Bhagat Y, Gangadhara K, Rabinal C, Chaudhari G, Ugale P (2015) Nanotechnology in agriculture: a review. J Pure App Microbiol 9:737–747

Bhattacharjee R, Kumar L, Mukerjee N, Anand U, Dhasmana A, Preetam S, Bhaumik S, Sihi S, Pal S, Khare T (2022) The emergence of metal oxide nanoparticles (NPs) as a phytomedicine: a two-facet role in plant growth, nano-toxicity and anti-phyto-microbial activity. Biomed Pharmacother 155:113658

Bolbanabad EM, Ashengroph M, Darvishi F (2020) Development and evaluation of different strategies for the clean synthesis of silver nanoparticles using Yarrowia lipolytica and their antibacterial activity. Process Biochem 94:319–328

Borghese R, Brucale M, Fortunato G, Lanzi M, Mezzi A, Valle F, Cavallini M, Zannoni D (2017) Reprint of "Extracellular production of tellurium nanoparticles by the photosynthetic bacterium Rhodobacter capsulatus". J Hazard Mater 324:31–38

Boroumand Moghaddam A, Namvar F, Moniri M, Tahir P, Azizi S, Mohamad R (2015) Nanoparticles biosynthesized by fungi and yeast: a review of their preparation, properties, and medical applications. Molecules 20(9):16540–16565

Chaudhry N, Dwivedi S, Chaudhry V, Singh A, Saquib Q, Azam A, Musarrat J (2018) Bio-inspired nanomaterials in agriculture and food: current status, foreseen applications and challenges. Microb Pathog 123:196–200

Chhipa H (2019) Mycosynthesis of nanoparticles for smart agricultural practice: a green and eco-friendly approach. In: Green synthesis, characterization and applications of nanoparticles. Elsevier, Amsterdam, pp 87–109

Chifiriuc MC, Holban AM, Curutiu C, Ditu L-M, Mihaescu G, Oprea AE, Grumezescu AM, Lazar V (2016) Antibiotic drug delivery systems for the intracellular targeting of bacterial pathogens. In: Smart drug delivery system. IntechOpen, London

Chourabi K, Elleuch L, Kloula S, Landoulsi A, Chatti A (2021) Antimicrobial and antibiofilm effects of silver nanoparticles produced by Yarrowia lipolytica against vegetative and starved shigella. Nano 16(8):2150088

Colililaa M (2013) Smart drug delivery from silica nanoparticles. Smart Mater Drug Delivery 2:63

David A, Kumar R, Jeba DP, Ashli J, Mathavan A (2022) Microbial synthesis of Pt nanoparticles–a nano review. ECS Trans 107(1):19627

Deb R, Pal P, Chaudhary P, Bhadsavle S, Behera M, Gautam D, Roshan M, Vats A, Ludri A, Gupta VK (2022) Development of gold nanoparticle-based visual assay for rapid detection of Escherichia coli specific DNA in milk of cows affected with mastitis. LWT 155:112901

Dhanasekaran S, Chopra S (2016) Getting a handle on smart drug delivery systems–A comprehensive view of therapeutic targeting strategies. Smart Drug Delivery Syst 1:31–62

Ding M, Zhao W, Song L-J, Luan S-F (2022) Stimuli-responsive nanocarriers for bacterial biofilm treatment. Rare Metals 41(2):482–498

Dolatabadi A, Noorbazargan H, Khayam N, Moulavi P, Zamani N, Asghari Lalami Z, Ashrafi F (2021) Ecofriendly biomolecule-capped Bifidobacterium bifidum-manufactured silver nanoparticles and efflux pump genes expression alteration in Klebsiella pneumoniae. Microb Drug Resist 27(2):247–257

Dolly S, Pandey A, Pandey BK, Gopal R (2015) Process parameter optimization and enhancement of photo-biohydrogen production by mixed culture of Rhodobacter sphaeroides NMBL-02 and Escherichia coli NMBL-04 using Fe-nanoparticle. Int J Hydrog Energy 40(46):16010–16020

Duarte KD, Frattini D, Kwon Y (2019) High performance yeast-based microbial fuel cells by surfactant-mediated gold nanoparticles grown atop a carbon felt anode. Appl Energy 256: 113912

Edison LK, Pradeep N (2020) Actinobacterial nanoparticles: green synthesis, evaluation and applications. In: Green nanoparticles: synthesis and biomedical applications. Elsevier, London, pp 371–384

El-Batal AI, Al-Hazmi NE, Mosallam FM, El-Sayyad GS (2018) Biogenic synthesis of copper nanoparticles by natural polysaccharides and Pleurotus ostreatus fermented fenugreek using gamma rays with antioxidant and antimicrobial potential towards some wound pathogens. Microb Pathog 118:159–169

Elshafei AM, Othman AM, Elsayed MA, Al-Balakocy NG, Hassan MM (2021) Green synthesis of silver nanoparticles using Aspergillus oryzae NRRL447 exogenous proteins: optimization via central composite design, characterization and biological applications. Environ Nanotechnol Monit Manage 16:100553

Fonseca MS, Rodrigues DM, Sokolonski AR, Stanisic D, Tomé LM, Góes-Neto A, Azevedo V, Meyer R, Araújo DB, Tasic L (2022) Activity of Fusarium oxysporum-based silver nanoparticles on Candida spp. oral isolates. Nanomaterials 12(3):501

Fouda A, Awad MA, Eid AM, Saied E, Barghoth MG, Hamza MF, Awad MF, Abdelbary S, Hassan SE-D (2021) An eco-friendly approach to the control of pathogenic microbes and anopheles stephensi malarial vector using magnesium oxide nanoparticles (Mg-NPs) fabricated by Penicillium chrysogenum. Int J Mol Sci 22(10):5096

Gahlawat G, Choudhury AR (2019) A review on the biosynthesis of metal and metal salt nanoparticles by microbes. RSC Adv 9(23):12944–12967

Gao X, Yu Z, Liu B, Yang J, Yang X, Yu Y (2020) A smart drug delivery system responsive to pH/enzyme stimuli based on hydrophobic modified sodium alginate. Eur Polym J 133:109779

Gheorghiu M, Polonschii C, Popescu O, Gheorghiu E (2021) Advanced optogenetic-based biosensing and related biomaterials. Materials 14(15):4151

Giese EC, Silva DD, Costa AF, Almeida SG, Dussán KJ (2020) Immobilized microbial nanoparticles for biosorption. Crit Rev Biotechnol 40(5):653–666

Gong J, Song X, Gao Y, Gong S, Wang Y, Han J (2018) Microbiological synthesis of zinc sulfide nanoparticles using Desulfovibrio desulfuricans. Inorg Nano-Metal Chem 48(2):96–102

Guerra JD, Sandoval G, Avalos-Borja M, Pestryakov A, Garibo D, Susarrey-Arce A, Bogdanchikova N (2020) Selective antifungal activity of silver nanoparticles: a comparative study between Candida tropicalis and Saccharomyces boulardii. Colloid Interf Sci Commun 37: 100280

Gupta P, Rai N, Verma A, Saikia D, Singh SP, Kumar R, Singh SK, Kumar D, Gautam V (2022) Green-based approach to synthesize silver nanoparticles using the fungal endophyte penicillium oxalicum and their antimicrobial, antioxidant, and in vitro anticancer potential. ACS Omega. https://doi.org/10.1021/acsomega.2c05605

Haldar C, Nath S (2020) Nanotechnology: A novel technique for aquaculture and fisheries development. Int J Fauna Biol Stud 7(6):23–27

Hamidi M, Jafari H, Siminska-Stanny J, Okoro OV, Fatimi A, Shavandi A (2022) Anionic exopolysaccharide from Cryptococcus laurentii 70766 as an alternative for alginate for biomedical hydrogels. Int J Biol Macromol 212:370–380

Harish V, Tewari D, Gaur M, Yadav AB, Swaroop S, Bechelany M, Barhoum A (2022) Review on nanoparticles and nanostructured materials: Bioimaging, biosensing, drug delivery, tissue engineering, antimicrobial, and agro-food applications. Nanomaterials 12(3):457

Hermida-Montero L, Pariona N, Mtz-Enriquez AI, Carrión G, Paraguay-Delgado F, Rosas-Saito G (2019) Aqueous-phase synthesis of nanoparticles of copper/copper oxides and their antifungal effect against Fusarium oxysporum. J Hazard Mater 380:120850

Herrmann IK, Wood MJA, Fuhrmann G (2021) Extracellular vesicles as a next-generation drug delivery platform. Nat Nanotechnol 16(7):748–759

Hosseinidoust Z, Mostaghaci B, Yasa O, Park B-W, Singh AV, Sitti M (2016) Bioengineered and biohybrid bacteria-based systems for drug delivery. Adv Drug Deliv Rev 106:27–44

Hsueh Y-H, Lin K-S, Ke W-J, Hsieh C-T, Chiang C-L, Tzou D-Y, Liu S-T (2015) The antimicrobial properties of silver nanoparticles in Bacillus subtilis are mediated by released Ag+ ions. PLoS One 10(12):e0144306

Huang Z, Zeng Z, Song Z, Chen A, Zeng G, Xiao R, He K, Yuan L, Li H, Chen G (2020) Antimicrobial efficacy and mechanisms of silver nanoparticles against Phanerochaete chrysosporium in the presence of common electrolytes and humic acid. J Hazard Mater 383: 121153

Hussein EAM, Mohammad AA-H, Harraz FA, Ahsan MF (2019) Biologically synthesized silver nanoparticles for enhancing tetracycline activity against staphylococcus aureus and klebsiella pneumoniae. Braz Arch Biol Technol 2019:62

Ilahi N, Haleem A, Iqbal S, Fatima N, Sajjad W, Sideeq A, Ahmed S (2022) Biosynthesis of silver nanoparticles using endophytic Fusarium oxysporum strain NFW16 and their in vitro antibacterial potential. Microsc Res Tech 85(4):1568–1579

Iswarya A, Anjugam M, Gopi N, Shanthi S, Govindarajan M, Alharbi NS, Kadaikunnan S, Alharbi MS, Sivakamavalli J, Vaseeharan B (2022) β-1, 3-Glucan binding protein-based silver nanoparticles enhance the wound healing potential and disease resistance in Oreochromis mossambicus against Aeromonas hydrophilla. Microb Pathog 162:105360

Janku F, Zhang HH, Pezeshki A, Goel S, Murthy R, Wang-Gillam A, Shepard DR, Helgason T, Masters T, Hong DS (2021) Intratumoral injection of clostridium novyi-NT spores in patients with treatment-refractory advanced solid tumors phase I study of intratumoral clostridium novyi-NT. Clin Cancer Res 27(1):96–106

Jassal PS, Kaur D, Prasad R, Singh J (2022) Green synthesis of titanium dioxide nanoparticles: development and applications. J Agric Food Res 10:100361. https://doi.org/10.1016/j.jafr.2022.100361

Jayaseelan C, Rahuman AA, Kirthi AV, Marimuthu S, Santhoshkumar T, Bagavan A, Gaurav K, Karthik L, Rao KB (2012) Novel microbial route to synthesize ZnO nanoparticles using Aeromonas hydrophila and their activity against pathogenic bacteria and fungi. Spectrochim Acta A Mol Biomol Spectrosc 90:78–84

Jia L, Zhang P, Sun H, Dai Y, Liang S, Bai X, Feng L (2021) Optimization of nanoparticles for smart drug delivery: a review. Nanomaterials 11(11):2790

Jin M, Zhao Q, Zhou Z, Zhu L, Zhang Z, Jiang L (2020) Draft genome sequence of a potential organic phosphorus-degrading bacterium Brevibacterium frigoritolerans GD44, isolated from radioactive soil in Xinjiang, China. Curr Microbiol 77:2896–2903

Jouzani GS, Valijanian E, Sharafi R (2017) Bacillus thuringiensis: a successful insecticide with new environmental features and tidings. Appl Microbiol Biotechnol 101:2691–2711

Juvet T, Mari A, Lajkosz K, Wallis CJ, Kuk C, Erlich A, Krimus L, Fleshner NE, Kulkarni GS, Zlotta AR (2020) Sequential administration of Bacillus Calmette-Guerin (BCG) and Electromotive Drug Administration (EMDA) of mitomycin C (MMC) for the treatment of high-grade nonmuscle invasive bladder cancer after BCG failure. In: Urologic oncology: seminars and original investigations, vol 11. Elsevier, Amsterdam, p 850

Kalaimurugan D, Vivekanandhan P, Sivasankar P, Durairaj K, Senthilkumar P, Shivakumar MS, Venkatesan S (2019) Larvicidal activity of silver nanoparticles synthesized by Pseudomonas fluorescens YPS3 isolated from the Eastern Ghats of India. J Clust Sci 30:225–233

Karthikeyan C, Varaprasad K, Venugopal SK, Shakila S, Venkatraman B, Sadiku R (2021) Biocidal (bacterial and cancer cells) activities of chitosan/CuO nanomaterial, synthesized via a green process. Carbohydr Polym 259:117762

Kaur T, Bala M, Kumar G, Vyas A (2022) Biosynthesis of zinc oxide nanoparticles via endophyte Trichoderma viride and evaluation of their antimicrobial and antioxidant properties. Arch Microbiol 204(10):620

Kavitha A, Doss A, Pole RPP, Pushpa Rani TPK, Prasad R, Satheesh S (2023) A mini review on plant-mediated zinc oxide nanoparticles and their antibacterial potency. Biocatal Agric Biotechnol. https://doi.org/10.1016/j.bcab.2023.102654

Khan MI, Hossain MI, Hossain MK, Rubel M, Hossain K, Mahfuz A, Anik MI (2022) Recent progress in nanostructured smart drug delivery systems for cancer therapy: a review. ACS Appl Biomater 5(3):971–1012

Khezerlou A, Alizadeh-Sani M, Azizi-Lalabadi M, Ehsani A (2018) Nanoparticles and their antimicrobial properties against pathogens including bacteria, fungi, parasites and viruses. Microb Pathog 123:505–526

Kim S, Song KB (2018) Antimicrobial activity of buckwheat starch films containing zinc oxide nanoparticles against Listeria monocytogenes on mushrooms. Int J Food Sci Technol 53(6): 1549–1557

Kim K, Bou-Ghannam S, Kameishi S, Oka M, Grainger DW, Okano T (2021) Allogeneic mesenchymal stem cell sheet therapy: a new frontier in drug delivery systems. J Control Release 330:696–704

Kiran GS, Sabu A, Selvin J (2010) Synthesis of silver nanoparticles by glycolipid biosurfactant produced from marine Brevibacterium casei MSA19. J Biotechnol 148(4):221–225

Koch N, Sonowal S, Prasad R (2023) Elucidate the smart tailored biogenic nanoparticles and their applications in remediation. Biotechnol Genet Eng Rev. https://doi.org/10.1080/02648725.2023.2219942

Komiyama M, Shigi N, Ariga K (2022) DNA-based nanoarchitectures as eminent vehicles for smart drug delivery systems. Adv Funct Mater 2022:2200924

Konar M, Nayak N, Priyadarsini S, Mishra M, Sahoo H (2019) Antimicrobial activity of nanoparticle-based dental fillers on novel chromogenic bacteria Enterobacter ludwigii. Mater Res Express 6(8):085407

Kong X, Liu Y, Huang X, Huang S, Gao F, Rong P, Zhang S, Zhang K, Zeng W (2019) Cancer therapy based on smart drug delivery with advanced nanoparticles. Anti Cancer Agents Med Chem 19(6):720–730

Kumar R, Gautam PK, Chandra A, Sharma VK (2014) Hydrogels-a novel a nd smart drug delivery system: an updated review. World J Pharm Res 2014:13

Kuyukina MS, Makarova MV, Pistsova ON, Glebov GG, Osipenko MA, Ivshina IB (2022) Exposure to metal nanoparticles changes zeta potentials of Rhodococcus cells. Heliyon 8(11): e11632

Kuzajewska D, Wszołek A, Żwierełło W, Kirczuk L, Maruszewska A (2020) Magnetotactic bacteria and magnetosomes as smart drug delivery systems: a new weapon on the battlefield with cancer? Biology 9(5):102

Lalitha K, Kalaimurgan D, Nithya K, Venkatesan S, Shivakumar MS (2020) Antibacterial, antifungal and mosquitocidal efficacy of copper nanoparticles synthesized from entomopathogenic nematode: Insect–host relationship of bacteria in secondary metabolites of Morganella morganii sp.(PMA1). Arab J Sci Eng 45:4489–4501

Lee S, Ahn J-H, Choi H, Seo J-M, Cho D, Koo K (2015) Natural magnetic nanoparticle containing droplet for smart drug delivery and heat treatment. In: 2015 37th annual international conference of the IEEE engineering in medicine and biology society (EMBC). IEEE, New York, pp 3541–3544

Lemos TS, de Souza JF, Fajardo AR (2021) Magnetic microspheres based on pectin coated by chitosan towards smart drug release. Carbohydr Polym 265:118013

Li Y, Fan J, Ju D (2018) Neurotoxicity concern about the brain targeting delivery systems. In: Brain targeted drug delivery systems: a focus on nanotechnology and nanoparticulates. Academic, Cambridge, pp 377–408

Li Z, Fan J, Tong C, Zhou H, Wang W, Li B, Liu B, Wang W (2019) A smart drug-delivery nanosystem based on carboxylated graphene quantum dots for tumor-targeted chemotherapy. Nanomedicine 14(15):2011–2025

Li H, Ahmad W, Rong Y, Chen Q, Zuo M, Ouyang Q, Guo Z (2020) Designing an aptamer based magnetic and upconversion nanoparticles conjugated fluorescence sensor for screening Escherichia coli in food. Food Control 107:106761

Li S, Yue H, Wang S, Li X, Wang X, Guo P, Ma G, Wei W (2022) Advances of bacteria-based delivery systems for modulating tumor microenvironment. Adv Drug Deliv Rev 2022:114444

Liu S, Qamar SA, Qamar M, Basharat K, Bilal M (2021) Engineered nanocellulose-based hydrogels for smart drug delivery applications. Int J Biol Macromol 181:275–290

Mahfuz A, Hossain MK, Khan MI, Hossain I, Anik MI (2022) Smart drug-delivery nanostructured systems for cancer therapy. Elsevier, Amsterdam

Maddela NR, Chakraborty S, Prasad R (2021) Nanotechnology for advances in medical microbiology. Springer Singapore. (ISBN 978-981-15-9915-6) https://www.springer.com/gp/book/9789811599156

Manivasagan P, Kim J, Jang E-S (2022) Recent progress in multifunctional conjugated polymer nanomaterial-based synergistic combination phototherapy for microbial infection theranostics. Coord Chem Rev 470:214701

Marathe K, Naik J, Maheshwari V (2021) Biogenic synthesis of silver nanoparticles using Streptomyces spp. and their antifungal activity against Fusarium verticillioides. J Clust Sci 32:1299–1309

Mohammed AN, Attia AS (2022) Control of biofilm-producing Aeromonas bacteria in the water tanks and drinkers of broiler poultry farms using chitosan nanoparticle-based coating thyme oil. Iraqi J Vet Sci 36(3):659–669

Mohd Yusof H, Mohamad R, Zaidan UH, Rahman NAA (2020) Sustainable microbial cell nanofactory for zinc oxide nanoparticles production by zinc-tolerant probiotic Lactobacillus plantarum strain TA4. Microb Cell Factories 19:1–17

Muras A, Romero M, Mayer C, Otero A (2021) Biotechnological applications of Bacillus licheniformis. Crit Rev Biotechnol 41(4):609–627

Oh D, Lee S, Kim J, Choi H, Seo J, Koo K-I (2014) Magnetically guided micro-droplet using biological magnetic material for smart drug delivery system. In: 2014 36th annual international conference of the IEEE engineering in medicine and biology society. IEEE, New York, pp 1390–1393

Oliveira E, Santos HM, Jorge S, Rodríguez-González B, Novio F, Lorenzo J, Ruiz-Molina D, Capelo JL, Lodeiro C (2019) Sustainable synthesis of luminescent CdTe quantum dots coated with modified silica mesoporous nanoparticles: towards new protein scavengers and smart drug delivery carriers. Dyes Pigments 161:360–369

Ozalp VC, Eyidogan F, Oktem HA (2011) Aptamer-gated nanoparticles for smart drug delivery. Pharmaceuticals 4(8):1137–1157

Pallavi S, Rudayni HA, Bepari A, Niazi SK, Nayaka S (2022) Green synthesis of Silver nanoparticles using Streptomyces hirsutus strain SNPGA-8 and their characterization, antimicrobial activity, and anticancer activity against human lung carcinoma cell line A549. Saudi J Biol Sci 29(1):228–238

Park J, Chariou PL, Steinmetz NF (2020) Site-specific antibody conjugation strategy to functionalize virus-based nanoparticles. Bioconjug Chem 31(5):1408–1416

Patil MP, Kim G-D (2018) Marine microorganisms for synthesis of metallic nanoparticles and their biomedical applications. Colloids Surf B Biointerfaces 172:487–495

Prasad R (2014) Synthesis of silver nanoparticles in photosynthetic plants. J Nanoparticles 2014:963961. https://doi.org/10.1155/2014/963961

Prasad R (2016) Advances and applications through fungal nanobiotechnology. Springer, International Publishing Switzerland. (ISBN: 978-3-319-42989-2)

Prasad R (2017) Fungal nanotechnology: applications in agriculture, industry, and medicine. Springer Nature Singapore Pte Ltd. (ISBN 978-3-319-68423-9)

Prasad R, Jha A, Prasad K (2018) Exploring the realms of nature for nanosynthesis. Springer International Publishing. (ISBN 978-3-319-99570-0) https://www.springer.com/978-3-319-99570-0

Prasad R, Pandey R, Barman I (2016) Engineering tailored nanoparticles with microbes: quo vadis. WIREs Nanomed Nanobiotechnol 8:316–330. https://doi.org/10.1002/wnan.1363
Prasad R, Pandey R, Varma A, Barman I (2017a) Polymer based nanoparticles for drug delivery systems and cancer therapeutics. In: Kharkwal H, Janaswamy S (eds) Natural Polymers for Drug Delivery. CAB International, Wallingford, pp 53–70
Prasad R, Kumar M, Kumar V (2017b) Nanotechnology: an agriculture paradigm. Springer Nature Singapore Pte Ltd. (ISBN: 978-981-10-4573-8)
Prasad R, Kumar V, Kumar M (2017c) Nanotechnology: food and environmental paradigm. Springer Nature Singapore Pte Ltd. (ISBN 978-981-10-4678-0)
Prema P, Ranjani SS, Kumar KR, Veeramanikandan V, Mathiyazhagan N, Nguyen V-H, Balaji P (2022) Microbial synthesis of silver nanoparticles using Lactobacillus plantarum for antioxidant, antibacterial activities. Inorg Chem Commun 136:109139
Qin Y, Zhao R, Qin H, Chen L, Chen H, Zhao Y, Nie G (2021) Colonic mucus-accumulating tungsten oxide nanoparticles improve the colitis therapy by targeting Enterobacteriaceae. Nano Today 39:101234
Qu J, Zhao X, Ma PX, Guo B (2018) Injectable antibacterial conductive hydrogels with dual response to an electric field and pH for localized "smart" drug release. Acta Biomater 72:55–69
Rajesh S, Dharanishanthi V, Kanna AV (2015) Antibacterial mechanism of biogenic silver nanoparticles of Lactobacillus acidophilus. J Exp Nanosci 10(15):1143–1152
Rajkumar R, Ezhumalai G, Gnanadesigan M (2021) A green approach for the synthesis of silver nanoparticles by Chlorella vulgaris and its application in photocatalytic dye degradation activity. Environ Technol Innov 21:101282
Rao SV, Anuhya E, Padmalatha K (2019) Nanoparticles: a smart drug delivery. J Drug Delivery Therapeut 9(2):590–593
Rather M, Sharma R, Aklakur M, Ahmad S, Kumar N, Khan M, Ramya V (2011) Nanotechnology: a novel tool for aquaculture and fisheries development. A prospective mini-review. Fish Aquac J 16(1-5):3
Reshetnikov VV, Smolskaya SV, Feoktistova SG, Verkhusha VV (2022) Optogenetic approaches in biotechnology and biomaterials. Trends Biotechnol 40:858–874
Romano I, Vitiello G, Gallucci N, Di Girolamo R, Cattaneo A, Poli A, Di Donato P (2022) Extremophilic microorganisms for the green synthesis of antibacterial nanoparticles. Microorganisms 10(10):1885
Roychoudhury A (2020) Yeast-mediated green synthesis of nanoparticles for biological applications. Indian J Pharm Biol Res 8(3):26–31
Rozene J, Morkvenaite-Vilkonciene I, Bruzaite I, Dzedzickis A, Ramanavicius A (2021) Yeast-based microbial biofuel cell mediated by 9, 10-phenantrenequinone. Electrochim Acta 373: 137918
Salem MF, Tayel AA, Alzuaibr FM, Bakr RA (2022) Innovative approach for controlling black rot of persimmon fruits by means of nanobiotechnology from nanochitosan and rosmarinic acid-mediated selenium nanoparticles. Polymers 14(10):2116
Sambi M, Qorri B, Malardier-Jugroot C, Szewczuk M (2017) Advancements in polymer science: 'smart' drug delivery systems for the treatment of cancer. MOJ Polym Sci 1:113–118
Sanchez-Moreno P, Ortega-Vinuesa JL, Peula-Garcia JM, Marchal JA, Boulaiz H (2018) Smart drug-delivery systems for cancer nanotherapy. Curr Drug Targets 19(4):339–359
Santos LM, Stanisic D, Menezes UJ, Mendonça MA, Barral TD, Seyffert N, Azevedo V, Durán N, Meyer R, Tasic L (2019) Biogenic silver nanoparticles as a post-surgical treatment for Corynebacterium pseudotuberculosis infection in small ruminants. Front Microbiol 10:824
Saravanakumar K, Wang M-H (2018) Trichoderma based synthesis of anti-pathogenic silver nanoparticles and their characterization, antioxidant and cytotoxicity properties. Microb Pathog 114:269–273
Shanmugam S, Krishnaswamy S, Chandrababu R, Veerabagu U, Pugazhendhi A, Mathimani T (2020) Optimal immobilization of Trichoderma asperellum laccase on polymer coated Fe3O4@

SiO2 nanoparticles for enhanced biohydrogen production from delignified lignocellulosic biomass. Fuel 273:117777
Shi J, Votruba AR, Farokhzad OC, Langer R (2010) Nanotechnology in drug delivery and tissue engineering: from discovery to applications. Nano Lett 10(9):3223–3230
Siddiqui J, Taheri M, Alam AU, Deen MJ (2022) Nanomaterials in smart packaging applications: a review. Small 18(1):2101171
Singh P, Kim YJ, Singh H, Mathiyalagan R, Wang C, Yang DC (2015) Biosynthesis of anisotropic silver nanoparticles by Bhargavaea indica and their synergistic effect with antibiotics against pathogenic microorganisms. J Nanomater 2015:4–4
Singh P, Kim Y-J, Zhang D, Yang D-C (2016a) Biological synthesis of nanoparticles from plants and microorganisms. Trends Biotechnol 34(7):588–599
Singh P, Kim YJ, Wang C, Mathiyalagan R, Yang DC (2016b) Weissella oryzae DC6-facilitated green synthesis of silver nanoparticles and their antimicrobial potential. Artif Cells Nanomed Biotechnol 44(6):1569–1575
Singh BN, Singh BR, Gupta VK, Kharwar RN, Pecoraro L (2018) Coating with microbial hydrophobins: a novel approach to develop smart drug nanoparticles. Trends Biotechnol 36(11):1103–1106
Singh N, Naik B, Kumar V, Kumar V, Gupta S (2021) Actinobacterial pigment assisted synthesis of nanoparticles and its biological activity: nanoparticles and its biological activity. J Microbiol Biotechnol Food Sci 10(4):604–608
Soliman KA, Ullah K, Shah A, Jones DS, Singh TR (2019) Poloxamer-based in situ gelling thermoresponsive systems for ocular drug delivery applications. Drug Discov Today 24(8): 1575–1586
Soltani Nejad M, Samandari Najafabadi N, Aghighi S, Pakina E, Zargar M (2022) Evaluation of phoma sp. biomass as an endophytic fungus for synthesis of extracellular gold nanoparticles with antibacterial and antifungal properties. Molecules 27(4):1181
Spagnuolo G, Genovese F, Fortunato L, Simeone M, Rengo C, Tatullo M (2019) The impact of optogenetics on regenerative medicine. Appl Sci 10(1):173
Srinath B, Namratha K, Byrappa K (2018) Eco-friendly synthesis of gold nanoparticles by Bacillus subtilis and their environmental applications. Adv Sci Lett 24(8):5942–5946
Srivastava S, Usmani Z, Atanasov AG, Singh VK, Singh NP, Abdel-Azeem AM, Prasad R, Gupta G, Sharma M, Bhargava A (2021) Biological nanofactories: using living forms for metal nanoparticle synthesis. Mini-Rev Med Chem 21(2):245–265
Sun W, Hu Q, Ji W, Wright G, Gu Z (2017) Leveraging physiology for precision drug delivery. Physiol Rev 97(1):189–225
Sundaramanickam A, Maharani V (2021) Antibiotic and antioxidant activities biogenic silver nanoparticles synthesized using Escherichia coli (VM1) bacterium
Szalewski DA, Hinrichs VS, Zinniel DK, Barletta RG (2018) The pathogenicity of Aspergillus fumigatus, drug resistance, and nanoparticle delivery. Can J Microbiol 64(7):439–453
Tarver S, Gray D, Loponov K, Das DB, Sun T, Sotenko M (2019) Biomineralization of Pd nanoparticles using Phanerochaete chrysosporium as a sustainable approach to turn platinum group metals (PGMs) wastes into catalysts. Int Biodeterior Biodegrad 143:104724
Tračuma E, Loca D (2020) Hyaluronic acid/polylysine composites for local drug delivery: a review. Key Eng Mater 850:213–218
Uddin MS (2019) Nanoparticles as nanopharmaceuticals: smart drug delivery systems. In: Nanoparticulate drug delivery systems. Apple Academic Press, Palm Bay, pp 85–120
Unsoy G, Gunduz U (2018) Smart drug delivery systems in cancer therapy. Curr Drug Targets 19(3):202–212
Veeramalini J, Kumar PS, Selvakumari IA, Sreejith R (2022) Process amelioration for production of biohydrogen using mutated Rhodobacter M 19 and Enterobacter aerogenesco-culture: Influence of nanoparticles. Fuel 317:123558
Velea AI, Vollebregt S, Hosman T, Pak A, Giagka V (2019) Towards a microfabricated flexible graphene-based active implant for tissue monitoring during optogenetic spinal cord

stimulation. In: 2019 IEEE 14th nanotechnology materials and devices conference (NMDC). IEEE, New York, pp 1–5

Ventura-Aguilar RI, Díaz-Galindo EP, Bautista-Baños S, Mendoza-Acevedo S, Munguía-Cervantes JE, Correa-Pacheco ZN, Bosquez-Molina E (2021) Monitoring the infection process of Rhizopus stolonifer on strawberry fruit during storage using films based on chitosan/polyvinyl alcohol/polyvinylpyrrolidone and plant extracts. Int J Biol Macromol 182:583–594

Vyshnava SS, Kanderi DK, Panjala SP, Pandian K, Bontha RR, Goukanapalle PKR, Banaganapalli B (2016) Effect of silver nanoparticles against the formation of biofilm by Pseudomonas aeruginosa an in silico approach. Appl Biochem Biotechnol 180:426–437

Vyshnava SS, Pandluru G, Kanderi DK, Panjala SP, Banapuram S, Paramasivam K, Anupalli RR, Bontha RR, Dowlatabad MR (2020) Gram scale synthesis of QD 450 core–shell quantum dots for cellular imaging and sorting. Appl Nanosci 10:1257–1268

Vyshnava SS, Kanderi DK, Dowlathabad MR (2022a) Confocal laser scanning microscopy study of intercellular events in filopodia using 3-mercaptopropoinc acid capped CdSe/ZnS quantum dots. Micron 153:103200

Vyshnava SS, Pandluru G, Kumar KD, Panjala SP, Banapuram S, Paramasivam K, Devi KV, Anupalli RR, Dowlatabad MR (2022b) Quantum dots based in-vitro co-culture cancer model for identification of rare cancer cell heterogeneity. Sci Rep 12(1):5868

Wang C, Kim YJ, Singh P, Mathiyalagan R, Jin Y, Yang DC (2016a) Green synthesis of silver nanoparticles by Bacillus methylotrophicus, and their antimicrobial activity. Artif Cells Nanomed Biotechnol 44(4):1127–1132

Wang Q, Jian-Ying H, Li H-Q, Chen Z, Zhao AZ-J, Wang Y, Ke-Qin Z, Hong-Tao S, Al-Deyab SS, Lai Y-K (2016b) TiO2 nanotube platforms for smart drug delivery: a review. Int J Nanomedicine 11:4819

Wang D, Yang C, Saleh MA, Alotaibi MD, Mohamed ME, Xu D, Gu T (2022) Conductive magnetite nanoparticles considerably accelerated carbon steel corrosion by electroactive Desulfovibrio vulgaris biofilm. Corros Sci 205:110440

Weeranantanapan O, Chudapongse N, Limphirat W, Nantapong N (2022) Streptomyces chiangmaiensis SSUT88A mediated green synthesis of silver nanoparticles: characterization and evaluation of antibacterial action against clinical drug-resistant strains. RSC Adv 12(7): 4336–4345

Wei Q, Ji J, Shen J (2008) Synthesis of near-infrared responsive gold nanorod/pnipaam core/shell nanohybrids via surface initiated atrp for smart drug delivery. Macromol Rapid Commun 29(8): 645–650

Xu P, Zuo H, Chen B, Wang R, Ahmed A, Hu Y, Ouyang J (2017) Doxorubicin-loaded platelets as a smart drug delivery system: an improved therapy for lymphoma. Sci Rep 7(1):1–16

Yang J, Kim EK, McDowell A, Kim Y-K (2018) Microbe-derived extracellular vesicles as a smart drug delivery system. Transl Clin Pharmacol 26(3):103

Yao Q, Kou L, Tu Y, Zhu L (2018) MMP-responsive 'smart' drug delivery and tumor targeting. Trends Pharmacol Sci 39(8):766–781

Yaqoob AA, Ahmad H, Parveen T, Ahmad A, Oves M, Ismail IM, Qari HA, Umar K, Mohamad Ibrahim MN (2020) Recent advances in metal decorated nanomaterials and their various biological applications: a review. Front Chem 8:341

Yeh Y-C, Huang T-H, Yang S-C, Chen C-C, Fang J-Y (2020) Nano-based drug delivery or targeting to eradicate bacteria for infection mitigation: a review of recent advances. Front Chem 8:286

Zhang H, Fan T, Chen W, Li Y, Wang B (2020) Recent advances of two-dimensional materials in smart drug delivery nano-systems. Bioactive Mater 5(4):1071–1086

Zhao S, Chen Z, Khan A, Wang J, Kakade A, Kulshrestha S, Liu P, Li X (2021) Elevated Cr (VI) reduction in a biocathode microbial fuel cell without acclimatization inversion based on strain Corynebacterium vitaeruminis LZU47-1. Int J Hydrog Energy 46(4):3193–3203

Bactericidal Effects: Microbial Nanoparticles as Next-Generation Antimicrobials

12

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Abstract

There is a serious health problem worldwide due to the alarming rise in multidrug-resistant (MDR) microorganisms. To circumvent this issue, scientists are striving to develop drugs for the treatment of such microbial infections. It demands the quest for alternative pharmaceutical therapies and methods of infection control. In the realm of antimicrobial therapy, nanotechnology provides opportunities as an alternative to using antibiotics today. Nanoparticles (NPs) exhibit distinctive and amazing capabilities which are very different from those of their bulk counterparts due to their varied structures and small size. *Actinomycetes*, yeast, fungi, and bacteria produce inorganic nanoparticles (NPs) enzymatically, both extracellularly and intracellularly. Numerous metallic NPs, including gold, copper, silver, titanium, and magnesium, have been well-reported for having antibacterial, antiviral, and antifungal effects. These NPs' antimicrobial abilities may be explained by their capacity to disrupt biofilm formation, create gaps in bacterial cell walls, disturb membrane structure, and more. By producing ROS (reactive oxygen species), the majority of metal oxide nanoparticles, including zinc oxide and magnesium oxide nanoparticles, exhibit bactericidal characteristics. Additionally, a variety of bioactive substances can be used to create nanoparticles. A functional network of nanoparticles can deliver medications to the target areas precisely and safely because of their small,

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controllable size. This chapter provides a comprehensive explanation of the synthesis of microbial nanoparticles, their mechanism of action, and one's potential as bacteriostatic/bactericidal agents. As a result, the development of environmentally benign methods to combat microbial resistance and control diseases is becoming increasingly important, and microbial-mediated creation of nanoparticles is attracting a lot of attention as a potential answer.

Keywords

Nanoparticles · Microorganisms · Synthesis · Bactericidal · Antimicrobials

12.1 Introduction

In light of newly emergent and resistant strains of pathogenic bacteria, fungi, viruses, and protozoa that are resistant to conventional medical treatment, microbial infections have recently become a major worldwide health burden (MacGowan and Macnaughton 2017). As a result, there is a greater chance of fatality, delayed treatment, increased healthcare costs, and a short life span. Since current antimicrobial drugs are ineffectual against these "superbug" comprising viruses, bacteria, fungus, and protozoa, it is necessary to look for new, safer antimicrobial alternatives. New antimicrobials have started emerging with the advent of biomedical nanomaterials, either as novel or enhancing the actions of the current traditional antimicrobial drugs (Pelgrift and Friedman 2013). The extensive physiochemical and functionalization (ligand attachment) characteristics of nanoparticles serve as the driving force behind this (Mubeen et al. 2021). The physicochemical characteristics of NPs are extremely diverse and have a wide assortment of biomedical applications, including medication delivery and antibacterial (Qayyum and Khan 2016). Silver nanoparticles, carbon nanotubes, gold nanoparticles (AuNPs), zinc oxide nanoparticles (NPs), iron oxide nanoparticles (FeO-NPs), and quantum dots (graphene and carbon-based) are a few types of such biomedical nanomaterials (Jafari 2021).

Compounds that have at least a single dimension (1–100 nm) in the nanometre scale range or whose fundamental unit in 3D space are in this range are referred to as nanomaterials (Edmundson et al. 2013). Particularly NPs have proven to provide broad-spectrum antibacterial effects against both Gram-positive and Gram-negative microorganisms. For instance, silver nanoparticles exhibit density-dependent antibacterial action against *E. coli* and *P. aeruginosa*, whereas ZnO NPs were reported to show inhibition against *S. aureus* (Ramalingam et al. 2016; Abdel et al. 2021). Generally speaking, one of three models—oxidative stress generation, metal ion releases, or non-oxidative mechanisms—adheres to the antibacterial mechanisms of action of NPs (Gurunathan et al. 2012; Ramalingam et al. 2016). These three different mechanisms can all take place at the same time. According to certain research, silver NPs cause the bacterial membrane's surface electric charge to be neutralised and alter its penetrability, which ultimately results in bacterial

mortality (Liao et al. 2019). Moreover, the production of ROS impairs its antioxidant system and harms cells mechanically. Existing research indicates that the following key mechanisms underlie the antibacterial actions of NPs: (a) bacteria's cell membrane breakdown, (b) production of ROS, (c) penetration of bacterial cell membrane, and (d) initiation of intracellular antimicrobial properties, especially associations with DNA and proteins (Prasad et al. 2016).

In that context, this review examines the current state of nanomaterials as substitute antimicrobials in terms of their ability to pass challenging membrane barriers and deliver and inhibit intracellular pathogens for an extended period of time, their roles in different antimicrobial activities, and their mechanisms related to mechanisms of action with a throw on antibacterial activity of artificial nanoparticles, quantum dots (QDs).

12.1.1 Need of Nanoparticles in Multidrug-Resistant (MDR) Microorganisms

Multidrug-resistant bacteria are thought to be the cause of at least 700,000 deaths each year worldwide, notably 23,000 deaths in the United States and 25,000 fatalities in the EU. Roughly 80% of multidrug-resistant bacteria are caused by improper or excessive use of antibiotics, as per reports from WHO, and all these infections are associated with substantial side effects. Additionally, it is anticipated that ten million people will die worldwide from bacterial infections by the year 2050 if nothing is done to address bacterial resistance or develop new medications. There aren't many available therapeutic and preventative alternatives at the moment as MDR infections as well as other resistant organisms grow. The search for new potent medicines is compelled by the failure of conventional antibiotics. The majority of bacterial infections, especially those brought on by MDR pathogens, can be treated successfully with nanoparticles (Mba and Nweze 2020). Nanoparticles and antibiotics can be used independently or together to have powerful synergistic effects. Three bacterial targets are the focus of the main classes of antibiotics currently in use: the machinery involved in DNA replication, translation, and cell wall construction. Sadly, bacterial resistance to each of these ways of action can emerge. The majority of the antibiotic resistance mechanisms don't really apply to nanoparticles since they interact directly with the cell walls of bacteria rather than penetrating them, which offers hope that Nanoparticles will not be as likely to cause microbial resistance as antibiotics. As a result, interest has been drawn to innovative and interesting NP-based materials that have antibacterial property (Li et al. 2017).

The main justification for considering NPs as alternatives to antibiotics is that, in some circumstances, NPs can successfully avoid microbial drug resistance. Numerous risks to public health have emerged as a result of the widespread use of antibiotic drugs, including superbugs that are resistant to all known medications and epidemics that are unaffected by medical intervention (Khameneh et al. 2016). To address antibiotic resistance, it is important to find new, powerful bactericidal materials, and NPs have been shown to be more effective than antibiotics at doing so. As a result,

interest has been drawn to innovative and interesting NP-based materials that have antimicrobial property (Hetta et al. 2023).

12.2 Biosynthesis of Nanoparticles from Microorganisms

It is believed that biosynthesis is superior to both physical and chemical synthesis methods (Moghaddam 2010). The following are potential causes:

1. It is a clean, environmentally friendly solution that eliminates the need for costly, hazardous chemicals.
2. Compared to current methods, bio-nanoparticle synthesis would be more commercially viable, result in significant energy and reductant cost savings, and have a high production rate.
3. Large-scale operations using both physical and chemical methods often produce particles larger than a few micrometres, whereas biosynthesis can be employed to produce small nanoparticles.
4. It is more difficult to create the conditions for physical and chemical procedures since they both require high temperatures and pressure.
5. In addition to being simple to handle, prokaryotes can be easily manipulated employing genetic engineering techniques to increase the expression of certain enzymes.
6. The particles produced biologically have a higher specific surface area and catalytic reactivity.
7. A stabiliser is required in practically all chemical procedures for creating nanoparticles in order to stop the aggregation of small particles. This is because capped proteins, which are released by bacteria, stabilise nanoparticles in solution.

12.2.1 Synthesis by Bacteria

One of the finest possibilities for the creation of nanoparticles is bacteria because of their extraordinary capacity to decrease heavy metal ions. For instance, certain bacterial species have learned to fend off pressures like the poisoning of heavy-metal ions or metals by using particular defence mechanisms. Some of them, such as *P. stutzeri* and *P. aeruginosa*, were shown to be able to grow and live at high concentrations of metal ions. They discovered that bacteria were able to bind a substantial number of metallic cations. Additionally, some of these bacteria can produce inorganic materials, such as the magnetotactic bacteria that produce intracellular magnetite nanoparticles (Mba and Nweze 2020). The majority of the species of bacteria used in the production of nanoparticles are tabulated below (Table 12.1).

Table 12.1 Types of bacterial nanoparticles and their mechanism of action (modified from Ghaderi et al. (2021))

	Type of NPs	Bactericidal effect	Mechanism of action (MoA) of NPs
Bacteria	Silver	*S. aureus*, *S. epidermidis* *E. faecium* and *K. pneumoniae*	• Prevents DNA replication and ETC • Degradation of the cell wall • Antibiofilms • Generation of ROS
	Gold	MRSA (Methicillin-resistant *Staphylococcus aureus*), *P. mirabilis,* *E. coli*, *P. aeruginosa*, *S. aureus*	• Generation of ROS • Antibiofilm • DNA synthesis inhibition and damage
	Selenium	*E. coli*, *P. aeruginosa*, *S. aureus*	• Generation ROS • Prevent the growth of bacteria
	Titanium dioxide	*S. aureus*, *E. coli*	• Generation of ROS • DNA damage
	Zinc oxide	*S. aureus*, *E. coli*, *L. monocytogenes*, *Salmonella* sp.	• Generation of ROS • Disintegration of cell with release of cell contents
	Iron	*S. aureus*, *S. epidermidis*, and *E. coli*	• Generation of oxidative stress through the production of reactive
	Carbon quantum dots (CQDs)	*E. coli*, *E. faecium*, *Streptococcus* sp., *Shewanella*, *Yersinia pestis*, and *K. pneumonia*	• Interference with ETC • Cell wall disintegration

12.2.2 Synthesis by *Actinomycetes*

Microorganisms are known as *Actinomycetes* which share key traits with fungi and prokaryotes (Hetta et al. 2021). *Thermomonospora* sp. reduced extracellular metal ions when exposed to gold ions, producing gold nanoparticles with significantly increased miscibility (Rangel-López et al. 2020; Elbahnasawy et al. 2021). Hetta et al. described an alkalotolerant actinnomycete (*Rhodococcus* sp.) that can produce gold nanoparticles with good monodispersity that are generated on the cytosolic membrane and cell walls (Hetta et al. 2021) (Table 12.2).

12.2.3 Synthesis by Fungi

The production of nanomaterials by fungus and their subsequent use, particularly in medicine, is known as myco-nanotechnology. When compared to other organisms, fungi get a number of benefits for the synthesis of nanoparticles, particularly since they are very simple to identify and culture, secrete a lot of hydrolytic enzymes, and

Table 12.2 Microorganisms producing nanoparticles (modified from Ghaderi et al. (2021))

Microbe	NPs with size	Organism producing NPs
Fungi	Gold	*Endophytic* fungus, *Colletotrichum* sp.
	Silver	*Penicillium brevicompactum*, *Aspergillus flavus*
	Zirconia	*Fusarium oxysporum*
	Cerium oxide	*Humicola* sp.
	Magnite	*Fusarium oxysporum* and *Verticillium* sp.
	Cadmium sulphate	*Fusarium oxysporum*
	Zinc oxide	*Aspergillus aeneus*
	Platinum	*Fusarium oxysporum*
Virus	Cadmium	Cowpea mosaic virus
	Ferric	Tobacco mosaic virus
	Zinc oxide	M13 bacteriophage
Yeast	Cadmium	*Candida glabrata*, *Schizosaccharomyces pombe*
	Gold	*Yarrowia lipolytica*
	Silver	*Candida guilliermondii*
Actinomycetes	Gold	*Thermomonospora*, *Rhodococcus*
	Silver	*Nocardiopsis* sp.

have a broad range and diversity (Prasad 2016, 2017, Prasad et al. 2018). Additionally, fungi can be used to produce nanoparticles with great monodispersity and dimensions (Hashem et al. 2022) (Table 12.2). When *Verticillium* was subjected to aqueous AgNO3, the metal ions were reduced, and silver nanoparticles were produced (Baghdadi et al. 2022). Gold, silver, and platinum nanoparticles have all been produced by *Fusarium oxysporum* extracellularly (Rangel-López et al. 2020) in watery media, crystals. *Trichoderma asperellum* and *Penicillium* sp. have also been observed to produce silver nanoparticles. It was recently reported that using *Aspergillus niger*, *A. flavus*, and *A. fumigates* caused an accumulation of AgNPs on the surface of the cell walls (Hashem et al. 2022; Donadu et al. 2021). *Hormoconis* sp., a filamentous fungus, may also produce AgNPs (Abu-Elghait et al. 2021).

12.2.4 Synthesis by Yeast

It has long been known that yeasts are primarily used in the production of semiconductor nanoparticles among eukaryotes. The semiconducting quantum dots researched in solid-state physics are comparable to peptide-coated nanoparticles generated from yeast species. But one of the major drawbacks of chemical and physical synthetic pathways—the aggregation into bigger particles—is solved by the yeast synthesis method. The phytochelatin layer stabilises nanocrystals made by yeast organically and efficiently regulates the size of the particles (Algammal et al. 2021). Three crucial characteristics for the stability of nanoparticles in biomedical application are demonstrated by yeast-derived CdS nanoparticles: the particles' crystallinity, their small size range, and their high-water solubility. When *Candida*

glabrata is exposed to Cd^{2+} ions, CdS QDs develop inside the cells (Wasef et al. 2021). *Torulopsis* sp. can produce PbS and gold nanoparticles intracellularly (Meshaal et al. 2021) (Table 12.2).

12.2.5 Virus Particle-Based Synthesis

It's interesting to note that the *tobacco mosaic virus* was used as a template for the oxidative hydrolysis synthesis of iron oxides, the co-crystallisation of both CdS and PbS. Glutamate and aspartate exterior groups on the virus's outer surface assisted in its occurrence (Usai et al. 2019; Han et al. 2021). The nucleation and assembling of inorganic nano-materials can be templated by viral scaffolds (Table 12.2).

12.3 Mechanism of Action of Nanoparticles as Antimicrobials

A growth in research investigating putative antimicrobial mechanisms of NPs has been conducted as a result of the growing usage of NPs in therapeutics (Meshaal et al. 2021). Metal oxide nanoparticles, for instance, can alter the metabolism of bacteria (Mabrok et al. 2023). When attempting to eradicate bacteria in order to treat ailments, this capability is quite advantageous. NPs must come into contact with bacterial cells in order to exert their antibacterial activity. When NPs travel through bacterial membranes and build up along the metabolic pathway, they then have an impact on the structure and functionality of the cell membrane. Examples of acceptable forms of contact include electrostatic, van der Waal, receptor-ligand interactions, and hydrophobic interactions (Roca et al. 2015). Following this, NPs interact with the fundamental elements of bacterial cells, including DNA, ribosomes, and enzymes, causing reactive oxygen species (ROS), heterogeneous alterations, modifications in cell membrane permeability, problems with enzyme inhibition, protein deactivation, and alterations in gene expression (Algammal et al. 2021; Aziz et al. 2014, 2015, 2016, 2019). The most commonly discussed mechanisms in contemporary research are oxidative stress, metal ion release, and non-oxidative mechanisms as shown in Fig. 12.1 (Yang et al. 2021).

12.3.1 Release of Soluble Metal Ions

The release of metal ions by metal oxide is the next significant process. Metal ions are gradually expelled from metal oxide, thereafter directly interact with functional groups like the nucleic acids and proteins after being absorbed via the cell membrane. In bacterial cells, this contact modifies cell shape, impairs enzymatic activity, and interferes with routine physiological processes (Abd Ellah et al. 2019).

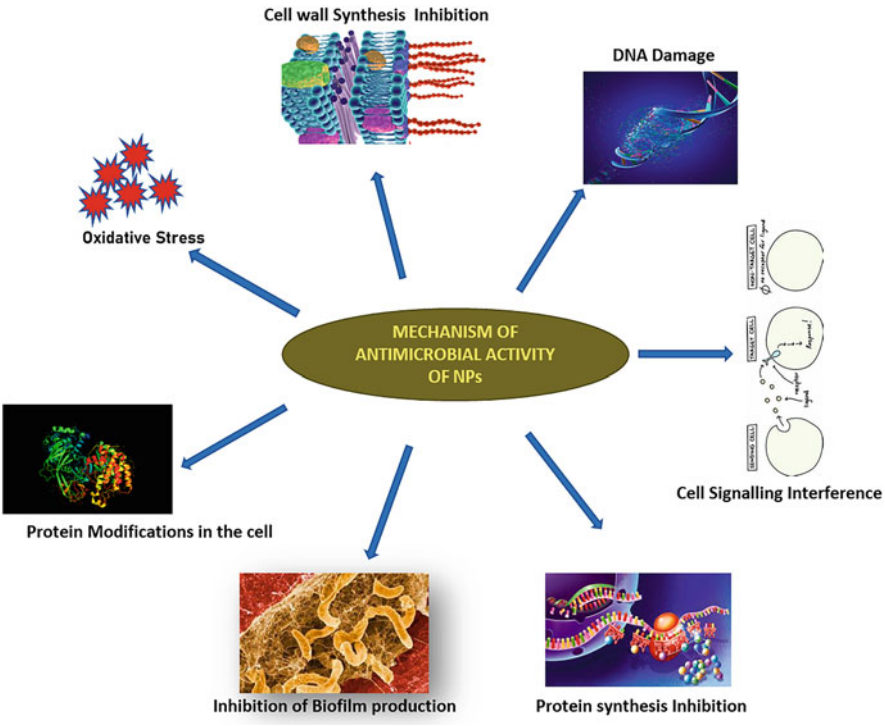

Fig. 12.1 Mechanisms of action of microbially synthesised nanoparticles

12.3.2 Interaction of Nanoparticles with Bacterial Membrane

According to studies, Gram-positive and Gram-negative bacteria interact differently with cell membranes due to their unique structural differences. Gram-negative bacterium has a special cell wall component called lipopolysaccharide (LPS), which generates a negatively charged surface and absorbs nanoparticles. The phosphate molecular structure is dispersed together with the nanoparticles in gram-positive bacteria, where teichoic is just expressed in the cell wall. As a result, the nanoparticles prevent the phosphate molecular structure from accumulating (Cheng et al. 2018). Numerous studies have demonstrated that nanoparticles are more effective in killing Gram-positive bacteria than Gram-negative bacteria when it comes to antibacterial activity. Nanoparticles can transfer reactive species of oxygen into bacteria via diffusion. Gram-positive bacteria have selenium nanoparticles deposited on their surface, which will kill the bacteria (Adeyemi et al. 2020). Titanium oxide nanoparticles can stick to the surface of bacterial cells in order to produce reactive oxygen species and harm the makeup and structure of cell membranes. This disrupts the function of cell membranes, leads to cell leakage,

and kills the bacteria in the long run. According to studies, nanoparticles also interfere with the bacterial cell membranes' ability to breathe (Gupta et al. 2019).

12.3.3 Inhibiting the Synthesis of Proteins and DNA

Researchers have paid a lot of attention lately to how nanoparticles affect the production of bacterial proteins. Proteomic bioinformatics investigation revealed that copper nanoparticles control proteins that are involved in N2 metabolism, electron transport, and material transport once they enter the cell. Additionally, nanoparticles can prevent bacteria from synthesising proteins and DNA by preventing the binding of ribosomal subunits to tRNA or by limiting the activity of the enzyme ATPase, which lowers the amounts of ATP (Abd Ellah et al. 2019). According to studies, nanoparticles can form stable connections with the proteins in cell membranes. As a response, they inhibit the activity of proteins that work to mediate the passage of ions across cell membranes and the synthesis of membrane ATP (Teixeira et al. 2018).

12.3.4 By Regulating Gene Expression

Nanoparticles control the expression of the genes involved in metabolism. In addition to controlling cell membrane penetration, nanoparticles can obstruct molecular pathways. The development and reproduction of bacteria are significantly influenced by bacterial metabolic activities. They may also make microorganisms pathogenic. As a result, bacterial pathogenicity can be controlled by specifically changing the metabolic activity of the bacteria. For instance, it has been found that copper nanoparticles may considerably decrease the activities of nitrate reductase and nitrite reductase as well as control the expression of the proteins related to bacterial nitrogen metabolism. According to Slavin and his researchers, some genetic components can be covalently coupled to silver nanoparticles and modified without going through laborious alteration methods (Slavin et al. 2017).

12.3.5 Oxidative Stress by ROS

ROS-induced oxidative stress is a key component of NPs' antibacterial defence system. It has the ability to damage proteins and lower some periplasmic enzymes' function. Additionally, ROS are excellent at increasing the gene expression of oxidative proteins, which are believed to be a key factor in the death of bacterial cells (Khalid and El-Sawy 2017; Song et al. 2021). It can eliminate the membrane, DNA, and mitochondria of the pathogens, which can cause apoptosis (Qayyum and Khan 2016; Liu et al. 2019). One of the most crucial oxidation-reduction systems of disulphide that bacteria employ to combat oxidative stress is interaction with the thioredoxin system (Wang et al. 2020).

12.3.6 By Adsorption

By using diffusion, nanoparticles can deliver ROS to bacteria. In a study, Blanco demonstrated how the formation of significant levels of hydroxyl radicals and penetration into bacterial cells allowed iron and graphene oxide nanoparticles to inactivate superbug, MRSA (Blanco et al. 2015). In a phenomenon known as biological adsorption, metal oxide nanoparticles get released into the surrounding environment and bind to negatively charged bacterial cell membrane groups like carboxylic and phosphate groups. It was also found that copper nanoparticle surface charges have a considerable impact on how well they adhere to the membrane surface.

12.4 Factors Affecting Bactericidal Effects of NPs

The physicochemical characteristics of NPs, which are important factors that control how well NPs interact with bacterial cells, include their size, charges, zeta potential, surface, and degree of crystallinity. Additionally, the bacterial strain, the exposure duration, and ambient circumstances also have a significant role in the antibacterial actions of nanoparticles (Lemire et al. 2013). Numerous studies have also demonstrated that an extremely large surface, relatively high energy, and an absence of atomic ligands cause metal oxide NPs to aggregate. Therefore, it is crucial to talk about the key elements affecting nanoparticles' antibacterial activity. Below are some of the factors affecting bactericidal activity of nanoparticles.

12.4.1 Size

The growth of bacterial biofilms by the well-known process of bacterial adhesion makes the particular organisms significantly more resistant to or immune to the effects of conventional antibiotics. According to recent studies, a metal nanoparticle's size has a significant impact on how effective it is against germs. Smaller NPs are more likely to pass through the cell membrane of bacteria because of their larger surface areas compared to bigger nanoparticles (Jijie et al. 2017). However, when the diameters of three different kinds of magnesium hydroxide nanoparticles were analysed, Cheeseman et al. (2020) discovered that the smallest magnesium nanoparticles had the least antibacterial impact. As a result, the variation is not the key element. Therefore, the physicochemical properties should be carefully considered while exploring their bactericidal mechanisms.

12.4.2 Shape

Shape plays a significant role in antibacterial action. By means of interactions with periplasmic enzymes, nanoparticles of various forms can harm bacterial cells to

diverse degrees (Hochvaldová et al. 2022). Additionally, it has been demonstrated that ZnO in the form of a pyramid inhibits enzyme deterioration and exhibits photocatalytic activity by obstructing and rebuilding the enzymes (Gupta et al. 2019). Greater bactericidal activity against *P. desmolyticum* and *S. aureus* has been shown for prismatic-shaped Y2-NPs. AgNPs with a cube shape have more potent antibacterial properties than AgNPs with spherical or wire shapes (Wang et al. 2017). Slavin et al. (2017) and Wang et al. (2005) found in earlier studies that the geometry of a silver nanoparticle had no impact on the susceptibility of bacteria.

12.4.3 Roughness

Few studies have examined the impact of roughness, in contrast to the considerable research regarding the impacts of various NP properties on bacterial cells. According to Natan and Banin (2017), when NPs become rougher, their size and surface area-to-mass ratio encourage the sorption of bacterial proteins, which is then followed by a decrease in bacterial adherence.

12.4.4 Zeta Potential

Recent research has shown that NPs' zeta potential significantly affects bacterial adherence. Vascular permeability is raised by the propensity of nanoparticles to selectively congregate at bacterial infection sites. By reducing bacterial adhesion, cationic NP accumulation helps to prevent bacterial growth. Somehow, very little NP infiltration into the outer *S. aureus* envelope results in high germicidal efficiency (Chakraborty et al. 2022). Negatively charged nanoparticles do not bind to bacteria because of the negative charge on both, and positively charged analogues have been thought to increase ROS generation. Negatively charged NPs exhibit some antibacterial activity at greater concentrations, as per Fahimmunisha et al. (2020), because molecular crowding causes interactions.

12.4.5 Environmental Conditions

12.4.5.1 Temperature

Numerous studies have shown that antimicrobial activity differs significantly depending on the environment in important ways. For instance, the environment's temperature has a significant impact on antibacterial activity since it affects the rate at which ROS are produced. Electrons are accumulated at the binding sites when temperature stimulates ZnO NPs. After that, the electrons collide with oxygen and create ROS, which increases ZnO NPs' antibacterial efficiency.

12.4.5.2 pH

In addition, the environment's pH affects *in vitro* antibacterial action. ZnO NPs dissolve more quickly when the pH is lower, giving them more antibacterial abilities (Sutherland 2001) Predominantly, a 3- to-5-fold increase in NP adherence to the bacterial surface was observed to be related to pH. Positively charged NP surfaces at low pH are advantageous for interacting with negatively charged bacterial cell barrier groups and causing strong multivalent electrostatic control. Aquatic chemistry diversification may activate AgNPs, increasing their antibacterial activity through the discharge of silver ions.

12.5 Role of Microbially Synthesised Nanoparticles as Antimicrobials

Viruses, bacteria, fungi, and protozoa that are multidrug-resistant have spread globally, making it challenging to treat infectious diseases using traditional methods. Therefore, it is crucial to find novel classes of antiviral, antibiotic, antifungal, and antiprotozoal drugs that can address resistant strains (Pinna et al. 2020; Algammal et al. 2021). Research has demonstrated that these newly developed broad-spectrum antimicrobial nanomaterials have the ability to eradicate a wide range of harmful bacteria (Abdellatif et al. 2021; Mubeen et al. 2021). Nanoparticles as multifunctional antimicrobial agents have shown to be effective against bacteria, fungi, viruses, parasites, and swelling (Spengler et al. 2022; Tripathi and Goshisht 2022). Below is the illustration for the multirole of nanoparticles as antimicrobials (Fig. 12.2).

12.5.1 In Drug Resistance

One of the main problems with illnesses is microbial infection, which places a heavy strain on the patient and the medical system. Moreover, the use of therapeutic drugs, particularly antibiotics, is restricted by multidrug-resistant bacteria, MDR (Spengler et al. 2022; Tawre et al. 2022). The ability of the NPs to inhibit a variety of multidrug-resistant bacterial strains that have resisted conventional antibiotic therapy makes them potential broad-spectrum antibiotics (Hetta et al. 2021).

Cell wall lysis is one of the methods by which nanoparticles exert antibacterial effects. Using Au/CuS NPs, for instance, Donadu's investigation on the development of transducer agents for photothermal therapy discovered that *Bacillus* genus cell membranes were destroyed. This study's eradication of *Bacillus* species demonstrated the effectiveness of Au/CuS NPs as NP-antimicrobial agents (Donadu et al. 2021). For instance, it was discovered in the study of Ahmadian that silver nanoparticles could suppress infections of *S. aureus, K. pneumoniae, E. coli,* or *P. aeruginosa* that were pan-multidrug resistant to all antibiotic drugs (Ahmadian-Fard-Fini et al. 2019). Additionally, earlier research by Fayaz et al. demonstrated that condoms coated with silver NPs exhibit antiviral, antibacterial, and antifungal

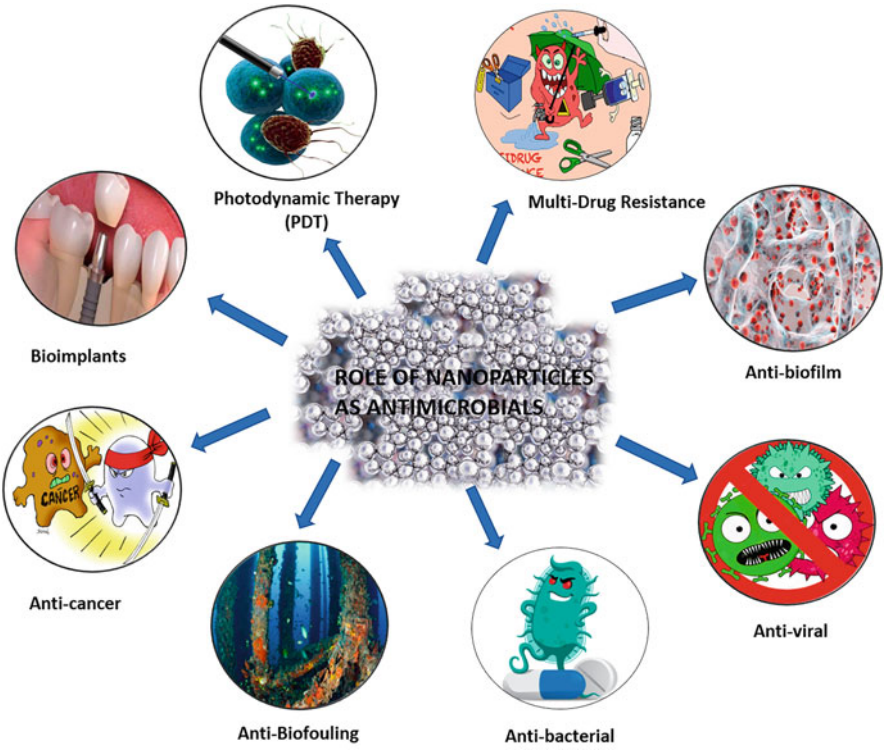

Fig. 12.2 Role of nanoparticles as antimicrobials

capabilities. This implies that all multidrug-resistant infections from different phyla and from all clinical sources can be treated with NPs (Mohammed Fayaz et al. 2012).

Additionally, to their antibacterial properties, hybrid nanomaterials have been discovered to have strong antimicrobial properties towards *E. coli*, *Staphylococcus aureus*, and *Enterococcus faecalis*. Examples of these hybrids include cholesterol-containing liposomes, phytonanosilver, and CNTs (Han et al. 2021). This demonstrates that the broad-spectrum action of the nano-antimicrobial drugs is generally enhanced when two or more nanoparticles are coupled. When CNTs and silver nanoparticle were mixed, the hybrid behaviour was also seen, and the resultant hybrid biocomposite was reported to have stronger and good antibacterial capabilities (Hashem et al. 2022). Chitosan-CNT hybrid also demonstrated strong antibacterial properties against bacteria (Pelgrift and Friedman 2013).

Additionally, it has been discovered that cefalexin-immobilised multi-walled CNTs significantly increase the antibacterial activity against a variety of pathogens, such as *E. coli, P. aeruginosa*, *S. aureus*, and *B. subtilis*. The filtration and antibacterial opportunities against any and all types of bacteria have also been reported to be improved by the coupling of AgNPs and CNTs, particularly

CNT-AgNPs (Song et al. 2021) on fibre membranes. The MWCNT-AgNP hybrid membrane has been discovered to greatly minimise biofilm development in addition to filtration and showing antibacterial capabilities, and this finding can be simply applied to various kinds of supporting membranes (Song et al. 2021).

12.5.2 In PDT (Photodynamic Therapies)

In contrast to antibiotic medication, photodynamic therapy (PDT) has indeed been suggested as a new method to inactivate germs because it does not select mutant-resistant strains. Because the ROS generated during the irradiation of a photosensitizer (PS) can react with microorganisms and cause their death, antimicrobial photodynamic therapy, APDT has been proposed as a treatment for infections. The notion that bacterial inactivation is the end consequence of a multi-target approach raises additional interest in the antibacterial usage of this technology. PDT also affects DNA, and reports of cytoplasm material leaking from damaged cell membranes have been made (Donadu et al. 2021; Meshaal et al. 2021; Yang et al. 2021). Given all of these various targets, it has been considered that there is little chance that bacteria will develop resistance. In several ways, nanoparticles have increased the effectiveness of APDT, boosting PS delivery to microorganisms. PS-loaded nanoparticles have been employed as carriers to introduce PS into bacteria and enhance antimicrobial effectiveness (Adeyemi et al. 2020). It has also been demonstrated that inorganic nanoparticles can photodynamically inactivate bacteria (Chaturvedi et al. 2020).

12.5.3 In Antibacterial Coating of Bioimplants

Human implants with antimicrobial properties come in two different varieties. The first category includes completely implantable devices like heart valves and dental implants. In order to prevent thrombosis, the antibacterial coating of cardiovascular devices in particular needs to be compatible with blood. Relying on pore structure, nanoparticle enrichment with titanium oxide coatings is applied to implants. The coating prevents the development of infections around the implant by preventing the adherence and proliferation of bacteria such as *Streptococcus* sp. and *E. coli* (Hong et al. 2021). The second category of devices includes partially implantable ones such as catheters, intravenous catheters, and neurosurgical catheters that are more likely to become colonised by bacteria, raising the chance of infection in clinical settings. Specifically, catheter biofilm formation can be slowed by using nanopolymers as antibacterial materials. Invasive neurosurgery catheters can be coated with nanoparticles (NPs) to decrease the likelihood of pathogenic bacterial infections and their consequences. *S. aureus* growth is considerably inhibited for 6 days after sustained discharge of NPs (Vasilev et al. 2019).

12.5.4 In Anti Biofouling and Antibiofilming

Biofilms cause operational issues in a number of industrial sectors, including transportation, water treatment, medicine, and sensor sensitivity. Bacterial adhesion begins as a minute monolayer and thickens over time when extracellular polymeric substances (EPS), or "biofilm," are produced as protective slimes. Biofilms are a source of contamination, inefficiency, and deterioration of quality, and their removal could be quite pricy. Silver nanoparticles, which already possess antimicrobial qualities, have sparked curiosity, and these particles offer a fresh field of study for the investigation of biofouling and biocorrosion prevention. Sol-gel (SG) and polymer-based coatings offer a framework for the addition of biocides and antimicrobial substances that provide this prevention. They offer an optically transparent platform that is reasonably priced that can be loaded with an antibacterial agent. Nanoparticles are injected into SG coatings in a study by Ielo et al. (2022) and examined for their effectiveness in reducing levels of biofouling. The results of a 7-day freshwater investigation revealed that MNPs can reduce levels of biofouling by up to 125% in the early phases of prevention when compared to the SG blank.

12.5.5 In Disinfections

The novel use of nanomaterials as disinfectants is related to their stability, high efficacy, and broad biocide spectrum like antiviral, bactericidal, and fungicidal, as well as antiparasitic properties (Algammal et al. 2021). A wide variety of NPs have demonstrated these remarkable disinfection qualities, in addition to the surface functionalization. According to Algammal et al. (2020), the NPs, which include those made of silver, copper, and gold, have outstanding cleaning and sanitising capabilities. Several of these nanoparticles are currently employed in hospitals as cleaning agents and disinfectants. In such instances, the cell surfaces are treated with powerful nanomaterials that are resistant to the superbug, MRSA, which causes the majority of nosocomial infections (Elkhawaga et al. 2020). The microbial burden on clinical surfaces, for instance, has been effectively reduced by silicone polymers containing AuNPs (Lebeaux et al. 2013).

When employed on hospital facemasks during extremely delicate clinical procedures, mixtures of silver and titanium dioxide nanoparticles have demonstrated to have significant protection against pathogenic bacteria (Lebeaux et al. 2013; Jassal et al. 2022).

Some NPs, like AgNPs, have a biocidal effect and are nontoxic; hence, they are frequently coated on medical equipment to fight infection (Hall-Stoodley et al. 2004). Additionally, silver nanoparticles are employed as cleansing, softening, and disinfectant agents in pet and animal shampoos. Additionally, NPs are being employed in packaging as preservatives to stop food from spoiling (Tanwar et al. 2014; Chausali et al. 2022).

12.5.6 Nanoparticle Antiparasitic Effect

Despite efforts to treat parasite infections, they are still on the rise, especially in tropical and low-income nations (Liu et al. 2019; Tawre et al. 2022). Drug toxicity, inefficiency, and the emergence of resistance to traditional antiparasitic medications are issues connected to parasitic illnesses. Due to the lack of effective antiparasitic medications, newer methods, like nanobiotechnology, have significantly improved the treatment of parasitic infections (Saleh et al. 2020; Tawre et al. 2022). Silver nanoparticles can inhibit *Leishmania* via ROS (Wang et al. 2020).

Animal model experiments have shown the use of other NPs, such as a mixture of gold, Ag, chitosan, and curcumin nanoparticles, can treat *Giardia lamblia* (Liu et al. 2019). The results also demonstrated that it is possible to completely remove *Giardia lamblia* from stools and intestines (Liu et al. 2019). Innovative synergic antimicrobial drugs, combined with 2/3 nano-antimicrobial drugs, to produce potency in the extinction of parasite illnesses are possible if the potential of NPs is fully realised.

12.5.7 In Treating Vector Borne Diseases

The manufacture of ecologically acceptable and secure NP pesticides synthesised from plants is currently available due to the rise in the frequency of vector-borne diseases. These include AgNPs produced from *Azadirachta indica* and *Heliotropium indicum* leaf extracts (Adeyemi et al. 2020; Chaturvedi et al. 2020). These pesticides are the most effective against mosquitoes that feed on blood (Adeyemi et al. 2020; Chaturvedi et al. 2020). This demonstrates the potential for eco-friendly NPs to prevent vector-transmitted diseases.

12.5.8 Inhibition of Pathogens in Macrophages

Infections that endure are brought on by pathogenic bacteria that can cross cell membranes and remain in neurons, and they are therefore challenging to cure (Algammal et al. 2020). Because of this, several medications have trouble penetrating these cells, which makes the elimination of such microbial diseases more difficult (Abd El-Baky et al. 2020). Due to the inability of standard antimicrobial medications to eradicate such germs, healthcare workers find it extremely challenging and frustrating while treating intravascular disease-causing pathogens. While the medications used to treat these conditions may not be ineffective, their effectiveness and efficiency may be constrained by low or ineffective intracellular diffusion and sustained drug density (Abd El-Baky et al. 2020).

12.5.9 Reversion of Multidrug Resistance in Tumour Cells by Chitosan

Since cancer cells are capable of generating mechanisms of resistance, anticancer medications may only have a limited amount of effectiveness against a variety of solid tumour forms, even if they are present in cancer (Liao et al. 2019). Tumours are able to avoid chemotherapy owing to these mechanisms. One of the most critical issues with chemotherapy is multidrug resistance (MDR). MDR is primarily caused by the cellular membrane pglycoprotein (Pgp), which can expel a variety of positive charge xenobiotics, along with some anticancer medications (Liao et al. 2019). The use of chitosan and its derivatives as nonviral vectors in gene therapy has shown considerable promise. These folic acid-linked hydroxypropyl-chitosan nanoparticles (FAHC-NPs) were created to decrease P-gp synthesis in order to combat tumour treatment resistance. These nanoparticles drastically decreased the levels of the *P-gp* gene and the multidrug resistance (MDR 1 gene) in both in vitro and in vivo, respectively. These findings revealed a potential strategy for overcoming cancer medication resistance.

12.6 Quantum Dots as Bactericidal

Quantum dots are man-made semiconducting nanoparticles that, depending on their composition and structure, can have a wide range of different properties. Man-made nanoscale crystals called quantum dots (QDs) have the ability to carry electrons. It's quantum dots. Due to how tiny they are, the dots demonstrate quantum effects. Since they are confined, the electron inside the dot can only occupy certain energy levels.

Quantum dots can have distinct electrical and optical properties compared to a vast number of the same substances since they can only access limited, discrete energy levels. Due to this, quantum dots can be used to further nanoscience (Jahangir et al. 2019).

The antibacterial activity of (QDs) is a crucial quality (Rajendiran et al. 2019). In comparison to traditional antibiotics, quantum dots not only exhibit exceptional structural stability but also photoluminescence characteristics for imaging and photodynamic therapy (PDT). QDs are frequently functionalized by polymers like PEG to increase their antibacterial effectiveness. The primary antibacterial mechanisms of QDs involve the production of free radicals, disruption of cell membranes and walls, and gene expression inhibition (Soheyli et al. 2019). QDs are able to show an antibacterial role in multidrug-resistant bacteria and fungi due to distinct processes from conventional antibiotics (Wasef et al. 2021). Since the QDs' toxicity to living organisms is relatively low, they are widely used in antibacterial research as a powerful substitute for conventional antimicrobials (Rajendiran et al. 2019).

QDs always are functionalized with polymers and photosensitizers (PS) to produce ROS and enhance their adhesion to bacteria in order to enhance their antibacterial effectiveness (Meshaal et al. 2021). Based on their ligands, diameter,

Table 12.3 List of quantum dots (QDs) and their mechanisms of inhibitory action on bacteria (modified from Rajendiran et al. (2019))

Quantum dots, QDs	Microbe producing	Mechanisms of action (moA)	Reference
Graphene QDs	*E. coli, S. aureus*, and *S. epidermis*	Production of ROS and cell damage	Fang et al. (2017)
Silver QDs	*Candida albicans*	Promotion of ROS production	Mir et al. (2018)
CdSe QDs	*P. aeruginosa*	Cell toxicity and gene toxicity	Priester et al. (2009)
ZnO QDs	*Escherichia coli*	ROS production and ETC modification	Joshi et al. (2009)

shape, surface charge, and charge transfer effect, functionalized QDs exhibit varying degrees of inhibitory action (Table 12.3).

12.7 Conclusion and Future Perspectives

A significant area of nanobiotechnology is the microbial production of nanoparticles. Microorganisms have the natural ability to synthesise nanoparticles because of their great diversity, and they could be considered promising biofactories for nanoparticle synthesis. According to research, nanoparticles can be functionalized, immobilised, and hybridised to increase their antibacterial properties against a variety of multi-resistant pathogens. A single type of nanoparticle antimicrobials, for instance, may exhibit a variety of antimicrobial activities against a variety of diseases. Due to their widespread antibacterial impact, these traits could also change the body's microbial flora and offer a variety of bactericidal, anticancer, antifungal, anti-biofouling, and antibiofilming properties. For the majority, nanoparticle antimicrobial medications are able to target and cross transmembrane barriers, which is a challenging phenomenon for classical antimicrobial drugs. To improve and expand their biological application, further knowledge about the toxicological consequences of NP-based antimicrobial drugs is required. Reliant on the nanoparticles' size, the particle may occasionally be harmful rather than have an antibacterial impact that inhibits infections. Contrarily, the majority of quantum dots (QDs) are safe for humans and do not harm human cells. QDs therefore provide greater potential for antibacterial application than nanoparticles. Further investigation into polymer-modified QDs can also aid in the development of pharmaceuticals with low animal cytotoxicity and broad-spectrum antimicrobial action.

References

Abd El-Baky RM, Masoud SM, Mohamed DS, Waly NG, Shafik EA, Mohareb DA, Hetta HF (2020) Prevalence and some possible mechanisms of colistin resistance among multidrug-

resistant and extensively drug-resistant *Pseudomonas aeruginosa*. Infect Drug Resist 13:323–332

Abd Ellah NH, Ahmed EA, Abd-Ellatief RB, Ali MF, Zahran AM, Hetta HF (2019) Metoclopramide nanoparticles modulate immune response in a diabetic rat model: association with regulatory T cells and proinflammatory cytokines. Int J Nanomedicine 14:2383

Abdellatif AA, Tawfeek HM, Abdelfattah A, Batiha GES, Hetta HF (2021) Recent updates in COVID-19 with emphasis on inhalation therapeutics: nanostructured and targeting systems. J Drug Deliv Sci Technol 63:102435

Abu-Elghait M, Hasanin M, Hashem AH, Salem SS (2021) Ecofriendly novel synthesis of tertiary composite based on cellulose and myco-synthesized selenium nanoparticles: characterization, antibiofilm and biocompatibility. Int J Biol Macromol 175:294–303

Adeyemi OS, Arowolo AT, Hetta HF, Al-Rejaie S, Rotimi D, Batiha GES (2020) Apoferritin and Apoferritin-capped metal nanoparticles inhibit arginine kinase of Trypanosoma brucei. Molecules 25(15):3432

Ahmadian-Fard-Fini S, Ghanbari D, Salavati-Niasari M (2019) Photoluminescence carbon dot as a sensor for detecting of *Pseudomonas aeruginosa* bacteria: hydrothermal synthesis of magnetic hollow NiFe2O4-carbon dots nanocomposite material. Compos Part B 161:564–577

Algammal AM, Hetta HF, Elkelish A, Alkhalifah DHH, Hozzein WN, Batiha GES, Mabrok MA (2020) Methicillin-resistant *Staphylococcus aureus* (MRSA): one health perspective approach to the bacterium epidemiology, virulence factors, antibiotic-resistance, and zoonotic impact. Infect Drug Resist 13:3255–3265

Algammal AM, Elsayed ME, Hashem HR, Ramadan H, Sheraba NS, El-Diasty EM, Hetta HF (2021) Molecular and HPLC-based approaches for detection of aflatoxin B 1 and ochratoxin A released from toxigenic Aspergillus species in processed meat. BMC Microbiol 21:1–10

Aziz N, Fatma T, Varma A, Prasad R (2014) Biogenic synthesis of silver nanoparticles using Scenedesmus abundans and evaluation of their antibacterial activity. J Nanoparticles 2014:689419. https://doi.org/10.1155/2014/689419

Aziz N, Faraz M, Pandey R, Sakir M, Fatma T, Varma A, Barman I, Prasad R (2015) Facile algae-derived route to biogenic silver nanoparticles: synthesis, antibacterial and photocatalytic properties. Langmuir 31:11605–11612. https://doi.org/10.1021/acs.langmuir.5b03081

Aziz N, Pandey R, Barman I, Prasad R (2016) Leveraging the attributes of Mucor hiemalis-derived silver nanoparticles for a synergistic broad-spectrum antimicrobial platform. Front Microbiol 7:1984. https://doi.org/10.3389/fmicb.2016.01984

Aziz N, Faraz M, Sherwani MA, Fatma T, Prasad R (2019) Illuminating the anticancerous efficacy of a new fungal chassis for silver nanoparticle synthesis. Front Chem 7:65. https://doi.org/10.3389/fchem.2019.00065

Baghdadi AM, Saddiq AA, Aissa A, Algamal Y, Khalil NM (2022) Structural refinement and antimicrobial activity of aluminum oxide nanoparticles. J Ceram Soc Jpn 130(3):257–263

Blanco E, Shen H, Ferrari M (2015) Principles of nanoparticle design for overcoming biological barriers to drug delivery. Nat Biotechnol 33(9):941–951

Chakraborty N, Banerjee J, Chakraborty P, Banerjee A, Chanda S, Ray K et al (2022) Green synthesis of copper/copper oxide nanoparticles and their applications: a review. Green Chem Lett Rev 15(1):187–215

Chaturvedi VK, Yadav N, Rai NK, Ellah NHA, Bohara RA, Rehan IF, Singh MP (2020) Pleurotus sajor-caju-mediated synthesis of silver and gold nanoparticles active against colon cancer cell lines: a new era of herbonanoceutics. Molecules 25(13):3091

Chausali N, Jyoti Saxena J, Prasad R (2022) Recent trends in nanotechnology applications of bio-based packaging. J Agric Food Res. https://doi.org/10.1016/j.jafr.2021.100257

Cheeseman S, Christofferson AJ, Kariuki R, Cozzolino D, Daeneke T, Crawford RJ et al (2020) Antimicrobial metal nanomaterials: from passive to stimuli-activated applications. Adv Sci 7(10):1902913

Cheng L, Li R, Liu G, Zhang Y, Tang X, Wang J et al (2018) Potential antibacterial mechanism of silver nanoparticles and the optimization of orthopedic implants by advanced modification technologies. Int J Nanomedicine 13:3311

Donadu MG, Mazzarello V, Cappuccinelli P, Zanetti S, Madléna M, Nagy ÁL, Gajdács M (2021) Relationship between the biofilm-forming capacity and antimicrobial resistance in clinical *acinetobacter baumannii* isolates: results from a laboratory-based in vitro study. Microorganisms 9(11):2384

Edmundson M, Thanh NT, Song B (2013) Nanoparticles based stem cell tracking in regenerative medicine. Theranostics 3(8):573

Elbahnasawy MA, Shehabeldine AM, Khattab AM, Amin BH, Hashem AH (2021) Green biosynthesis of silver nanoparticles using novel endophytic *Rothia endophytica*: characterization and anticandidal activity. J Drug Deliv Sci Technol 62:102401

Elkhawaga AA, Hetta HF, Osman NS, Hosni A, El-Mokhtar MA (2020) Emergence of Cronobacter sakazakii in cases of neonatal sepsis in upper Egypt: first report in North Africa. Front Microbiol 11:215

Fahimmunisha BA, Ishwarya R, AlSalhi MS, Devanesan S, Govindarajan M, Vaseeharan B (2020) Green fabrication, characterization and antibacterial potential of zinc oxide nanoparticles using aloe socotrina leaf extract: a novel drug delivery approach. J Drug Deliv Sci Technol 55:101465

Fang X, Ding J, Yuan N, Sun P, Lv M, Ding G, Zhu C (2017) Graphene quantum dot incorporated perovskite films: passivating grain boundaries and facilitating electron extraction. Phys Chem Chem Phys 19(8):6057–6063

Ghaderi RS, Kazemi M, Soleimanpour S (2021) Nanoparticles are more successful competitor than antibiotics in treating bacterial infections: a review of the literature. Iran J Med Microbiol 15(1): 18–45

Gupta A, Mumtaz S, Li CH, Hussain I, Rotello VM (2019) Combatting antibiotic-resistant bacteria using nanomaterials. Chem Soc Rev 48(2):415–427

Gurunathan S, Han JW, Dayem AA, Eppakayala V, Kim JH (2012) Oxidative stress-mediated antibacterial activity of graphene oxide and reduced graphene oxide in *Pseudomonas aeruginosa*. Int J Nanomedicine 7:5901–5914

Hall-Stoodley L, Costerton JW, Stoodley P (2004) Bacterial biofilms: from the natural environment to infectious diseases. Nat Rev Microbiol 2(2):95–108

Han HW, Patel KD, Kwak JH, Jun SK, Jang TS, Lee SH et al (2021) Selenium nanoparticles as candidates for antibacterial substitutes and supplements against multidrug-resistant bacteria. Biomol Ther 11(7):1028

Hashem AH, Al Abboud MA, Alawlaqi MM, Abdelghany TM, Hasanin M (2022) Synthesis of nanocapsules based on biosynthesized nickel nanoparticles and potato starch: antimicrobial, antioxidant, and anticancer activity. Starch-Stärke 74(1–2):2100165

Hetta HF, Al-Kadmy I, Khazaal SS, Abbas S, Suhail A, El-Mokhtar MA, Algammal AM (2021) Antibiofilm and antivirulence potential of silver nanoparticles against multidrug-resistant *Acinetobacter baumannii*. Sci Rep 11(1):1–11

Hetta HF, Ramadan YN, Al-Harbi AI, Ahmed EA, Battah B, Abd Ellah NH et al (2023) Nanotechnology as a promising approach to combat multidrug resistant bacteria: a comprehensive review and future perspectives. Biomedicine 11(2):413

Hochvaldová L, Večeřová R, Kolář M, Prucek R, Kvítek L, Lapčík L, Panáček A (2022) Antibacterial nanomaterials: upcoming hope to overcome antibiotic resistance crisis. Nanotechnol Rev 11(1):1115–1142

Hong Q, Huo S, Tang H, Qu X, Yue B (2021) Smart nanomaterials for treatment of biofilm in orthopedic implants. Front Bioeng Biotechnol 9:694635

Ielo I, Giacobello F, Castellano A, Sfameni S, Rando G, Plutino MR (2022) Development of antibacterial and antifouling innovative and eco-sustainable sol–gel based materials: from marine areas protection to healthcare applications. Gels 8(1):26

Jafari A (2021) Evaluation of magnesium oxide and zinc oxide nanoparticles against multi-drug-resistance *mycobacterium tuberculosis*. Indian J Tuberculosis 68(2):195–200

Jahangir MA, Gilani SJ, Muheem A, Jafar M, Aslam M, Ansari MT, Barkat MA (2019) Quantum dots: next generation of smart nano-systems. Pharma Nanotechnol 7(3):234–245

Jassal PS, Kaur D, Prasad R, Singh J (2022) Green synthesis of titanium dioxide nanoparticles: development and applications. J Agric Food Res 10:100361. https://doi.org/10.1016/j.jafr.2022.100361

Jijie R, Barras A, Teodorescu F, Boukherroub R, Szunerits S (2017) Advancements on the molecular design of nanoantibiotics: current level of development and future challenges. Mol Syst Design Eng 2(4):349–369

Joshi P, Chakraborti S, Chakrabarti P, Haranath D, Shanker V, Ansari ZA et al (2009) Role of surface adsorbed anionic species in antibacterial activity of ZnO quantum dots against *Escherichia coli*. J Nanosci Nanotechnol 9(11):6427–6433

Khalid M, El-Sawy HS (2017) Polymeric nanoparticles: promising platform for drug delivery. Int J Pharm 528(1–2):675–691

Khameneh B, Diab R, Ghazvini K, Bazzaz BSF (2016) Breakthroughs in bacterial resistance mechanisms and the potential ways to combat them. Microb Pathog 95:32–42

Lebeaux D, Chauhan A, Rendueles O, Beloin C (2013) From in vitro to in vivo models of bacterial biofilm-related infections. Pathogens 2(2):288–356

Lemire JA, Harrison JJ, Turner RJ (2013) Antimicrobial activity of metals: mechanisms, molecular targets and applications. Nat Rev Microbiol 11(6):371–384

Li TF, Li K, Wang C, Liu X, Wen Y, Xu YH et al (2017) Harnessing the cross-talk between tumor cells and tumor-associated macrophages with a nano-drug for modulation of glioblastoma immune microenvironment. J Control Release 268:128–146

Liao S, Zhang Y, Pan X, Zhu F, Jiang C, Liu Q et al (2019) Antibacterial activity and mechanism of silver nanoparticles against multidrug-resistant *Pseudomonas aeruginosa*. Int J Nanomedicine 14:1469

Liu T, Cui Q, Wu Q, Li X, Song K, Ge D, Guan S (2019) Mechanism study of bacteria killed on nanostructures. J Phys Chem B 123(41):8686–8696

Mabrok M, Algammal A, Sivaramasamy E, Hetta HF, Atwah B, Alghamdi S, Rodkhum C (2023) Tenacibaculosis caused by *Tenacibaculum maritimum*: updated knowledge of this marine bacterial fish pathogen. Front Cell Infect Microbiol 12:1068000

MacGowan A, Macnaughton E (2017) Antibiotic resistance. Medicine 45(10):622–628

Mba IE, Nweze EI (2020) The use of nanoparticles as alternative therapeutic agents against Candida infections: an up-to-date overview and future perspectives. World J Microbiol Biotechnol 36:1–20

Meshaal AK, Hetta HF, Yahia R, Abualnaja KM, Mansour AT, Al-Kadmy IM et al (2021) In vitro antimicrobial activity of medicinal plant extracts against some bacterial pathogens isolated from raw and processed meat. Life 11(11):1178

Mir IA, Radhakrishanan VS, Rawat K, Prasad T, Bohidar HB (2018) Bandgap tunable AgInS based quantum dots for high contrast cell imaging with enhanced photodynamic and antifungal applications. Sci Rep 8(1):1–12

Moghaddam K (2010) An introduction to microbial metal nanoparticle preparation method. J Young Investig 19(1)

Mohammed Fayaz A, Ao Z, Girilal M, Chen L, Xiao X, Kalaichelvan PT, Yao X (2012) Inactivation of microbial infectiousness by silver nanoparticles-coated condom: a new approach to inhibit HIV-and HSV-transmitted infection. Int J Nanomedicine 7:5007–5018

Mubeen B, Ansar AN, Rasool R, Ullah I, Imam SS, Alshehri S et al (2021) Nanotechnology as a novel approach in combating microbes providing an alternative to antibiotics. Antibiotics 10(12):1473

Natan M, Banin E (2017) From nano to micro: using nanotechnology to combat microorganisms and their multidrug resistance. FEMS Microbiol Rev 41(3):302–322

Pelgrift RY, Friedman AJ (2013) Nanotechnology as a therapeutic tool to combat microbial resistance. Adv Drug Deliv Rev 65(13–14):1803–1815. https://doi.org/10.1016/j.addr.2013.07.011

Pinna E, Le Gall S, Torralba E, Mula G, Cachet-Vivier C, Bastide S (2020) Mesopore formation and silicon surface nanostructuration by metal-assisted chemical etching with silver nanoparticles. Front Chem 8:658

Prasad R (2016) Advances and applications through fungal nanobiotechnology. Springer, International Publishing Switzerland. (ISBN: 978-3-319-42989-2)

Prasad R (2017) Fungal nanotechnology: applications in agriculture, industry, and medicine. Springer Nature Singapore Pte Ltd. (ISBN 978-3-319-68423-9)

Prasad R, Pandey R, Barman I (2016) Engineering tailored nanoparticles with microbes: quo vadis. WIREs Nanomed Nanobiotechnol 8:316–330. https://doi.org/10.1002/wnan.1363

Prasad R, Kumar V, Kumar M, Wang S (2018) Fungal nanobionics: principles and applications. Springer Nature Singapore Pte Ltd. (ISBN 978-981-10-8666-3) https://www.springer.com/gb/book/9789811086656

Priester JH, Stoimenov PK, Mielke RE, Webb SM, Ehrhardt C, Zhang JP et al (2009) Effects of soluble cadmium salts versus CdSe quantum dots on the growth of planktonic *Pseudomonas aeruginosa*. Environ Sci Technol 43(7):2589–2594

Qayyum S, Khan AU (2016) Nanoparticles vs. biofilms: a battle against another paradigm of antibiotic resistance. MedChemComm 7(8):1479–1498

Rajendiran K, Zhao Z, Pei DS, Fu A (2019) Antimicrobial activity and mechanism of functionalized quantum dots. Polymers 11(10):1670

Ramalingam B, Parandhaman T, Das SK (2016) Antibacterial effects of biosynthesized silver nanoparticles on surface ultrastructure and nanomechanical properties of gram-negative bacteria viz. *Escherichia coli* and *Pseudomonas aeruginosa*. ACS Appl Mater Interfaces 8(7): 4963–4976

Rangel-López L, Zaragoza-Bastida A, Valladares-Carranza B, Peláez-Acero A, Sosa-Gutiérrez CG, Hetta HF et al (2020) In vitro antibacterial potential of Salix babylonica extract against bacteria that affect Oncorhynchus mykiss and Oreochromis spp. Animals 10(8):1340

Roca I, Akova M, Baquero F, Carlet J, Cavaleri M, Coenen S et al (2015) The global threat of antimicrobial resistance: science for intervention. New Microbes New Infect 6:22–29

Saleh H, Nassar AM, Noreldin AE, Samak D, Elshony N, Wasef L et al (2020) Chemo-protective potential of cerium oxide nanoparticles against fipronil-induced oxidative stress, apoptosis, inflammation and reproductive dysfunction in male white albino rats. Molecules 25(15):3479

Slavin YN, Asnis J, Hńfeli UO, Bach H (2017) Metal nanoparticles: understanding the mechanisms behind antibacterial activity. J Nanobiotechnol 15:1–20

Soheyli E, Azad D, Sahraei R, Hatamnia AA, Rostamzad A, Alinazari M (2019) Synthesis and optimization of emission characteristics of water-dispersible ag-in-s quantum dots and their bactericidal activity. Colloids Surf B: Biointerfaces 182:110389

Song X, Liu P, Liu X, Wang Y, Wei H, Zhang J et al (2021) Dealing with MDR bacteria and biofilm in the post-antibiotic era: application of antimicrobial peptides-based nano-formulation. Mater Sci Eng C 128:112318

Spengler G, Gajdács M, Donadu MG, Usai M, Marchetti M, Ferrari M et al (2022) Evaluation of the antimicrobial and antivirulent potential of essential oils isolated from Juniperus oxycedrus L. ssp. macrocarpa aerial parts. Microorganisms 10(4):758

Sutherland IW (2001) The biofilm matrix–an immobilized but dynamic microbial environment. Trends Microbiol 9(5):222–227

Tanwar J, Das S, Fatima Z, Hameed S (2014) Multidrug resistance: an emerging crisis. Interdiscip Perspect Infect Dis 2014:1

Tawre MS, Shiledar A, Satpute SK, Ahire K, Ghosh S, Pardesi K (2022) Synergistic and antibiofilm potential of Curcuma aromatica derived silver nanoparticles in combination with antibiotics against multidrug-resistant pathogens. Front Chem 10:1029056

Teixeira MC, Sanchez-Lopez E, Espina M, Calpena AC, Silva AM, Veiga FJ et al (2018) Advances in antibiotic nanotherapy: overcoming antimicrobial resistance. Emerg Nanotechnol Immunol 233–259

Tripathi N, Goshisht MK (2022) Recent advances and mechanistic insights into antibacterial activity, antibiofilm activity, and cytotoxicity of silver nanoparticles. ACS Appl Bio Mater 5(4):1391–1463

Usai D, Donadu M, Bua A, Molicotti P, Zanetti S, Piras S et al (2019) Enhancement of antimicrobial activity of pump inhibitors associating drugs. J Infect Dev Ctries 13(02):162–164

Vasilev AA, Efimov MN, Bondarenko GN, Muratov DG, Dzidziguri EL, Ivantsov MI et al (2019) FeCo alloy nanoparticles supported on IR pyrolyzed chitosan as catalyst for Fischer-Tropsch synthesis. Chem Phys Lett 730:8–13

Wang X, Du Y, Fan L, Liu H, Hu Y (2005) Chitosan-metal complexes as antimicrobial agent: synthesis, characterization and structure-activity study. Polym Bull 55:105–113

Wang L, Hu C, Shao L (2017) The antimicrobial activity of nanoparticles: present situation and prospects for the future. Int J Nanomedicine 12:1227

Wang DY, Van der Mei HC, Ren Y, Busscher HJ, Shi L (2020) Lipid-based antimicrobial delivery-systems for the treatment of bacterial infections. Front Chem 7:872

Wasef L, Nassar AM, El-Sayed YS, Samak D, Noreldin A, Elshony N et al (2021) The potential ameliorative impacts of cerium oxide nanoparticles against fipronil-induced hepatic steatosis. Sci Rep 11(1):1310

Yang X, Ye W, Qi Y, Ying Y, Xia Z (2021) Overcoming multidrug resistance in bacteria through antibiotics delivery in surface-engineered nano-cargos: recent developments for future nano-antibiotics. Front Bioeng Biotechnol 9:696514

Microbiologically Synthesized Nanoparticles and Their Role in Biofilm Inhibition

13

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Abstract

Much research is being done on alternative antibacterial therapies that replace or supplement conventional antibiotics since multidrug-resistant bacterial infections are becoming more prevalent. Metallic nanoparticles have been demonstrated to destroy bacterial biofilms successfully. However, their chemical manufacture frequently results in harmful byproducts. Recent research has shown that the environmentally friendly production of metallic NPs may be accomplished using microbial and plant extracts. The NPs can effectively limit bacterial growth by passing through the exopolysaccharides of a biofilm matrix. A cluster of sessile microbial cells forms a biofilm group that may cling to surface biological and nonliving things, through glycocalyx and additional polymeric molecules. Such biofilms result in biofouling on implants and medical equipment and several chronic disorders. NPs that penetrate the biofilm change the QS gene pathways, impairing cell-to-cell communication and preventing the formation of the biofilm. Algae, which create a variety of biogenic chemicals, have been discovered to be capable of destroying biofilms without negatively affecting the ecosystem and other biotas. The main component of the algal extract with antibacterial and anti-biofilm properties is polyunsaturated fatty acids. The extracts from roughly 225 different species of cyanobacteria and microalgae exhibit anti-biofilm action. This section is focused on the "signal jamming effects" of different metallic and nonmetallic nanoparticles produced by microbial nanotechnologies on biofilms' development.

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13.1 Introduction

Most severe diseases in people are discovered in biological origin. According to Costerton et al. (1999), a biofilm is a microbial cell's symbiotic relationship. That continues to be attached to surfaces, whether biological or nonliving things, that include self-produced hydrated polymerized compounds. The growth of biological material is generated by bacteria in the plankton sticking to surfaces like those of medical equipment and prosthetics. In addition, it promotes the development of wound-associated infections, chronic otitis media, cystic fibrosis, and valve endocarditis (Donlan 2001; Santos et al. 2011; Abidi et al. 2013).

The method of cell-to-cell communication, which is concentrated and reliant on direct communication of chemical substance transfer (Lobedanz and Søgaard-Andersen 2003; Phelan et al. 2012), chemical signaling (Eberhard et al. 1981), and electrical signaling determines the capacity of bacterial cells to adapt and monitor a variety of environmental situations (Nielsen et al. 2010; Shrestha et al. 2013).

Quorum sensing is the name given to communication that is a density-dependent mechanism that is activated by minute molecules in bacteria (autoinducers) (QS). Initially, this process was noticed in *Vibrio fischeri* (Nealson et al. 1970), and Fuqua et al. (1994) created the acronym QS. Acyl-homoserine lactones (AHLs), a class of autoinducing peptides crucial in developing bacterial pathogenicity, make up the QS machinery. Exotoxin A, lection, pyocyanin, and elastase are only a few virulence factors generated by QS in *Pseudomonas aeruginosa*, In contrast, *Staphylococcus aureus* was shown to have protein A, enterotoxins, lipases, hemolysins, and fibronectin (Yarwood et al. 2004; Carnes et al. 2010).

Bacterial cells can avoid the pathogenicity of the host defense system with virulence determinants that have evolved. The transcription of several genes in the poly-step process that leads to the creation of biofilm is the planktonic stage of microbes from a single organism (Donlan 2002). The transformation of planktonic organisms into their sessile forms enhances numerous chemical compounds, which causes genetic alterations in the cells. The dense extracellular polymeric substance (EPS), made up of the sessile microcolonies, produces proteins, extracellular DNA, and other polymerized components that act as a natural barrier all around microbial cells. The quorum sensing (QS) pathway causes the biofilm to mature (Lahiri et al. 2019).

Lahiri et al. (2019) claim that the unpreventable attachment of microbial cells to the surface, the yield of QS compounds, the movement of materials inside the biofilm, the metabolic activity of the substrate by various immobile microcolonies, the progression of EPS, and eventually the metastasis of the sessile colonial possessions are the causes of the development of biofilm. Although antibiotics are the first choice to treat microbial diseases, the rapid rise in bacterial resistance due to uncontrolled antibiotic usage has emerged as a major health issue (Laxminarayan et al. 2013; Chioro et al. 2015; Zhao et al. 2017; Zhong and Zhao 2018; Ma et al. 2019; Sarkar et al. 2020).

A conventional method for treating biofilm consisted of combining several antibiotics with various killing mechanisms. However, because of the rise in

antibiotic resistance, standard medications cannot prevent biofilm development. The growth of EPS surrounding the microcolonies hinders or completely stops the spread of antibiotics inside the system of life. Growth of EPS surrounding microcolonies inhibits penetration, resulting in zero or little antibiotic dispersion within the physical system. Additionally, changes to the microenvironment inside biofilm matrices lead to establishing a concentration gradient of metabolites that inhibits or almost eliminates bacterial growth.

Additionally, it has been noted that changes in the microenvironment cause the nutrient supply to change, oxidative stress to be produced, water to become scarce, starvation to occur, and temperature to change, all of which cause the bacterial cells to develop a variety of stress-related adaptive mechanisms (Singh et al. 2017). Change of the microbial cells follows this into persisters. It also plays a big part in the development of drug tolerance. Persisters are a highly protected spore-like condition (Stewart 2002).

Various nanoparticles (NPs) have recently gained popularity as an alternative to antibiotics in treating bacterial infections. Nanoparticles act by bypassing drug resistance mechanisms in bacteria and inhibiting biofilm formation or other important processes related to their virulence potential. NPs have a completely different method of new strategies have emerged to attack bacteria without having to enter the microbial cell (Wang et al. 2017a). The production of nanoparticles by microbiology is shown to be more advantageous than that through chemical modification because it does not necessitate the same circumstances as a purified precursor material. The requirement of favorable circumstances and suitable temperature ranges (20–30°C) increase the viability of bacteriologically manufactured NPs in the marketplace (Vaseghi et al. 2018). Furthermore, a natural capping factor acts as a barrier toward oxidation, agglomeration, and clustering on certain microbiogenic nanomaterials, providing outstanding persistence (Durán and Seabra 2012). As a result, NPs created through microbiology are generally thought of as being preferable to antibacterial therapy (Capeness et al. 2019; Prasad et al. 2020; Maddela et al. 2021; Inamuddin et al. 2021; Saglam et al. 2021).

13.2 Synthesis of Microbial Nanoparticles

Owing to their elastic physicochemical properties, nanoparticles (NPs) have lately revolutionized employment in the health sector by introducing new properties, including thermal and electromagnetic conductivities, absorptivity, melting temperature, and the improvement of catalytic efficiency by altering the surface-to-volume ratio. Nanotechnology includes the production of nano-dimensional materials with different form- and size-dependent properties (Rafique et al. 2017). In the health sector, many NPs, particularly silver nanoparticles (AgNPs), display a wide range of applications, including the capacity to distribute medications, use biochemical detectors for medical imaging, and catalyze reactions. Other uses include memory chips, wireless electrical logic, computer transistors, and antibacterial effectiveness (Das et al. 2014; Prasad 2014; Prasad et al. 2018; Aziz et al. 2014, 2015, 2016, 2019).

The traditional techniques for producing NPs include ultrasonication, radiolysis, microwave, spray pyrolysis, electrospinning, the sol-gel method, chemical reduction, and inert condensation. However, the immediate demand for a quicker, cheaper, more effective, nontoxic, and environmentally friendly procedure has turned attention to greener methods (Khandel and Kumar-Shahi 2016; Fang et al. 2019).

The stabilization of NPs is effectively aided by biogenic sources such as bacteria, fungi, and other plant components (Durán et al. 2005). Microorganisms like fungus, yeast, and bacteria are used in the green synthesis of NPs as the process may be adjusted by changing the culture parameters, such as nutrition, pH, pressure, and temperature. The microbial system has an internal mechanism for producing nanoparticles (NPs) from metallic salts (Li et al. 2011; Prasad et al. 2016; Srivastava et al. 2021; Kisimba et al. 2023).

Studies have indicated that heavy metals being transformed into metallic NPs involve bacterial cells significantly. The creation of metallic NPs is caused by various interacting pathways present within bacterial cells. Bacterial cells can create sustainable nanoparticles on a vast scale, another benefit of using them (Fariq et al. 2017). Additionally, it has been shown that cells have subcellular enzymes that are involved in the generation of nanoparticles, especially in fungi (Fariq et al. 2017). Enzymes like nicotinamide adenine dinucleotide (NADH)-dependent reductase were used to synthesize metallic nanoparticles (Guilger-Casagrande and de Lima 2019; Prasad 2016, 2017).

The enzyme nitrate reductase and anthraquinones from *Fusarium oxysporum* had the responsibility of decreasing the silver ions. In a different work, extracellular NADH-dependent nitrate reductase was applied to create AgNPs utilizing identical fungi and quinolones (Anil Kumar et al. 2007). AuNPs are also created by a fungus enzyme called NADH-dependent oxidoreductase (Kitching et al. 2015). Furthermore, studies showed that the creation of NPs included the enzymes nitrate reductase and alpha-NADH-dependent reductase.

The output of NPs is often higher in fungi than in bacterial cells because they have more biomass. Although bacteria are more frequently utilized to make metallic NPs, the presence of mycelia in fungi may make them more valuable since they offer a larger surface area for interactions. Because fungi generate more enzymes than bacteria, turning metallic salts into metallic NPs happens more quickly. The metal ion absorption and reduction mechanism for the generation of NPs included the fungal cell wall (Khandel and Shahi 2018).

The interior elements of fungal cells, such as the cell wall, cytoplasmic membrane, protein, enzymes, and others, are crucial in the formation of the nanoparticles. The synthesis of AgNPs and other metallic NPs is affected by temperature, pH, biomass, and additional physiological characteristics. These nanoparticle antimicrobial (antibacterial, antifungal, and antiviral) capabilities, among other features, benefit human welfare. In actuality, no harmful substances are needed for the NP recovery and purification procedure since the method of biosynthesis of AgNPs by fungus or materials derived from fungi (Wei et al. 2009).

Mycogenic AgNPs do, however, have several drawbacks similar to other nanoparticles. Before use, it is essential to verify AgNPs' biocompatibility and biosafety, particularly in the healthcare industry. The majority of the known fungi species for producing nanoparticles have been documented will become harmful to both humans and plants, which poses the biggest challenge to the commercial production of myogenic metallic NPs. *Trichoderma reesei*, on the other hand, is a nonpathogenic fungus that has gained widespread acceptance for the production of AgNPs as an industrially suitable strain (Dorcheh and Vahabi 2016).

Higher manufacturing costs and greater biosynthesis times are other downsides of NPs produced by a fungus (Jeevanandam et al. 2016). Utilizing bacteria to produce NPs has the benefit of rapid growth and a more straightforward technique for controlling genetic expression (Lovley and Woodward 1996). Owing to their ability to withstand settings with higher levels of metallic particles, bacteria are frequently used to synthesize metallic NPs (Haefeli et al. 1984).

13.3 Microorganism-Assisted Nanoparticle Synthesis Mechanism

Microorganisms can produce nanoparticles (NP) intracellularly and extracellularly by synthesizing metals, metal oxides, or metalloids. In the literature, this procedure is well-documented (Patil and Chandrasekaran 2020). The extracellular process includes the discharge of metal ions for nanoparticle production by bacterial enzymes and proteins of microbial or fungal cell wall constituents or organic compounds present in the growth media. This is in contrast to the subcellular mechanism, which includes the early electrostatic interaction of metal ions by carboxylic acid groups of the bacteria cell wall, channel of metallic ions via cells, and reduction by subcellular proteins and cofactors to generate NPs (Siddiqi et al. 2018; Koch et al. 2023).

It is possible to identify bacterial resistance pathways for cellular detoxification in the biochemical processes involved in microorganism-mediated nanoparticle production. In this, enzyme, mediated degradation and nanostructure-based deposition change the dissolution of inorganic and dangerous ions. It has been suggested that there are techniques for extra- and intracellular biocatalytic production. These mechanisms primarily involve oxidoreductase enzymes and cellular transporters, such as NADH-dependent nitrate reductase, NADPH-dependent sulfite reductase flavoprotein subunit alpha, and cysteine desulfhydrase (Grasso et al. 2019). Cellular enzymes transform hazardous metal ions further into appropriate metal elements by binding specific ions from the environment and biosynthesizing nanomaterials in microorganisms. Based on how they are made, nanoparticles can be classified as intracellular or extracellular. In the intracellular method, ions are introduced within the microbial cell where they combine with enzymes to create nanoparticles. In the extracellular state, reduced ions and metal ions are confined on the surface of the cell when enzymes are present (Li et al. 2011).

13.4 Microbial Enzymes' Nanoparticle Bioreduction of Metal, Metalloid, and Nonmetal Ions

Extracellular enzymes from various bacteria and fungi can convert metal and metalloids into the appropriate nanoparticles. Extracellular enzymes, like nitrate reductase, can transfer electrons from specific donors (such as hydroxyl groups to Ag+), facilitating the conversion of Ag+ to metallic AgNPs. Functional groupings, such as -NH_2,-OH,-SH, or –COOH, help in the stabilization of microbial proteins.

Microbiological proteins aid in the stability of metal ions, which are later transformed into NPs on the cell wall or within the periplasm, of the NPs by serving as interaction sites for those ions. When NPs are formed and stabilized, proteins sometimes act as primary reducing or capping agents. By transferring electrons between cytoplasmic elements (such as NADH/NADPH), vitamins, and organic acids, it is also known that internal enzymes such as cytochrome oxidases support the conversion of metal ions into NPs. There are three ways that subcellular reductase can initiate synthesis and stability of nanomaterials: periplasmic reductase can actively reduce M^+ to M, bioreduction takes place in the cytosol or periplasm and generates M from M^+or, M^{2+} in the cytoplasm and M can be formed (Klaus et al. 1999; Mishra et al. 2017; Lv et al. 2018; Siddiqi et al. 2018).

Te^{2+} and Se^{2+} are poisonous metalloid species that degrade using toxic chemical reductants, which is terrible for the sake of the planet and human health (Presentato et al. 2018). As they produce little to no harmful byproducts during the whole degradation process their efficiency in disintegration, purification, and bioinspired reductants is one possibility. Rhodococcus, an actinomycete, breaks down SeO_3^{2-} aerobically to create Se-NPs. Greater free energy and less stability in solutions caused, Se-nucleation seeds to be produced during the reduction of SeO_3^{2-} to create Se-NPs, which were then assembled to form the suspension, and nanomaterials were precipitated as nanocrystals (Jana 2015). In a different investigation, the enzyme fumarate reductase with selenite reducing factor was used by *Enterobacter cloacae* to create Se-NPs both intracellularly and extracellularly. Microorganisms like *Citrobacter freundii* (anaerobic synthesis) and *Pseudomonas putida* could also produce Se-NPs (aerobic synthesis). During the earlier case, it is found that thiol-containing amino acids, such as cysteine, facilitate the chelate of SeO_3^{2-}, whereby creates Selena di-glutathione. As a substrate, this can cause glutathione reductase to produce the unstable intermediate Se0—additionally, microbiological species like *Stenotrophomonas maltophilia* SeITE02 and *Ochrobactrum* sp. MPV1 creates spherical nanoparticles of Se and Te. Black Te-NPs can be produced from tellurite using NADH-dependent reductase as a detoxifier (Song et al. 2017; Wang et al. 2017b; Xu et al. 2018).

With the aid of a few multicellular proteins, some bacteria, such as *Magnetospirillum magneticum*, have subcellular magnetosomes that help encapsulate Fe2O3-NPs in their dissolved state (e.g., ferritin or iron reductase enzymes). Biological membranes comprised of proteins, glycolipids, and phospholipids surround magnetic nanocrystals of the raw materials magnetite (Fe_3O_4) and greigite

(Fe_3S_4) that are employed by *magnetotactic* bacteria to move through the earth's electromagnetic field. Environmental factors, cellular stress, and cell growth cycles influence magnetosome synthesis. As the magnetosomes develop, when the iron is transported *Magnetosomes* are oriented in a chain, crystals are created, and produced are mature outside of the bacterial cell membranes (Kuzajewska et al. 2020). Due to differences in composition, the magnetosome membrane contrasts with the plasmalemma and offers the right conditions for biomineralization. The magnetosome island produces distinct protein sets to control this tightly regulated process of magnetosome formation (Barber-Zucker and Zarivach 2017). At the junction of the magnetosome membranes, supersaturating quantities of iron also led to the formation of magnetite. Vesicle formation has been seen to take place before the biomineralization event. Thus, using the MamB and MamM proteins, as in the case of *Magnetospirillum magneticum*, could make it simpler to pump vesicles with iron at supersaturation levels. A better nucleation process is made possible by interactions between the crystal's ions and its surface proteins. The physicochemical characteristics of the magnetite nanoparticles were also discovered to have an impact on their shape including pH, redox potential, temperature, the route in which iron is supplied, the quantity of stimulator and inhibitory ions or molecules, and supersaturation state (Faivre and Schüler 2008).

The usual precursor for these metal oxide nanoparticles is $FeCl_3$. For instance, *Morganella morganii* and *Erwinia herbicola* bacteria were employed to create metal oxide nanomaterials of CuO and SnO_2, respectively, employing redox processes and enzymes like NADH. The freshly generated metal NPs can be reduced and stabilized by the metabolites of microbes in the fermentation broth secreted (Srivastava and Mukhopadhyay 2014; Obayemi et al. 2015).

Several researchers have created transition metal chalcogenide nanoparticles. For instance, *Moorella thermoacetica* can produce CdS-NPs extracellularly by adding $Cd(NO_3)_2$ to the medium for bacterial growth that promotes photosynthetic CO_2 into acetic acid. *Desulfovibrio caledoniensis* manufacture CdS-NPs both extracellularly and intracellularly. Anaerobic sulfate reduction in bacteria is activated by ATP sulfurylase in a three-step process that also needs ferredoxin or NADH to reduce the succeeding adenosine-phosphosulfate (APS) complex to sulfite and assimilatory or dissimilatory sulfite reductase to convert sulfite to sulfide. Regulating the amount of poly-ethene glycol in the *Clostridiaceae* sp. can also produce PbS nanocrystals, where the sulfate-reducing bacteria first convert (SO4)2- to S_2 followed by S_2 which will slowly combine with Pb^{2+} to precipitate as PbS-NPs (Qi et al. 2016; Yue et al. 2016). Additionally, studies have revealed that *Shewanella oneidensis* MR-1 can create highly distributed Pd-Ag bimetallic NPs related to graphemes (Han et al. 2019). Crude polysaccharides derived from *Pleurotus* flagellates can transform graphene oxides into nanosheets (Dasgupta et al. 2017).

13.5 Microbial Exopolysaccharides for Nanoparticle Synthesis

Exopolysaccharides (EPSs) are produced extracellularly by bacterial cells and are essential for surface adhesion and cell-to-cell communication. In addition to having the capacity to create nanoparticles by reducing metal ions, EPSs also serve as a capping factor in stabilizing the NPs; thus, the EPSs act as a backup option for the microbiological creation of several metal nanomaterials. Bacterial EPSs, mostly made of noncarbohydrate components that give the EPSs their anionic nature, as well as carbohydrates such as D-glucose, L-fucose, D-mannose, D-galactose, and N-acetyl-D-glucosamine. Certain organic compounds typically produce EPSs are more lipophilic, affecting how well they interact with cations like metal ions. Chelated metal ions are diverse functional groupings that diminish and stabilize via electrostatic bonding after being in touch with EPS.

With -H bonding, the subsequent inhibition of their aggregation, and precipitation, the bonding in the nanoparticles stabilizes (Escárcega-González et al. 2018). To create NPs that have capping and chelating processes, various functional groups associated with Gram-positive and Gram-negative EPS function as stabilizing and lowering agents (Emam and Ahmed 2016). This helps to regulate the thickness, particle dispersal, and form of the NPs (Kanmani and Lim 2013). Mucoadhesion features help in the detection of non-specific protein transporters by the NPs allowing them to gain broader applicability (Kanmani and Lim 2013). Recent studies have demonstrated that the production of AgNPs involved the utilization of structurally characterized EPS from succinoglycan bacteria. *Sinorhizobium meliloti* produces a polymeric material that induces the aldehyde group to oxidize into a carboxyl group-mediated nucleophilic insertion in the reduction of the metal (Kwon et al. 2009). *Alcaligenes faecalis*, *Rhizobium* sp., and *Agrobacterium* sp. are the leading producers of curdlan, a different kind of EPS made up of (1, 3)-D-glucan repeating units connected by beta-(1, 3)-glycosidic linkages. Some are used in the synthesis and stabilization of nanoparticles (Zhang and Edgar 2014). To create derivatives of curdlan, a polymer that is insoluble in water can be carboxylated or oxidized. AgNPs were created by Leung et al. (2010) using carboxymethylated curdlan. It was easier to reduce the silver ions since the negatively-charged hydroxyl and carboxyl groups continued to exist. Another essential element of EPS that helps make graphene nanomaterials is dextran (Hu et al. 2016). Dextran is a multidimensional branched glucan produced mainly through some types of lactic acid bacteria, such as *Leuconostoc mesenteroides* and *Streptococcus mutans*. It is chemically made up of glucose residues linked together by alpha-(1,6) glycosidic bonds. Dextran, which worked as a stabilizing agent and reductant in an aqueous solution, was used to create size-controlled AgNPs by Bankura et al. (2012).

Delftia acidovorans and *Cupriavidus metallidurans* can also manufacture Au NPs greenly. The bacterial biofilms can be harvested for their gold nuggets (Johnston et al. 2013). The results from experiments revealed a nanoparticle Au could prevent the production of biofilms (Reith et al. 2010). By modifying the microbial cell membrane's surface chemistry, and hydrophobicity, they interact with lipids and proteins, and Au NPs prevent biofilm growth (Ikuma et al. 2015).

As a result, the NPs' ability to break through the biofilm is altered. The thickness of the nanoparticles, the surface charge, their chemistry, and their concentration all affect how well they can pierce the biofilm (Ikuma et al. 2015). Following that, the NPs interact with the biofilm's structural elements, which causes the biofilm to disintegrate (Qayyum and Khan 2016; Pinto et al. 2019). Furthermore, there is evidence that it's Au NPs changed groups can boost their ability to inhibit one or more types of biofilm cells. The biofilm can be efficiently interfered with by various factors, including Van der Waals, hydrogen bonds, electrostatic contacts, and hydrophobic interactions (Yu et al. 2018).

13.6 Microbial Biosurfactants for the Production of Nanoparticles

Biosurfactants are amphiphilic compounds with microbial surface activity primarily made by bacteria, fungi, and yeasts. The majority of its hydrophilic component is made up of long-chain or hydroxyl fatty acids. In contrast, their hydrophobic moiety comprises carbohydrates, cyclic peptides, amino acids, carboxylic acids, or phosphates. Glycolipids, lipopeptides, and phospholipids are examples of low-molecular-weight surface active agents (LMW). High-molecular-weight polymers, also known as bio-emulsifying agents like emulsan, are the two categories into which these are separated (Pati et al. 2020). They can alternatively be categorized as (a) glycolipids (rhamnolipids); (b) Mycolic acids, which are hydroxylated and cross-linked fatty acids; or (c) lipopolysaccharides. When metallic nanoparticles are synthesized using biogenic methods, biosurfactants can serve as good capping agents (Płaza et al. 2014). They work by adhering to metallic nanoparticles, stabilizing their surfaces, and preventing future aggregation, all of which contribute to stabilization (Kiran et al. 2011; Gahlawat and Choudhury 2019). Hydrophobic and hydrophilic molecular combinations in classes of amphipathic molecules biosurfactants divide variously polarized fluid stages with hydrogen bonding at their interface (Rodrigues et al. 2006). Microemulsions are water-solvable droplets, which serve as a micro-reactor. The droplet's size decreases as the surfactants' concentration rise, lowering the thickness of the particles. There being water significantly influences the size and form of the NPs. The molar ratio of water (R) determines the particle thickness and mono dispersity (Han et al. 2008).

13.7 Microbial Nanoparticle Synthesis via Biomineralization

Few microbes can reduce metal salts producing metallic ions that concentrate either within or without the microbial cells, mobilizing or immobilizing the salts of metal. They change the metals' oxidation condition through electrochemical reactions to achieve complexation and inactivation, followed by their precipitation, with the aid of efflux pumps.

For instance, gold (I)-thiosulfate is metabolized by *Acidithiobacillus thiooxidans* cells into Au(I) and thiosulfate (S2O32-) ions. Whenever Au (I) degrades to atomic gold inside the cells, thiosulfate is an energy source. This atomic gold precipitates within the microbial cells to create NPs throughout the late stationary stage and is subsequently liberated from the cells. Finally, the bulk solution's gold particles are turned into the wire at micron scales and octahedral gold (Lengke and Southam 2005).

Added research indicated one of three probable methods by which generation of iron sulfide, selective reducing actions, or a metabolic process are all possible ways that the sulfate-reducing bacteria will reduce the gold (I)-thiosulfate compound. The deposition of gold (I)-thiosulfate is essential in the initial stage, onto recently generated iron sulfide surfaces sulfate-reducing bacteria, resulting in the production of elemental gold. During the second step, using microbes that reduce sulfate will discharge through the outer membrane pores causing the hydrogen sulfide (HS-) to decrease the gold (I)-thiosulfate complex, which led to the precipitation of atomic gold. In the third step, the gold (I)-thiosulfate complex was broken down into the cells that liberate Au(I) and thiosulfate ions (Lengke and Southam 2005; Lengke et al. 2006).

13.8 Magnetic Nanoparticles Made by Microbes

There are numerous applications for the magnetic nanoparticle termed as magnetosomes, generated by magnetotactic bacteria (MTB), known as the bacterial magnetic nanoparticle (BMP) (Vargas et al. 2018). These are internal magnetic particulates composed of iron oxides and sulfides that work as bacterial compass needles to direct bacteria through oxygen variations in aquatic environments under the impact of Earth's geomagnetic. BMPs are typically transported by phospholipid vesicles and have the potential to spread in underwater mediums.

BMP biomineralization happens in several stages; the cytoplasmic membrane is invaded by a GTPase in the first stage, followed by building a linear chain throughout the cytoskeletal filaments. The second stage includes the accumulation of ferrous ions using transmembrane iron carriers within the vesicles. The third phase involves the induction of BMP proteins, which results in the gradual buildup of supersaturating iron levels and the fractional reduction and dehydrating of ferrihydrite to magnetite (Arakaki et al. 2008).

Shewanella oneidensis produced magnetite using passive and active methods in a different investigation. In a high-pH environment, ferrihydrite is actively used to produce Fe^{2+} as a supply of electron acceptor. The transition of Fe2+ and Fe3+ adjacent to negative-charged cell walls occurs next, which causes supersaturation and the precipitation of magnetite (Li et al. 2011). This membrane controls the thickness, crystallization, and shape of the particle. The phospholipid bilayer, which has 20–40 different surface protein species, can capture bacterial nanoparticles (Grünberg et al. 2004).

Although additional MTB species can be grown, the BMPs utilized in nanobiotechnology and nanomedicine are primarily derived from *Magnetospirillum magneticum* AMB-1 and *Magnetospirillum gryphiswaldense* MSR-1 (Chen et al. 2016).

13.9 Stable Quantum Dot Nanoparticles Made by Microbes

A wide range of biological, biomedical, optical, and optoelectronic application domains, including biosensors, photovoltaics, transistors, oil exploration, biomedicine, imaging, and solar cells, are recently becoming increasingly dependent on fluorescent or quantum dots (QDs) nanomaterials. This is because of their unique size-dependent characteristics. According to improved biocompatibility and lower production of harmful byproducts during their synthesis, they are more practical, pointing the way toward environmentally friendly technologies. Bidentate thiols, such as dithiothreitol (DTT), mercaptosuccinic acid (MSA), and mercaptopropionic acid (MPA), and CdS, CdSe, and CdTe QDs have currently been synthesized using ligands with different functional compounds (amino, hydroxyl, and a carboxylic acid, among others). These cadmium- and tellurite-resistant Antarctic bacteria, *Pseudomonas* (eight isolates), *Psychrobacter* (three isolates), and *Shewanella* (one isolate), may synthesize CdS and CdTe QDs in response to hazardous oxidizing heavy metals like Cd and Te with a time-dependent shift in fluorescence emission color (Plaza et al. 2016). One example of nanomaterials with fluorescent tags is CdSe. In *S. cerevisiae*, CdSe nanoparticles were produced intracellularly by Cui et al. (2009) utilizing genetic engineering methods. When in contact with inorganic ions, in yeast the glutathione production genes GSH1, GSH2, and GLR1 go inactive, which in turn causes a considerable decrease in fluorescence that is inversely correlated with the production of CdSe nanoparticles. It was discovered that Na2SeO3 was converted to selenocysteine $(Cys\text{-}Se)_2$, a selenium compound that comprises cysteine. After that, $CdCl_2$ was used to make CdSe nanomaterials. Halophilic bacteria like *Halobacillus* sp. were investigated in the following investigation by Bruna et al. (2019). DS2 built CdS QDs having improved NaCl resistance (Bruna et al. 2019). Órdenes-Aenishanslins et al. (2020) created a cation exchange-based, adjustable ternary CdSAg QD. By exposing the interaction between bacterial cells with cysteine and CdCl2, nanoparticles were also made extracellularly within the cells of the bacteria. The stabilization of the nanoparticle in this reaction was accomplished by cellular biomolecules and was reliant on the synthesis of S_2, which was carried out by enzymes called cysteine desulfhydrases.

13.10 The Synthesis of Nanoparticles from Microbial Organic Particles

Nanofibers are created using bacterial cellulose (BC), which is also employed to give the nanofibers a bactericidal quality. In a procedure that is regarded as green, bactericidal chitin (Ch) and bacterial cellulose (BC) nanofibers were combined to create a nanocomposite of BC-Ch. Additionally, Ch79d was fed to *Acetobacter aceti* to create 50–100 nm-wide nanofibrils and biosynthesize bio-BC-Ch79d nanocomposites (Butchosa et al. 2013).

The making of nanoparticles is discovered to involve a variety of microbial elements (Table 13.1). These nanoparticles are proven to operate as effective anti-biofilm agents by inhibiting the QS mechanism.

13.11 Quorum Sensing

The process of Quorum sensing is a density-dependent, interaction form of cell to cell communication related chemical substance substitutes (Lobedanz and Søgaard-Andersen 2003; Phelan et al. 2012), chemical signaling (Eberhard et al. 1981), signaling linked utilizing an electrical impulse (Nielsen et al. 2010; Shrestha et al. 2013), is what allows bacterial cells can adapt to and keep track of different circumstances in the environment. Quorum sensing was the term referring to a density-dependent communications medium in bacteria that is caused by tiny chemicals (autoinducers) (QS). *Vibrio fischeri* was the first organism to exhibit this mechanism (Nealson et al. 1970). QS is a word conceptualized by Fuqua et al. (1994).

Its multistep methodology that results in the formation of biofilms involves the manifestation of many different reactions of genes to the same organism's planktonic form of microbial cells (Donlan 2002). The transformation of unicellular organisms into their motile forms causes the production of different chemicals that promote genetic alterations within the cells. As a reaction, microcolonies that are sessile create an extracellular polymer that is dense (EPS) that wraps the bacterial cells physically. Such EPS is composed of exopolysaccharides, proteins, exogenous DNA (e DNA), and other molecular components. Through the quorum sensing process, this situation causes the biofilm to develop QS (Lahiri et al. 2019; Sonawane et al. 2022).

The biofilm structure is caused by the permanent attachment of microbial cells to surfaces, which is preceded by the synthesis of QS particles, mobility of biofilm particles, substrate digestion by diverse sessile microcolonies, the development of EPS, and ultimately spreading of the sessile populations (Lahiri et al. 2019).

The foundation of QS was the production of extracellular substances called autoinducers (AIs), which allow bacterial cells to interact with one another. This technique aids in organizing the many expressions of bacterial cells so they can react to environmental changes. Gram-positive, as well as Gram-negative, bacterial cells exhibit this method. According to studies, Gram-positive microorganisms employ

Table 13.1 Formation of nanoparticles by microbes

Classification	Microorganism	Element used	Size of nanoparticles (nm)	Reference
Actinomycetes	*Streptacidiphilus durhamensis* *Streptomyces griseoruber*	Ag Au	8–48 5–50	Buszewski et al. (2018) Ranjitha and Rai (2017)
	Streptomyces xinghaiensis OF *Rhodococcus* sp. NCIM 2891	Ag Ag	5–20 10–15	Wypij et al. (2018) Otari et al. (2014)
Fungi	*Penicillium diversum* *Fusarium oxysporum* JT1 *Trichoderma harzianum* *Aspergillus terrous* *Colletotrichum* sp.	Ag Au CdS ZnO AlO	10–15 22 3–8 28–63 30–50	Ganachari et al. (2012) Thakker et al. (2013) Bhadwal et al. (2014) Baskar et al. (2015) Suryavanshi et al. (2017)
Yeast	*Rhodosporidium diobovatum* *Saccharomyces cerevisiae*	PbS Ag.Au Nanopiates	2–5 2–20	Seshadri et al. (2011) Korbekand et al. (2016) Yang et al. (2017)
	Pichia kudriavzevia	ZnO	10–60	Moghaddam et al. (2017)
	Rhodotoruia glutinis	Ag	15	Cunha et al. (2018)
Virus	Tobacco mosaic virus (TMV)	Pd.Au	3–4,5	Kobayashi et al. (2012) Fan et al. (2013)
	M13 virus	TiO_2	20–40	Chen et al. (2013)
	Hepatitis E virus	Nanoconjugate	27–34	Chen et al. (2018)
	Potato virus X Muticum	Nanocarriers ZnD	13 0.57	Le et al. (2017) Sanaeimehr et al. (2018)
Algae	*Sargassum amansit* *Gelidium*	Ag Ag	27–54 51	Pugazhendhi et al. (2018) Kim et al. (2016)
	Laminaria japonica	Au	8	González-Ballesteros et al. (2017)
	Cystoseira baccata *Chlorella vulgaris* *Spirogyra varians* *Chlorelix vulgaris*	Pd Ag Au	5–20 35 2–10	Garole et al. (2019) Salari et al. (2016) Annamala and Nallomuthu

(continued)

Table 13.1 (continued)

Classification	Microorganism	Element used	Size of nanoparticles (nm)	Reference
Bacteria	*Bacillus subtilis* *Lactobacillus* sp. *Lactobacillus* sp.	TiO_2 TiO_2 TiO_2	10–30 50–100 50–100	Dhandapani et al. (2012) Ahmad et al. (2014) Ahmad et al. (2013)
	Escherichia coli *Exiguobacterium aurantiacumm* *Brevundimonas diminuta*	Ag Ag Ag	5–50 5–50 5–50	Saeed et al. (2020) Saeed et al. (2020) Saeed et al. (2020)
	Acinetobacter sp. SW30 *Lactobacillus kimchicus* DCY51 *Paracoccus haeundaensis* BC74171 *Micrococcus yunnanensis* *Mycobacterium* sp.	Au Au Au Au Au	15–40 5–30 20.93 ± 3.46 53.8 5–55	Wadhwani et al. (2016) Markus et al. (2016) Patil et al. (2019) Jafari et al. (2018) Camas et al. (2018)
	Lactobacillus sp. *Lactobacillus sporogenes*	CdS ZnO	2.5–5.5 145.70	Prasad and Jha (2010) Mishra et al. (2013)
	Lactobacillus fermentum *Shewanella loihica*	Iron oxide Cu	10–15 10–16+	Park et al. (2014) Lv et al. (2018)

autoinducing proteins (AIPs) to communicate, while Gram-negative microorganisms include three major groups of AIs (Raffa et al. 2005). Quorum quenching (QQ) is a method for inhibiting the QS system (Dong et al. 2002). Multiple techniques, including competitive inhibition and QS output cleavage, are required for the QQ process.

From *Bacillus* sp. bacterial quorum sensing (QS) utilizes quorum sensor molecules, which were isolated and separated. The quenching of the quorum ability of the nanocatalyst r-AiiA-MNP was assessed following their molecular attachment to their magnetic nanoparticles (MNPs), and it was shown to be successful in reducing QS (Beladiya et al. 2015). The las network is composed of the regulating element las R, which produces the Las R protein, and the *las I* gene, which controls the production of the 3-oxo-C12-HSL chemical messengers linked with the AHL group. The virulence gene is triggered by the LasR/3-oxo-C12-HSL. The rhlR and

rhlI genes make up the real system. These further cause the las I system, which is in charge of synthesizing pyocyanin, rhamnolipids, and swarming motilities, to be activated. The las control is the rhl system. Among the other two networks, PQS functions as an intermediary. The PqsA E controls the conversion of 2-heptyl-4-quinolones (HHQ) into 2-heptyl-3-hydroxy-4-quinolone, acting as a precursor for HHQ.

13.12 Mechanism of Gram-Negative Microorganism Quorum Sensing

The messenger molecules known as autoinducers (AI), such as acetyl homoserine lactone (AHL) and additional compounds whose formation is reliant upon S-adenosylmethionine (SAM), were employed by Gram-negative bacterial cells to interact (Walker et al. 2011). SAM functions as an amino acid remover necessary for the synthesis of acyl-homoserine lactones (Whitehead et al. 2001). According to a report, SAM is needed for the manufacture of N-(3-oxo octanoyl)-L-homoserine lactone in *E. coli* via plasmid-associated Lux I (Hanzelka and Greenberg 1996).

The cell membrane's outer layer isn't a barrier to the AIs generated by the bacterial cells. High cell density (HCD) causes an increase in AIs, which controls the regulatory elements for the proteins linked to the QS process. Numerous messenger molecules, such as 2-heptyl-3-hydroxy-4-quinolone from *P. aeruginosa* and 3-hydroxy-palmitic acid from *Ralstonia solanacearum*, are linked to the Gram-negative microbial cells (Flavier et al. 1997). Another one is a nosocomial reactive illness bacterium that is still linked to illnesses such as cystic fibrosis (CF), respiratory infections, and several forms of cutaneous and burned serious infections (Ammons et al. 2009). There are three main QS circuits in these Gram-negative bacteria. One such circuit includes the protein LasR, which codes for the transcriptional regulator LasR, and the protein LasI, which is responsible for producing the autoinducer. Both the gene rhlR, which promotes the transcriptional regulator RhlR, and the protein rhlI, which is involved in the generation of the autoinducer N-(butonyl)-L-Homoserine lactone, make up a significant QS circuit (Pearson et al. 1994, 1995). Alkyl quinolones, particularly 2-heptyl-3-hydroxy-4-quinolones, are linked with the third QS loop, which is also present in P. aeruginosa and predominantly controlled by the pqsABCDEH and PqsR activator proteins (Pesci et al. 1999).

13.13 Quorum Sensing Suppression by Microbiogenic Nanoparticles

The capacity of NPs to stop the proliferation of microbial cells and hence combat harmful organisms makes them the most often used drug delivery system. NPs have a variety of inhibitory mechanisms for microbial and biofilm growth. Numerous

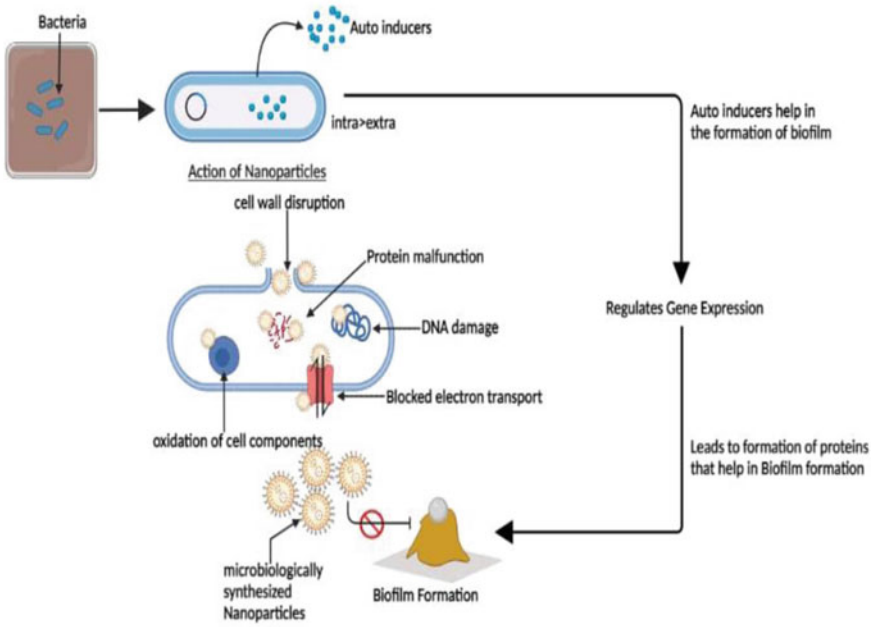

Fig. 13.1 Nanoparticles synthesized from microbes and their role in biofilm inhibition

investigations were carried out to figure out the most likely method by which the NPs might prevent microbial growth (Fig. 13.1).

Due to the small number of research that has been conducted, information about the reduction of the QS procedure by NPs is quite restricted, despite the field's potential being intriguing. By interfering with the medium of cell-cell interaction or by muzzling the stimuli connected to the QS system, NPs function as strong inhibitors of QS. As a result, they hamper the production of numerous signaling elements and prohibit the synthesis of molecule-receptor complexes. As a result, the signaling molecules loop is stopped (Sadekuzzaman et al. 2015); due to their potent antibacterial action, AgNPs or silver nanoparticles, have been used as QQ regulators (Castellano et al. 2007; Chen and Schluesener 2008).

AgNPs' broad range of antimicrobial properties (Kim et al. 2007; Lara et al. 2011; Brandt et al. 2012), ease of action due to their physicochemical properties, and surface area to volume proportion have all piqued the attention of the scientific community (Kim et al. 2007). Other NPs from microorganisms, including AuNPs, TiO2, SiO2, and ZnO, are effective at suppressing the QS system and preventing the formation of the biofilm (Shah et al. 2008; Samanta et al. 2017; Al-Shabib et al. 2018).

13.14 Quorum Sensing Suppression by Silver Nanoparticles (AgNPs)

Ever since the dawn of time, people have been aware of the antibacterial characteristics of noble metals. Silver compounds, metallic silver, and salts have all been used to successfully inhibit microbial development since antiquity. Silver nanoparticles (AgNPs) were created, thanks to advancements in nanotechnology, and because of their huge surface area-to-volume proportion, they demonstrate excellent antimicrobial activity against several pathogenic infections. Multiple investigations have shown the efficacy of AgNPs against both multidrug-resistant bacterial biofilms and planktonic bacterial cells.

AgNPs have a significant surface area to volume proportion, a neutral nature, configurable physical parameters like size and shape, and biocompatibility and have shown bactericidal or bacteriostatic activities at very low concentrations, among other benefits for anti-biofilm applications. Directly acting as an antibacterial agent are AgNPs and the silver ions (Ag+) are produced when AgNPs dissolve. Multiple elements of both unicellular microbial species and biofilms can interact with both AgNPs and Ag+ ions. They hinder bacterial metabolism and exterior cellular operations through these interactions. AgNPs' overall antimicrobial effect is a result of a mixture of cell membrane breakdown, specific proteins dislocation, cellular membrane downregulation, protein denaturation, blocking of the electron transport chain (ETC), oxidative stress brought on by the generation of reactive oxygen species (ROS), impairing of nucleic acids, and oxidative stress itself (Gupta et al. 2018; Prasad et al. 2017).

Furthermore, it has been shown that green-synthesized NPs were crucial in preventing infections brought on by microorganisms. According to studies, AgNPs may prevent the production of messenger elements by suppressing LasI/Rhl I synthase. AgNPs may inhibit *P. aeruginosa*'s quorum sensing (Ali et al. 2017).

The reduction of silver nitrate solution using *Azadirachta indica*-mediated leaf extract to produce silver nanomaterials. Gram-positive *Staphylococcus aureus* and model Gram-negative *Escherichia coli* bacteria were utilized to examine the antimicrobial activities of the generated AgNPs. The zone of Inhibitory activity against *S. aureus* and *E. coli* was found to be 10 mm and 13 mm, correspondingly, and the biofilm assessment revealed a substantial influence on nanoparticle concentration. The creation of biofilms is necessary for the production and secretion of EPS (exopolymeric substances). In general, bacteria create biofilms and colonize in response to their environment. According to certain findings, 100 nm-sized AgNPs can reduce biofilm activity by 90–95%. According to certain publications, biofilm development has become more distinct as the number of nanoparticles has increased. This indicates that microorganisms can withstand the toxicity of nanoparticles and may provide better remediation in the future. AgNPs generated extracellularly by *Cedecea* sp. stand out for their exceptional physical stability, which results in unabated antibacterial activity for periods longer than a year.

AgNPs can lock the reactive groups of numerous molecules, including LasI or RhlI synthase, as well as their neighboring groups being available, according to *in*

silico investigations employing molecular docking. AgNPs successfully block the reactive sites and strongly inhibit the quorum sensing (QS) process. AgNPs can disrupt the transcriptional factors that inactivate the LasR or RhlR mechanism, hence lowering the activity of the QS proteins. AgNPs can also successfully block messenger molecules like LasI and RhlI so that they are acting anti-QS agents. Studies have also revealed that *Rhizopus arrhizus* metabolites used to generate AgNPs in microfabricated forms hinder *P. aeruginosa*'s QS system (Singh et al. 2015). At a dosage of 0–25 g/ml, it was demonstrated that these microfabricated AgNPs could significantly lower the synthesis of signaling molecules. Furthermore, it has been shown that these nanostructured NPs can downregulate the action of the lasA and lasB proteins up to 79–84%. The AHL-LasR complex induces the action of the specific QS elements, including lasA, lasB, lasI, lasR, rhlI, rhlR, rhlA, phzA1, and fabH2. The nanostructured AgNPs were successful in lowering the activity of the QS genes.

Contrary to what researchers observed about the effects on planktonic cells, it has been observed that *V. vinifera* cane extract inhibits the metabolic activity of biofilm cells. The greatest extract concentration (2% (v/v)) reduced metabolic activity by 32% relative to the control. Similar to how they affected planktonic cells, polydisperse AgNPs were more successful in reducing the activity of the cells that make up biofilms. At a dosage of 20 mg/L pAgNPs/e, the strongest reduction in metabolic activity (80% relative) was noted. Less than 50% metabolic activity was reduced in the biofilm cells by the monodisperse AgNPs (20 mg/L).

Cyperus esculentus extracts were effectively employed as efficient reductants in the work by (Ajayi et al. 2015) to create silver nanomaterials. In these methods, *Cyperus esculentus* extracts are made by crushing and spending a lot of time incubating. The outcome shows that the produced particles are active in avoiding biofilm formation, improving the efficiency of antibiotic and antifungal drugs through synergistic interactions, and suppressing microbial growth.

13.15 Quorum Sensing Inhibition Using Microbiogenic Gold Nanoparticles

Due to its straightforward manufacturing process, ease of usage, and relative lack of toxicity when compared to other commonly used nanomaterials, Au NPs have several uses (Capek 2014). *Salmonella typhi*, Bacillus Calmette-Guerin, and methicillin-resistant *S. aureus* (MRSA) are just a few of the bacteria that Au NPS effectively combated (Zhao et al. 2010; Lima et al. 2013; Bindhu and Umadevi 2014). Investigations have demonstrated that the acyl-homoserine lactone lactonase enzyme connected to gold NP involves in preventing *Proteus* sp. quorum sensing (Vinoj et al. 2015). N-acyl-homoserine lactonase that was present on their surface helps in the breakdown of N-hexanoyl-L-homoserine lactone.

Additionally, the proteobacterium *Shewanella oneidensis* MR-1 was used to biogenically synthesize gold-silver bimetallic nanoparticles. These particles demonstrated antibacterial characteristics and were used to prevent the biofilm

formation of *P. aeruginosa*, *S. aureus*, *E. coli*, and *Enterococcus faecalis* cultures at a dosage of 250 μM. (Ramasamy and Lee 2016).

Hence, they were able to limit EPS generation and metabolic processes, which prevented the development of biofilm and altered the microbial cells' hydrophobicity (Samanta et al. 2017). The consistency of the NPs, which in turn played a considerable impact in decreasing pyocyanin synthesis from *P. aeruginosa*, was brought about by the Au NP formed from Laccaria fraternal's mycelium (Samanta et al. 2017).

13.16 Quorum Sensing Suppression by ZnO Nanoparticles

Green synthesis sometimes referred to as biosynthesis, is a natural process of creating ZnO NPs that employ microorganisms as the reducing agents. These microorganisms include algae, fungi, yeast, bacteria, and plant extracts (Bhuyan et al. 2015; Kavitha et al. 2023). Even if utilizing microbes as reducing and stabilizing agents during the manufacture of ZnO nanomaterials has its advantages, more vigilance is used due to the virulence of some microorganisms and incubation problems. Rhizosphere microorganisms called plant growth-promoting microbes (PGPMs) can invade the root habitat. Among the microorganisms that are present in this region are fungi and bacteria that can enter the soil around the roots and rhizosphere. Some *Trichoderma* species that have been shown to interact symbiotically or as endophytes with plant roots are included in the group of fungi that promote plant growth (PGPFs). Numerous studies on *Trichoderma* as a biological control agent, biofertilizer, fungicide, and plant development booster have been conducted (Prasad and Rai 2023). The therapeutic capacity of *Trichoderma* compounds has, however, received scant attention.

Trichoderma spp. was chosen to biosynthesize ZnO NPs and examine their antimicrobial efficacy against the human diseases *S. aureus* and *E. coli* along with their ability to prevent biofilm formation (*S. aureus*) when used at various ZnO NP doses. Using a 96-well microplate, the anti-biofilm abilities of ZnO NPs and tetracycline were assessed. Planktonic *S. aureus* treated with reagents for 24 h at a time was examined for biofilm formation inhibition. An established crystal violet assay for biofilm biomass revealed that ZnO NPs were highly effective than tetracycline at removing the formed biofilm generated by *S. aureus*.

In a *P. aeruginosa* colony obtained through cystic fibrosis (CF; García-Lara et al. 2015), the quorum sensing (QS) mechanism's suppression had a significant impact on the biofilm's development. The QS elements within Gram-negative microbial cells can be downregulated by these NPs. Researchers demonstrated that downregulating lasR, lasI, rhl I, and rhl R allowed ZnO NPs to block QS in *P. aeruginosa* (Saleh et al. 2019). Additional research demonstrated the efficacy of ZnO NPs inhibiting the pqs and las mechanism of QS as well as their ability to decrease the floating and clumping motility of *P. aeruginosa* (Khan et al. 2020). ZnO nanoparticles caused the production of the pyocyanin-associated phz operon to be repressed as a consequence of the efflux of the zinc ion efflux pump of the czc

operon and various other transcriptional activators, including the porin protein opdT and type III inhibitor ptrA. Additionally, *P. aeruginosa*'s membrane hydrophobicity can be increased by the ZnO NPs (Lee et al. 2014).

13.17 Quorum Sensing Suppression by Various Other Nanoparticles

Other nanomaterials from microbial sources, including AuNPs, TiO_2, SiO_2, and ZnO, are effective against the QS technique and prevent the production of the biofilm (Shah et al. 2008; Samanta et al. 2017; Al-Shabib et al. 2018).

According to experimental results, AgCl-TiO_2 nanomaterials were an excellent anti-quorum sensing material that inhibits violaceum (Naik and Kowshik 2014). Additionally, it has been observed that the silver in Ag nanomaterials can stop the development of violacein, which can specifically disrupt the QS process. Additionally, AgCl-TiO_2 NPs were shown to block QS even without having oxo-octanoyl homoserine lactone.

Studies have demonstrated that NPs covered with cyclodextrin help in the suppression of *V. fischeri*'s AHL-dependent QS (Miller 2015). According to the research, having cyclodextrin in combination with Si-NP is utilized in removing the AHL compound from the surrounding and lowering bioluminescence. Further research revealed that these NPs can suppress the LuxA and LuxR proteins.

13.18 Conclusion

Quorum sensing, which involves examining the synthesis of autoinducers, allows microbial organisms to detect the presence of other organisms in their environment. The formation of a biofilm is facilitated by this process, which also enables bacterial cells to interact with one another. The major modes of action of QS inhibition include signal receptor blockade, inhibition of messenger production, and interrupting the QS pathway. At the moment, the topic is concentrated on developing chemicals with microbial origins to stop the bacterial QS mechanism. Infections related to medical implants are more frequently caused by microbial biofilm. Therefore, the need for innovative treatment methods for infections caused by device-associated biofilms is critical. By removing the exopolysaccharides (EPS) of the biofilm membrane and eliminating the pathogen, the usage of nanomaterials has developed as a successful tactic for preventing biofilm development. Nanomaterials' low cytotoxicity and unique modes of action are major considerations in their use for biofilm therapy. Physicochemical characteristics of nanoparticles, like their dimensions, shape, surface properties, organization, aggregation status, and cellular components under interaction with the nanomaterials, all have a significant impact on how poisonous they are. The time-consuming methods involved in purification and our limited understanding of the mechanics are the few drawbacks of microbial nanoparticle manufacturing. Furthermore, it is crucial to manage the dimensions,

forms, and monodispersity of the solution phase. Building up production-level manufacturing for commercial purposes is a significant task. Therefore, it is necessary to address several crucial situations, which include determining the best organism based on their development rates, metabolic activities, and biosynthetic pathways, selecting the catalytic state (microbial proteins), that can either be complete cells, unprocessed proteins, or purified compounds and can speed up reactions, and finding the better environments for cell development and metabolic activity. Maximum biomass synthesis, appropriate reaction circumstances for improved elimination of undesirable excess substances and byproducts, enhanced extraction and separation processes (freeze-thawing, heating processes, and osmotic shock) of the nanoparticles, and improved containment of the generated NPs without accumulation. A novel chemical that may be utilized to downregulate the operon linked to quorum-sensing genes or boost quorum-quenching action to avoid biofilm formation. Anyhow QS suppression has a lot of promise as an anti-infective, further study and research are required to help in understanding the nature of its action and therapeutic relevance. Although there is still a requirement for further advances to avoid regrowth following biofilm therapy, it is anticipated that nanomaterial-based treatment approaches will continue to develop more complicated or sophisticated processes of removing the EPS and destroying the microorganism.

References

Abidi SH, Sherwani SK, Siddiqui TR, Bashir A, Kazmi SU (2013) Drug resistance profile and biofilm forming potential of Pseudomonas aeruginosa isolated from contact lenses in Karachi-Pakistan. BMC Ophthalmol 13:57. https://doi.org/10.1186/1471-2415-13-57

Ahmad R, Khatoon N, Sardar M (2013) Biosynthesis, characterization and application of TiO2 nanoparticles in biocatalysis and protein folding. J Proteins Proteomics 4:115–121

Ahmad R, Khatoon N, Sardar M (2014) Antibacterial effect of green synthesized TiO2 nanoparticles. Adv Sci Lett 20:1616–1620. https://doi.org/10.1166/asl.2014.5563

Ajayi IA, Raji AA, Ogunkunle EO (2015) Green synthesis of silver nanoparticles from seed extracts of Cyperus esculentus and Butyrospermum paradoxum. IOSR J Pharm Biol Sci Ver I 10(4): 2319–7676

Ali SG, Ansari MA, Sajid Jamal QM, Khan HM, Jalal M, Ahmad H, Mahdi AA (2017) Antiquorum sensing activity of silver nanoparticles in P. aeruginosa: an in silico study. In Silico Pharmacol 5: 1–7

Al-Shabib NA, Husain FM, Hassan I, Khan MS, Ahmed F, Qais FA et al (2018) Biofabrication of zinc oxide nanoparticle from Ochradenus baccatus leaves: broad-spectrum Antibiofilm activity, protein binding studies, and in vivo toxicity and stress studies. J Nanomater 2018:8612158. https://doi.org/10.1155/2018/8612158

Ammons MCB, Ward LS, Fisher ST, Wolcott RD, James GA (2009) In vitro susceptibility of established biofilms composed of a clinical wound isolate of Pseudomonas aeruginosa treated with lactoferrin and xylitol. Int J Antimicrob Agents 33(3):230–236

Anil Kumar S, Abyaneh MK, Gosavi SW, Kulkarni SK, Pasricha R, Ahmad A et al (2007) Nitrate reductase-mediated synthesis of silver nanoparticles from AgNO3. Biotechnol Lett 29:439–445. https://doi.org/10.1007/s10529-006-9256-7

Arakaki A, Nakazawa H, Nemoto M, Mori T, Matsunaga T (2008) Formation of magnetite by bacteria and its application. J R Soc Interface 5:977–999. https://doi.org/10.1098/rsif.2008.0170

Aziz N, Fatma T, Varma A, Prasad R (2014) Biogenic synthesis of silver nanoparticles using Scenedesmus abundans and evaluation of their antibacterial activity. J Nanoparticles 2014:689419. https://doi.org/10.1155/2014/689419

Aziz N, Faraz M, Pandey R, Sakir M, Fatma T, Varma A, Barman I, Prasad R (2015) Facile algae-derived route to biogenic silver nanoparticles: synthesis, antibacterial and photocatalytic properties. Langmuir 31:11605–11612. https://doi.org/10.1021/acs.langmuir.5b03081

Aziz N, Pandey R, Barman I, Prasad R (2016) Leveraging the attributes of Mucor hiemalis-derived silver nanoparticles for a synergistic broad-spectrum antimicrobial platform. Front Microbiol 7:1984. https://doi.org/10.3389/fmicb.2016.01984

Aziz N, Faraz M, Sherwani MA, Fatma T, Prasad R (2019) Illuminating the anticancerous efficacy of a new fungal chassis for silver nanoparticle synthesis. Front Chem 7:65. https://doi.org/10.3389/fchem.2019.00065

Bankura KP, Maity D, Mollick MMR, Mondal D, Bhowmick B, Bain MK et al (2012) Synthesis, characterization and antimicrobial activity of dextran stabilized silver nanoparticles in aqueous medium. Carbohydr Polym 89:1159–1165. https://doi.org/10.1016/j.carbpol.2012.03.089

Barber-Zucker S, Zarivach R (2017) A look into the biochemistry of magnetosome biosynthesis in magnetotactic bacteria. ACS Chem Biol 12:13–22. https://doi.org/10.1021/acschembio.6b01000

Baskar G, Chandhuru J, Sheraz Fahad K, Praveen AS, Chamundeeswari M, Muthukumar T (2015) Anticancer activity of fungal l-asparaginase conjugated with zinc oxide nanoparticles. J Mater Sci Mater Med 26:43. https://doi.org/10.1007/s10856-015-5380-z

Beladiya C, Tripathy RK, Bajaj P, Aggarwal G, Pande AH (2015) Expression, purification and immobilization of recombinant AiiA enzyme onto magnetic nanoparticles. Protein Expr Purif 113:56–62

Bhadwal AS, Tripathi RM, Gupta RK, Kumar N, Singh RP, Shrivastav A (2014) Biogenic synthesis and photocatalytic activity of CdS nanoparticles. RSC Adv 4:9484–9490. https://doi.org/10.1039/c3ra46221h

Bhuyan T, Mishra K, Khanuja M, Prasad R, Varma A (2015) Biosynthesis of zinc oxide nanoparticles from *Azadirachta indica* for antibacterial and photocatalytic applications. Mater Sci Semicond Process 32:55–61

Bindhu MR, Umadevi MJML (2014) Antibacterial activities of green synthesized gold nanoparticles. Mater Lett 120:122–125

Brandt O, Mildner M, Egger AE, Groessl M, Rix U, Posch M et al (2012) Nanoscalic silver possesses broad-spectrum antimicrobial activities and exhibits fewer toxicological side effects than silver sulfadiazine. Nanomedicine 8(4):478–488

Bruna N, Collao B, Tello A, Caravantes P, Díaz-Silva N, Monrás JP et al (2019) Synthesis of salt-stable fluorescent nanoparticles (quantum dots) by polyextremophile halophilic bacteria. Sci Rep 9:1953. https://doi.org/10.1038/s41598-018-38330-8

Buszewski B, Railean-Plugaru V, Pomastowski P, Rafińska K, Szultka-Mlynska M, Golinska P et al (2018) Antimicrobial activity of biosilver nanoparticles produced by a novel Streptacidiphilusdurhamensis strain. J Microbiol Immunol Infect 51:45–54. https://doi.org/10.1016/j.jmii.2016.03.002

Butchosa N, Brown C, Larsson PT, Berglund LA, Bulone V, Zhou Q (2013) Nanocomposites of bacterial cellulose nanofibers and chitin nanocrystals: fabrication, characterization and bactericidal activity. Green Chem 15:3404–3413. https://doi.org/10.1039/c3gc41700j

Capek I (2014) Preparation and functionalization of gold nanoparticles. J Surf Sci Technol 29:1–18

Capeness MJ, Echavarri-Bravo V, Horsfall LE (2019) Production of biogenic nanoparticles for the reduction of 4-Nitrophenol and oxidative laccase-like reactions. Front Microbiol 10:997. https://doi.org/10.3389/fmicb.2019.00997

Camas M, Camas AS, Kyeremeh K (2018) Extracellular synthesis and characterization of gold nanoparticles using Mycobacterium sp. BRS2A-AR2 isolated from the aerial roots of the Ghanaian mangrove plant, Rhizophora racemosa. Indian J Microbiol 58:214–221. https://doi.org/10.1007/s12088-018-0710-8

Carnes EC, Lopez DM, Donegan NP, Cheung A, Gresham H, Timmins GS et al (2010) Confinement-induced quorum sensing of individual Staphylococcus aureus bacteria. Nat Chem Biol 6:41–45. https://doi.org/10.1038/nchembio.264

Castellano JJ, Shafii SM, Ko F, Donate G, Wright TE, Mannari RJ et al (2007) Comparative evaluation of silver-containing antimicrobial dressings and drugs. Int Wound J 4(2):114–122

Chen X, Schluesener HJ (2008) Nanosilver: a nanoproduct in medical application. Toxicol Lett 176(1):1–12

Chen PY, Dang X, Klug MT, Qi J, Dorval Courchesne NM, Burpo FJ et al (2013) Versatile three-dimensional virus-based template for dye-sensitized solar cells with improved electron transport and light harvesting. ACS Nano 7:6563–6574. https://doi.org/10.1021/nn4014164

Chen C, Wang P, Li L (2016) Applications of bacterial magnetic nanoparticles in nanobiotechnology. J Nanosci Nanotechnol 16:2164–2171. https://doi.org/10.1166/jnn.2016.10954

Chen CC, Stark M, Baikoghli M, Cheng RH (2018) Surface functionalization of hepatitis E virus nanoparticles using chemical conjugation methods. J Vis Exp 2018:e57020. https://doi.org/10.3791/57020. PMID: 29806824

Chioro A, Coll-Seck AM, Høie B, Moeloek N, Motsoaledi A, Rajatanavin R et al (2015) Antimicrobial resistance: a priority for global health action. Bull World Health Organ 93:439. https://doi.org/10.2471/BLT.15.158998

Costerton JW, Stewart PS, Greenberg EP (1999) Bacterial biofilms: a common cause of persistent infections. Science 284:1318–1322. https://doi.org/10.1126/science.284.5418.1318

Cui R, Liu HH, Xie HY, Zhang ZL, Yang YR, Pang DW et al (2009) Living yeast cells as a controllable biosynthesizer for fluorescent quantum dots. Adv Funct Mater 19:2359–2364. https://doi.org/10.1002/adfm.200801492

Cunha FA, da Cunha MCSO, da Frota SM, Mallmann EJJ, Freire TM, Costa LS et al (2018) Biogenic synthesis of multifunctional silver nanoparticles from Rhodotorula glutinis and Rhodotorula mucilaginosa: antifungal, catalytic and cytotoxicity activities. World J Microbiol Biotechnol 34:127. https://doi.org/10.1007/s11274-018-2514-8

Das VL, Thomas R, Varghese RT, Soniya EV, Mathew J, Radhakrishnan EK (2014) Extracellular synthesis of silver nanoparticles by the Bacillus strain CS 11 isolated from industrialized area. 3 Biotech 4:121–126. https://doi.org/10.1007/s13205-013-0130-8

Dasgupta A, Sarkar J, Ghosh M, Bhattacharya A, Mukherjee A, Chattopadhyay D et al (2017) Green conversion of graphene oxide to graphene nanosheets and its biosafety study. PLoS One 12:e0171607. https://doi.org/10.1371/journal.pone.0171607

Dhandapani P, Maruthamuthu S, Rajagopal G (2012) Bio-mediated synthesis of TiO2 nanoparticles and its photocatalytic effect on aquatic biofilm. J Photochem Photobiol B Biol 110:43–49. https://doi.org/10.1016/j.jphotobiol.2012.03.003

Dong YH, Gusti AR, Zhang Q, Xu JL, Zhang LH (2002) Identification of quorum-quenching N-acyl homoserine lactonases from bacillus species. Appl Environ Microbiol 68(4):1754–1759

Donlan RM (2001) Biofilms and device-associated infections. Emerg Infect Dis 7:277–281. https://doi.org/10.3201/eid0702.010226

Donlan RM (2002) Biofilms: microbial life on surfaces. Emerg Infect Dis 8:881–890. https://doi.org/10.3201/eid0809.020063

Dorcheh S, Vahabi K (2016) Biosynthesis of nanoparticles by fungi: large-scale production. In: Mérillon J, Ramawat K (eds) Fungal metabolites. Springer, (Switzerland, pp 395–414

Durán N, Seabra AB (2012) Metallic oxide nanoparticles: state of the art in biogenic syntheses and their mechanisms. Appl Microbiol Biotechnol 95:275–288. https://doi.org/10.1007/s00253-012-4118-9

Durán N, Marcato PD, Alves OL, De Souza GIH, Esposito E (2005) Mechanistic aspects of biosynthesis of silver nanoparticles by several Fusarium oxysporum strains. J Nanobiotechnology 3:8. https://doi.org/10.1186/1477-3155-3-8

Eberhard A, Burlingame AL, Eberhard C, Kenyon GL, Nealson KH, Oppenheimer NJ (1981) Structural identification of autoinducer of Photobacterium fischeri luciferase. Biochemistry 20: 2444–2449. https://doi.org/10.1021/bi00512a013

Emam HE, Ahmed HB (2016) Polysaccharides templates for assembly of nanosilver. Carbohydr Polym 135:300–307. https://doi.org/10.1016/j.carbpol.2015.08.095

Escárcega-González CE, Garza-Cervantes JA, Vázquez-Rodríguez A, Morones-Ramírez JR (2018) Bacterial exopolysaccharides as reducing and/or stabilizing agents during synthesis of metal nanoparticles with biomedical applications. Int J Polym Sci 2018:7045852. https://doi.org/10.1155/2018/7045852

Faivre D, Schüler D (2008) Magnetotactic bacteria and magnetosomes. Chem Rev 108:4875–4898. https://doi.org/10.1021/cr078258w

Fan XZ, Pomerantseva E, Gnerlich M, Brown A, Gerasopoulos K, McCarthy M et al (2013) Tobacco mosaic virus: a biological building block for micro/nano/bio systems. J Vac Sci Technol A 31:050815. https://doi.org/10.1116/1.4816584

Fang X, Wang Y, Wang Z, Jiang Z, Dong M (2019) Microorganism assisted synthesized nanoparticles for catalytic applications. Energies 12:190. https://doi.org/10.3390/en12010190

Fariq A, Khan T, Yasmin A (2017) Microbial synthesis of nanoparticles and their potential applications in biomedicine. J Appl Biomed 15:241–248. https://doi.org/10.1016/j.jab.2017.03.004

Flavier AB, Clough SJ, Schell MA, Denny TP (1997) Identification of 3-hydroxypalmitic acid methyl ester as a novel autoregulator controlling virulence in Ralstonia solanacearum. Mol Microbiol 26(2):251–259

Fuqua WC, Winans SC, Greenberg EP (1994) Quorum sensing in bacteria: the LuxR-LuxI family of cell density- responsive transcriptional regulators. J Bacteriol 176:269–275. https://doi.org/10.1128/JB.176.2.269-275.1994

Gahlawat G, Choudhury AR (2019) A review on the biosynthesis of metal and metal salt nanoparticles by microbes. RSC Adv 9:12944. https://doi.org/10.1039/C8RA10483B

Ganachari SV, Bhat R, Deshpande R, Venkataraman A (2012) Extracellular biosynthesis of silver nanoparticles using fungi Penicillium diversum and their antimicrobial activity studies. Bionanoscience 2:316–321. https://doi.org/10.1007/s12668-012-0046-5

García-Lara B, Saucedo-Mora MÁ, Roldán-Sánchez JA, Pérez-Eretza B, Ramasamy M, Lee J et al (2015) Inhibition of quorum-sensing-dependent virulence factors and biofilm formation of clinical and environmental Pseudomonas aeruginosa strains by ZnO nanoparticles. Lett Appl Microbiol 61(3):299–305

Garole VJ, Choudhary BC, Tetgure SR, Garole DJ, Borse AU (2019) Palladium nanocatalyst: green synthesis, characterization and catalytic application. Int J Environ Sci Technol 16:7885–7892. https://doi.org/10.1007/s13762-018-2173-1

González-Ballesteros N, Prado-López S, Rodríguez-González JB, Lastra M, Rodríguez-Argüelles MC (2017) Green synthesis of gold nanoparticles using brown algae Cystoseira baccata: its activity in colon cancer cells. Colloids Surf B: Biointerfaces 153:190–198. https://doi.org/10.1016/j.colsurfb.2017.02.020

Grasso G, Zane D, Dragone R (2019) Microbial nanotechnology: challenges and prospects for green biocatalytic synthesis of nanoscale materials for sensoristic and biomedical applications. Nanomaterials 10:11. https://doi.org/10.3390/nano10010011

Grünberg K, Müller E-C, Otto A, Reszka R, Linder D, Kube M et al (2004) Biochemical and proteomic analysis of the magnetosome membrane in Magnetospirillum gryphiswaldense. Appl Environ Microbiol 70:1040–1050. https://doi.org/10.1128/AEM.70.2.1040-1050.2004

Guilger-Casagrande M, de Lima R (2019) Synthesis of silver nanoparticles mediated by fungi: a review. Front Bioeng Biotechnol 7:287. https://doi.org/10.3389/fbioe.2019.00287

Gupta N, Upadhyaya CP, Singh A, Abd-Elsalam KA, Prasad R (2018) Applications of silver nanoparticles in plant protection. In: Abd-Elsalam K, Prasad R (eds) Nanobiotechnology applications in plant protection. Springer International Publishing AG, pp 247–266

Haefeli C, Franklin C, Hardy K (1984) Plasmid-determined silver resistance in Pseudomonas stutzeri isolated from a silver mine. J Bacteriol 158:389–392. https://doi.org/10.1128/JB.158.1.389-392.1984

Han D, Yang H, Zhu C, Wang F (2008) Controlled synthesis of CuO nanoparticles using TritonX-100-based water-in-oil reverse micelles. Powder Technol 185:286–290. https://doi.org/10.1016/j.powtec.2007.10.018

Han R, Song X, Wang Q, Qi Y, Deng G, Zhang A et al (2019) Microbial synthesis of graphene-supported highlydispersed Pd-Ag bimetallic nanoparticles and its catalytic activity. J Chem Technol Biotechnol 94:3375–3383. https://doi.org/10.1002/jctb.6150

Hanzelka BL, Greenberg EP (1996) Quorum sensing in Vibrio fischeri: evidence that S-adenosylmethionine is the amino acid substrate for autoinducer synthesis. J Bacteriol 178(17):5291–5294

Hu Y, He L, Ding J, Sun D, Chen L, Chen X (2016) One-pot synthesis of dextran decorated reduced graphene oxide nanoparticles for targeted photo-chemotherapy. Carbohydr Polym 144:223–229. https://doi.org/10.1016/j.carbpol.2016.02.062

Ikuma K, Decho AW, Lau BLT (2015) When nanoparticles meet biofilms-interactions guiding the environmental fate and accumulation of nanoparticles. Front Microbiol 6:591. https://doi.org/10.3389/fmicb.2015.00591

Inamuddin, Ahamed MI, Prasad R (2021) Advanced antimicrobial materials and applications. Springer Singapore. (ISBN: 978-981-15-7098-8) https://www.springer.com/gp/book/9789811570971

Jafari M, Rokhbakhsh-Zamin F, Shakibaie M, Moshafi MH, Ameri A, Rahimi HR et al (2018) Cytotoxic and antibacterial activities of biologically synthesized gold nanoparticles assisted by Micrococcus yunnanensis strain J2. Biocatal Agric Biotechnol 15:245–253. https://doi.org/10.1016/j.bcab.2018.06.014

Jana S (2015) Advances in nanoscale alloys and intermetallics: low temperature solution chemistry synthesis and application in catalysis. Dalton Trans 44:18692–18717. https://doi.org/10.1039/C5DT03699b

Jeevanandam J, Chan YS, Danquah MK (2016) Biosynthesis of metal and metal oxide nanoparticles. Chem Bio Eng Rev 3:55–67. https://doi.org/10.1002/cben.201500018

Johnston CW, Wyatt MA, Li X, Ibrahim A, Shuster J, Southam G et al (2013) Gold biomineralization by a metallophore from a gold-associated microbe. Nat Chem Biol 9:241–243. https://doi.org/10.1038/nchembio.1179

Kanmani P, Lim ST (2013) Synthesis and structural characterization of silver nanoparticles using bacterial exopolysaccharide and its antimicrobial activity against food and multidrug resistant pathogens. Process Biochem 48:1099–1109. https://doi.org/10.1016/j.procbio.2013.05.011

Kavitha A, Doss A, Pole RPP, Pushpa Rani TPK, Prasad R, Satheesh S (2023) A mini review on plant-mediated zinc oxide nanoparticles and their antibacterial potency. Biocatal Agric Biotechnol. https://doi.org/10.1016/j.bcab.2023.102654

Khan MF, Husain FM, Zia Q, Ahmad E, Jamal A, Alaidarous M et al (2020) Anti-quorum sensing and anti-biofilm activity of zinc oxide nanospikes. ACS Omega 5(50):32203–32215

Khandel P, Kumar-Shahi S (2016) Microbes mediated synthesis of metal nanoparticles: current status and future prospects. Int J Nanomater Biostruct 6:1–24

Khandel P, Shahi SK (2018) Mycogenic nanoparticles and their bio-prospective applications: current status and future challenges. J Nanostruct Chem 8:369–391. https://doi.org/10.1007/s40097-018-0285-2

Kim JS, Kuk E, Yu KN, Kim JH, Park SJ, Lee HJ et al (2007) Antimicrobial effects of silver nanoparticles. Nanomedicine 3(1):95–101

Kim DY, Saratale RG, Shinde S, Syed A, Ameen F, Ghodake G (2016) Green synthesis of silver nanoparticles using Laminaria japonica extract: characterization and seedling growth assessment. J Clean Prod 172:2910–2918. https://doi.org/10.1016/j.jclepro.2017.11.123

Kiran GS, Selvin J, Manilal A, Sujith S (2011) Biosurfactants as green stabilizers for the biological synthesis of nanoparticles. Crit Rev Biotechnol 31:354–364. https://doi.org/10.3109/07388551.2010.539971

Kisimba K, Krishnan A, Faya M, Byanga K, Kasumbwe K, Vijayakumar K, Prasad R (2023) Synthesis of metallic nanoparticles based on green chemistry and their medical biochemical applications: synthesis of metallic nanoparticles. J Renew Mater 11(6):2575–2591. https://doi.org/10.32604/jrm.2023.026159

Kitching M, Ramani M, Marsili E (2015) Fungal biosynthesis of gold nanoparticles: mechanism and scale up. Microb Biotechnol 8:904–917. https://doi.org/10.1111/1751-7915.12151

Klaus T, Joerger R, Olsson E, Granqvist CG (1999) Silver-based crystalline nanoparticles, microbially fabricated. Proc Natl Acad Sci U S A 96:13611–13614. https://doi.org/10.1073/pnas.96.24.13611

Kobayashi M, Tomita S, Sawada K, Shiba K, Yanagi H, Yamashita I et al (2012) Chiral metamolecules consisting of gold nanoparticles and genetically engineered tobacco mosaic virus. Opt Express 20:24856–24863. https://doi.org/10.1364/OE.20.024856

Koch N, Sonowal S, Prasad R (2023) Elucidate the smart tailored biogenic nanoparticles and their applications in remediation. Biotechnol Genet Eng Rev. https://doi.org/10.1080/02648725.2023.2219942

Korbekandi H, Mohseni S, Jouneghani RM, Pourhossein M, Iravani S (2016) Biosynthesis of silver nanoparticles using Saccharomyces cerevisia. Artif Cells Nanomed Biotechnol 44:235–239. https://doi.org/10.3109/21691401.2014.937870

Kuzajewska D, Wszołek A, Żwierełło W, Kirczuk L, Maruszewska A (2020) Magnetotactic bacteria and magnetosomes as smart drug delivery systems: anew weapon on the battlefield with cancer? Biology 9:102. https://doi.org/10.3390/biology9050102

Kwon C, Park B-H, Kim H-W, Jung S-H (2009) Green synthesis of silver nanoparticles by sinorhizobial octasaccharide isolated from Sinorhizobium meliloti. Bull Kor Chem Soc 30:1651–1654. https://doi.org/10.5012/bkcs.2009.30.7.1651

Lahiri D, Dash S, Dutta R, Nag M (2019) Elucidating the effect of the anti-biofilm activity of bioactive compounds extracted from plants. J Biosci 44:52. https://doi.org/10.1007/s12038-019-9868-4

Lara HH, Garza-Treviño EN, Ixtepan-Turrent L, Singh DK (2011) Silver nanoparticles are broad-spectrum bactericidal and virucidal compounds. J Nanobiotechnol 9:1–8

Laxminarayan R, Duse A, Wattal C, Zaidi AKM, Wertheim HFL, Sumpradit N et al (2013) Antibiotic resistance-the need for global solutions. Lancet Infect Dis 13:1057–1098. https://doi.org/10.1016/S1473-3099(13)70318-9

Lee JH, Kim YG, Cho MH, Lee J (2014) ZnO nanoparticles inhibit Pseudomonas aeruginosa biofilm formation and virulence factor production. Microbiol Res 169(12):888–896

Le DHT, Lee KL, Shukla S, Commandeur U, Steinmetz NF (2017) Potato virus X, a filamentous plant viral nanoparticle for doxorubicin delivery in cancer therapy. Nanoscale 9:2348–2357. https://doi.org/10.1039/C6NR09099K

Lengke MF, Southam G (2005) The effect of thiosulfate-oxidizing bacteria on the stability of the gold-thiosulfate complex. Geochim Cosmochim Acta 69:3759–3772. https://doi.org/10.1016/j.gca.2005.03.012

Lengke MF, Fleet ME, Southam G (2006) Synthesis of plantinum nanoparticles by reaction of filamentous cyanobacteria with plantinum(IV)- chloride complex. Langmuir 22:7318–7323. https://doi.org/10.1021/la060873s

Leung TC-Y, Wong CK, Xie Y (2010) Green synthesis of silver nanoparticles using biopolymers, carboxymethylated-curdlan and fucoidan. Mater Chem Phys 121:402–405. https://doi.org/10.1016/j.matchemphys.2010.02.026

Li X, Xu H, Chen ZS, Chen G (2011) Biosynthesis of nanoparticles by microorganisms and their applications. J Nanomater 2011:270974. https://doi.org/10.1155/2011/270974

Lima E, Guerra R, Lara V, Guzmán A (2013) Gold nanoparticles as efficient antimicrobial agents for Escherichia coli and rjrnella typhi. Chem Cent J 7:1–7

Lobedanz S, Søgaard-Andersen L (2003) Identification of the C-signal, a contact-dependent morphogen coordinating multiple developmental responses in Myxococcus xanthus. Genes Dev 17:2151–2161. https://doi.org/10.1101/gad.274203

Lovley DR, Woodward JC (1996) Mechanisms for chelator stimulation of microbial Fe(III)-oxide reduction. Chem Geol 132:19–24. https://doi.org/10.1016/S0009-2541(96)00037-X

Lv Q, Zhang B, Xing X, Zhao Y, Cai R, Wang W et al (2018) Biosynthesis of copper nanoparticles using Shewanella loihica PV-4 with antibacterial activity: novel approach and mechanisms investigation. J Hazard Mater 347:141–149. https://doi.org/10.1016/j.jhazmat.2017.12.070

Ma Y, Lan G, Li C, Cambaza EM, Liu D, Ye X et al (2019) Stress tolerance of Staphylococcus aureus with different antibiotic resistance profiles. Microb Pathog 133:103549. https://doi.org/10.1016/j.micpath.2019.103549

Maddela NR, Chakraborty S, Prasad R (2021) Nanotechnology for advances in medical microbiology. Springer Singapore. (ISBN 978-981-15-9915-6) https://www.springer.com/gp/book/9789811599156

Markus J, Mathiyalagan R, Kim Y-J, Abbai R, Singh P, Ahn S et al (2016) Intracellular synthesis of gold nanoparticles with antioxidant activity by probiotic Lactobacillus kimchicus DCY51T isolated from Korean kimchi. Enzyme Microb Technol 95:85–93. https://doi.org/10.1016/j.enzmictec.2016.08.018

Miller KP (2015) Bacterial communication and its role as a target for nanoparticle-based antimicrobial therapy (Doctoral dissertation)

Mishra M, Paliwal JS, Singh SK, Selvarajan E, Subathradevi C, Mohanasrinivasan V (2013) Studies on the inhibitory activity of biologically synthesized and characterized zinc oxide nanoparticles using lactobacillus sporogens against Staphylococcus aureus. J Pure Appl Microbiol 7:1–6

Mishra S, Singh BR, Naqvi AH, Singh HB (2017) Potential of biosynthesized silver nanoparticles using Stenotrophomonas sp. BHU-S7 (MTCC 5978) for management of soil-borne and foliar phytopathogens. Sci Rep 7:45154. https://doi.org/10.1038/srep4515

Moghaddam AB, Moniri M, Azizi S, Rahim RA, Ariff AB, Saad WZ et al (2017) Biosynthesis of ZnO nanoparticles by a new Pichia kudriavzevii yeast strain and evaluation of their antimicrobial and antioxidant activities. Molecules 22:872. https://doi.org/10.3390/molecules22060872

Naik K, Kowshik M (2014) Anti-quorum sensing activity of AgCl-TiO_2 nanoparticles with potential use as active food packaging material. J Appl Microbiol 117:972–983. https://doi.org/10.1111/jam.12589

Nealson KH, Platt T, Hastings JW (1970) Cellular control of the synthesis and activity of the bacterial luminescent system. J Bacteriol 104:313–322. https://doi.org/10.1128/JB.104.1.313-322.1970

Nielsen LP, Risgaard-Petersen N, Fossing H, Christensen PB, Sayama M (2010) Electric currents couple spatially separated biogeochemical processes in marine sediment. Nature 463:1071–1074. https://doi.org/10.1038/nature08790

Obayemi JD, Dozie-Nwachukwu S, Danyuo Y, Odusanya OS, Anuku N, Malatesta K et al (2015) Biosynthesis and the conjugation of magnetite nanoparticles with luteinizing hormone releasing hormone (LHRH). Mater Sci Eng C 46:482–496. https://doi.org/10.1016/j.msec.2014.10.081

Órdenes-Aenishanslins N, Anziani-Ostuni G, Monrás JP, Tello A, Bravo D, Toro-Ascuy D et al (2020) Bacterial synthesis of ternary cdsag quantum dots through cation exchange: tuning the composition and properties of biological nanoparticles for bioimaging and photovoltaic applications. Microorganisms 8:631. https://doi.org/10.3390/microorganisms8050631

Otari SV, Patil RM, Nadaf NH, Ghosh SJ, Pawar SH (2014) Green synthesis of silver nanoparticles by microorganism using organic pollutant: its antimicrobial and catalytic application. Environ Sci Pollut Res 21:1503–1513. https://doi.org/10.1007/s11356-013-1764-0

Park K-Y, Jeong J-K, Lee Y-E, Daily Iii JW (2014) Health benefits of kimchi (Korean fermented vegetables) as a probiotic food. J Med Food 17:6–20. https://doi.org/10.1089/jmf.2013.3083

Pati S, Chatterji A, Dash BP, Nelson BR, Sarkar T, Shahimi S et al (2020) Structural characterization and antioxidant potential of chitosan by γ-irradiation from the carapace of horseshoe crab. Polymers 12:2361. https://doi.org/10.3390/polym12102361

Patil MP, Kang M-J, Niyonizigiye I, Singh A, Kim J-O, Seo YB et al (2019) Extracellular synthesis of gold nanoparticles using the marine bacterium Paracoccus haeundaensis BC74171T and evaluation of their antioxidant activity and antiproliferative effect on normal and cancer cell lines. Colloids Surf B Biointerfaces 183:110455. https://doi.org/10.1016/j.colsurfb.2019.110455

Patil S, Chandrasekaran R (2020) Biogenic nanoparticles: a comprehensive perspective in synthesis, characterization, application and its challenges. J Genet Eng Biotechnol 18:67. https://doi.org/10.1186/s43141-020-00081-3

Pearson JP, Gray KM, Passador L, Tucker KD, Eberhard A, Iglewski BH, Greenberg EP (1994) Structure of the autoinducer required for expression of Pseudomonas aeruginosa virulence genes. Proc Natl Acad Sci 91(1):197–201

Pearson JP, Passador L, Iglewski BH, Greenberg EP (1995) A second N-acylhomoserine lactone signal produced by Pseudomonas aeruginosa. Proc Natl Acad Sci 92(5):1490–1494

Pesci EC, Milbank JB, Pearson JP, McKnight S, Kende AS, Greenberg EP, Iglewski BH (1999) Quinolone signaling in the cell-to-cell communication system of Pseudomonas aeruginosa. Proc Natl Acad Sci 96(20):11229–11234

Phelan VV, Liu WT, Pogliano K, Dorrestein PC (2012) Microbial metabolic exchange-the chemotype-to-phenotype link. Nat Chem Biol 8:26–35. https://doi.org/10.1038/nchembio.739

Pinto RM, Lopes-de-Campos D, Martins MCL, Van Dijck P, Nunes C, Reis S (2019) Impact of nanosystems in Staphylococcus aureus biofilms treatment. FEMS Microbiol Rev 43:622–641. https://doi.org/10.1093/femsre/fuz021

Płaza GA, Chojniak J, Banat IM (2014) Biosurfactant mediated biosynthesis of selected metallic nanoparticles. Int J Mol Sci 15:13720–13737. https://doi.org/10.3390/ijms150813720

Plaza DO, Gallardo C, Straub YD, Bravo D, Pérez-Donoso JM (2016) Biological synthesis of fluorescent nanoparticles by cadmium and tellurite resistant Antarctic bacteria: exploring novel natural nanofactories. Microb Cell Factories 15:76. https://doi.org/10.1186/s12934-016-0477-8

Prasad R (2014) Synthesis of silver nanoparticles in photosynthetic plants. J Nanoparticles, Article ID 963961:2014. https://doi.org/10.1155/2014/963961

Prasad R (2016) Advances and applications through fungal nanobiotechnology. Springer, International Publishing Switzerland. (ISBN: 978-3-319-42989-2)

Prasad R (2017) Fungal nanotechnology: applications in agriculture, industry, and medicine. Springer Nature Singapore Pte Ltd. (ISBN 978-3-319-68423-9)

Prasad K, Jha AK (2010) Biosynthesis of CdS nanoparticles: an improved green and rapid procedure. J Colloid Interface Sci 342:68–72. https://doi.org/10.1016/j.jcis.2009.10.003

Prasad R, Rai S (2023) Trichoderma for biotechnological applications: current insight and future prospects. Elsevier

Prasad R, Pandey R, Barman I (2016) Engineering tailored nanoparticles with microbes: quo vadis. WIREs Nanomed Nanobiotechnol 8:316–330. https://doi.org/10.1002/wnan.1363

Prasad R, Gupta N, Kumar M, Kumar V, Wang S, Abd-Elsalam KA (2017) Nanomaterials act as plant defense mechanism. In: Prasad R, Kumar M, Kumar V (eds) Nanotechnology. Springer Nature Singapore Pte Ltd, pp 253–269

Prasad R, Jha A, Prasad K (2018) Exploring the realms of nature for nanosynthesis. Springer International Publishing. (ISBN 978-3-319-99570-0) https://www.springer.com/978-3-319-99570-0

Prasad R, Siddhardha B, Dyavaiah M (2020) Nanostructures for antimicrobial and antibiofilm applications. Springer International Publishing. (ISBN 978-3-030-40336-2) https://www.springer.com/gp/book/9783030403362

Presentato A, Piacenza E, Anikovskiy M, Cappelletti M, Zannoni D, Turner RJ (2018) Biosynthesis of selenium-nanoparticles and -nanorods as a product of selenite bioconversion by the aerobic bacterium Rhodococcus aetherivorans BCP1. New Biotechnol 41:1–8. https://doi.org/10.1016/j.nbt.2017.11.002

Pugazhendhi A, Prabakar D, Jacob JM, Karuppusamy I, Saratale RG (2018) Synthesis and characterization of silver nanoparticles using Gelidium amansii and its antimicrobial property against various pathogenic bacteria. Microb Pathog 114:41–45. https://doi.org/10.1016/j.micpath.2017.11.013

Qayyum S, Khan AU (2016) Nanoparticles vs. biofilms: a battle against another paradigm of antibiotic resistance. MedChemComm 7:1479–1498. https://doi.org/10.1039/C6MD00124F

Qi P, Zhang D, Zeng Y, Wan Y (2016) Biosynthesis of CdS nanoparticles: a fluorescent sensor for sulfate-reducing bacteria detection. Talanta 147:142–146. https://doi.org/10.1016/j.talanta.2015.09.046

Raffa RB, Iannuzzo JR, Levine DR, Saeid KK, Schwartz RC, Sucic NT et al (2005) Bacterial communication ("quorum sensing") via ligands and receptors: a novel pharmacologic target for the design of antibiotic drugs. J Pharmacol Exp Ther 312(2):417–423

Rafique M, Sadaf I, Rafique MS, Tahir MB (2017) A review on green synthesis of silver nanoparticles and their applications. Artif Cells Nanomed Biotechnol 45:1272–1291. https://doi.org/10.1080/21691401.2016.1241792

Ramasamy M, Lee J (2016) Recent nanotechnology approaches for prevention and treatment of biofilm-associated infections on medical devices. Biomed Res Int 2016:1851242. https://doi.org/10.1155/2016/1851242

Ranjitha VR, Rai VR (2017) Actinomycetes mediated synthesis of gold nanoparticles from the culture supernatant of Streptomyces griseoruber with special reference to catalytic activity. 3 Biotech 7:299. https://doi.org/10.1007/s13205-017-0930-3

Reith F, Fairbrother L, Nolze G, Wilhelmi O, Clode PL, Gregg A et al (2010) Nanoparticle factories: biofilms hold the key to gold dispersion and nugget formation. Geology 63:1227–1230. https://doi.org/10.1130/G31052.1

Rodrigues L, Banat IM, Teixeira J, Oliveira R (2006) Biosurfactants: potential applications in medicine. J Antimicrob Chemother 57:609–618. https://doi.org/10.1093/jac/dkl024

Sadekuzzaman M, Yang S, Mizan MFR, Ha SD (2015) Current and recent advanced strategies for combating biofilms. Compr Rev Food Sci Food Saf 14(4):491–509

Saeed S, Iqbal A, Ashraf MA (2020) Bacterial-mediated synthesis of silver nanoparticles and their significant effect against pathogens. Environ Sci Pollut Res 27:37347–37356. https://doi.org/10.1007/s11356-020-07610-0

Saglam N, Korkusuz F, Prasad R (2021) Nanotechnology applications in health and environmental sciences. Springer International Publishing. (ISBN: 978-3-030-64410-9) https://www.springer.com/gp/book/9783030644093

Salari Z, Danafar F, Dabaghi S, Ataei SA (2016) Sustainable synthesis of silver nanoparticles using macroalgae Spirogyra varians and analysis of their antibacterial activity. J Saudi Chem Soc 20:459–464. https://doi.org/10.1016/j.jscs.2014.10.004

Saleh MM, Sadeq RA, Latif HKA, Abbas HA, Askoura M (2019) Zinc oxide nanoparticles inhibits quorum sensing and virulence in Pseudomonas aeruginosa. Afr Health Sci 19(2):2043–2055

Samanta S, Singh BR, Adholeya A (2017) Intracellular synthesis of gold nanoparticles using an ectomycorrhizal strain EM-1083 of Laccaria fraterna and its nanoanti-quorum sensing potential against Pseudomonas aeruginosa. Indian J Microbiol 57:448–460

Sanaeimehr Z, Javadi I, Namvar F (2018) Antiangiogenic and antiapoptotic effects of green-synthesized zinc oxide nanoparticles using Sargassum muticum algae extraction. Cancer Nanotechnol 9:3. https://doi.org/10.1186/s12645-018-0037-5

Santos APA, Watanabe E, de Andrade D (2011) Biofilm on artificial pacemaker: fiction or reality? Arq Bras Cardiol 97:113–120. https://doi.org/10.1590/S0066-782X2011001400018

Sarkar T, Salauddin M, Chakraborty R (2020) In-depth pharmacological and nutritional properties of bael (Aegle marmelos): a critical review. J Agric Food Res 2:100081. https://doi.org/10.1016/j.jafr.2020.100081

Seshadri S, Saranya K, Kowshik M (2011) Green synthesis of lead sulfide nanoparticles by the lead resistant marine yeast, Rhodosporidium diobovatum. Biotechnol Prog 27:1464–1469. https://doi.org/10.1002/btpr.651

Shah MSAS, Nag M, Kalagara T, Singh S, Manorama SV (2008) Silver on PEG-PU-TiO2 polymer nanocomposite films: an excellent system for antibacterial applications. Chem Mater 20(7): 2455–2460

Shrestha PM, Rotaru AE, Summers ZM, Shrestha M, Liu F, Lovley DR (2013) Transcriptomic and genetic analysis of direct interspecies electron transfer. Appl Environ Microbiol 79(7): 2397–2404

Siddiqi KS, Husen A, Rao RAK (2018) A review on biosynthesis of silver nanoparticles and their biocidal properties. J Nanobiotechnology 16:14. https://doi.org/10.1186/s12951-018-0334-5

Singh R, Shedbalkar UU, Wadhwani SA, Chopade BA (2015) Bacteriagenic silver nanoparticles: synthesis, mechanism, and applications. Appl Microbiol Biotechnol 99:4579–4593

Singh S, Singh SK, Chowdhury I, Singh R (2017) Understanding the mechanism of bacterial biofilms resistance to antimicrobial agents. Open Microbiol J 11:53–62. https://doi.org/10.2174/1874285801711010053

Sonawane JM, Rai AK, Sharma M, Tripathi M, Prasad R (2022) Microbial biofilms: recent advances and progress in environmental bioremediation. Sci Total Environ. https://doi.org/10.1016/j.scitotenv.2022.153843

Song D, Li X, Cheng Y, Xiao X, Lu Z, Wang Y et al (2017) Aerobic biogenesis of selenium nanoparticles by Enterobacter cloacae Z0206 as a consequence of fumarate reductase mediated selenite reduction. Sci Rep 7:3239. https://doi.org/10.1038/s41598-017-03558-3

Srivastava N, Mukhopadhyay M (2014) Biosynthesis of SnO2 nanoparticles using bacterium Erwinia herbicola and their photocatalytic activity for degradation of dyes. Ind Eng Chem Res 53:13971–13979. https://doi.org/10.1021/ie5020052

Srivastava S, Usmani Z, Atanasov AG, Singh VK, Singh NP, Abdel-Azeem AM, Prasad R, Gupta G, Sharma M, Bhargava A (2021) Biological nanofactories: using living forms for metal nanoparticle synthesis. Mini-Rev Med Chem 21(2):245–265

Stewart PS (2002) Mechanisms of antibiotic resistance in bacterial biofilms. Int J Med Microbiol 292:107–113. https://doi.org/10.1078/1438-4221-00196

Suryavanshi P, Pandit R, Gade A, Derita M, Zachino S, Rai M (2017) Colletotrichum sp.- mediated synthesis of sulphur and aluminium oxide nanoparticles and its in vitro activity against selected food-borne pathogens. LWT 81:188–194. https://doi.org/10.1016/j.lwt.2017.03.038

Thakker JN, Dalwadi P, Dhandhukia PC (2013) Biosynthesis of gold nanoparticles using Fusarium oxysporum f. sp. cubense JT1, a plant pathogenic fungus. ISRN Biotechnol 2013:515091. https://doi.org/10.5402/2013/515091

Vargas G, Cypriano J, Correa T, Leão P, Bazylinski DA, Abreu F (2018) Applications of magnetotactic bacteria, magnetosomes and magnetosome crystals in biotechnology and nanotechnology: mini-review. Molecules 23:1–25. https://doi.org/10.3390/molecules23102438

Vaseghi Z, Nematollahzadeh A, Tavakoli O (2018) Green methods for the synthesis of metal nanoparticles using biogenic reducing agents: a review. Rev Chem Eng 34:529–559. https://doi.org/10.1515/revce-2017-0005

Vinoj G, Pati R, Sonawane A, Vaseeharan B (2015) In vitro cytotoxic effects of gold nanoparticles coated with functional acyl homoserine lactone lactonase protein from Bacillus licheniformis and their antibiofilm activity against Proteus species. Antimicrob Agents Chemother 59(2): 763–771

Wadhwani SA, Shedbalkar UU, Singh R, Vashisth P, Pruthi V, Chopade BA (2016) Kinetics of synthesis of gold nanoparticles by Acinetobacter sp. SW30 isolated from environment. Indian J Microbiol 56:439–444. https://doi.org/10.1007/s12088-016-0598-0

Walker AK, Jacobs RL, Watts JL, Rottiers V, Jiang K, Finnegan DM et al (2011) A conserved SREBP-1/phosphatidylcholine feedback circuit regulates lipogenesis in metazoans. Cell 147(4): 840–852

Wang L, Hu C, Shao L (2017a) The antimicrobial activity of nanoparticles: present situation and prospects for the future. Int J Nanomedicine 12:1227–1249. https://doi.org/10.2147/IJN.S121956

Wang X, Zhang D, Pan X, Lee DJ, Al-Misned FA, Mortuza MG et al (2017b) Aerobic and anaerobic biosynthesis of nano-selenium for remediation of mercury contaminated soil. Chemosphere 170:266–273. https://doi.org/10.1016/j.chemosphere.2016.12.020

Wei D, Sun W, Qian W, Ye Y, Ma X (2009) The synthesis of chitosan-based silver nanoparticles and their antibacterial activity. Carbohydr Res 344:2375–2382. https://doi.org/10.1016/j.carres.2009.09.001

Whitehead NA, Barnard AM, Slater H, Simpson NJ, Salmond GP (2001) Quorum-sensing in gram-negative bacteria. FEMS Microbiol Rev 25(4):365–404

Wypij M, Czarnecka J, Świecimska M, Dahm H, Rai M, Golinska P (2018) Synthesis, characterization and evaluation of antimicrobial and cytotoxic activities of biogenic silver nanoparticles synthesized from Streptomyces xinghaiensis OF1 strain. World J Microbiol Biotechnol 34:23. https://doi.org/10.1007/s11274-017-2406-3

Xu C, Qiao L, Guo Y, Ma L, Cheng Y (2018) Preparation, characteristics and antioxidant activity of polysaccharides and proteins-capped selenium nanoparticles synthesized by Lactobacillus casei ATCC 393. Carbohydr Polym 195:576–585. https://doi.org/10.1016/j.carbpol.2018.04.110

Yang Z, Li Z, Lu X, He F, Zhu X, Ma Y et al (2017) Controllable biosynthesis and properties of gold nanoplates using yeast extract. Nano-Micro Lett 9:5. https://doi.org/10.1007/s40820-016-0102-8

Yarwood JM, Bartels DJ, Volper EM, Greenberg EP (2004) Quorum sensing in Staphylococcus aureus biofilms. J Bacteriol 186:1838–1850. https://doi.org/10.1128/JB.186.6.1838-1850.2004

Yu S, Liu J, Yin Y, Shen M (2018) Interactions between engineered nanoparticles and dissolved organic matter: a review on mechanisms and environmental effects. J Environ Sci 63:198–217. https://doi.org/10.1016/j.jes.2017.06.021

Yue L, Wang J, Zhang Y, Qi S, Xin B (2016) Controllable biosynthesis of high-purity lead-sulfide (PbS) nanocrystals by regulating the concentration of polyethylene glycol in microbial system. Bioprocess Biosyst Eng 39:1839–1846. https://doi.org/10.1007/s00449-016-1658-x

Zhang R, Edgar KJ (2014) Properties, chemistry applications of the bioactive polysaccharide curdlan. Biomacromolecules 15:1079–1096. https://doi.org/10.1021/bm500038g

Zhao Y, Tian Y, Cui Y, Liu W, Ma W, Jiang X (2010) Small molecule-capped gold nanoparticles as potent antibacterial agents that target gram-negative bacteria. J Am Chem Soc 132(35):12349–12356

Zhao X, Zhao F, Wang J, Zhong N (2017) Biofilm formation and control strategies of foodborne pathogens: food safety perspectives. RSC Adv 7:36670–36683. https://doi.org/10.1039/C7RA02497E

Zhong J, Zhao X (2018) Isothermal amplification technologies for the detection of foodborne pathogens. Food Anal Methods 11:1543–1560. https://doi.org/10.1007/s12161-018-1177-2

Microbially Synthesized Nanoparticles in Sustainable Agriculture

14

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Abstract

Advances in synthesizing nanomaterials have demonstrated that biological systems and microbes play an essential role in nanoscience and nanotechnology. These organisms can produce and accumulate nanoparticles (NPs) of different shapes and sizes without harming the environment. For the synthesis of NPs, microbial enzymes and proteins have been used as reducing agents more recently than in physical and chemical approaches. It is a fast, cost-effective, and environmentally friendly method. Fungi and bacteria are preferred among biogenic sources due to their ease of cultivation and ability to control synthesized nanoparticles' size and morphology, which can lower the cost of large-scale manufacturing. Additionally, they have a higher concentration of the reductase enzyme required to convert ionic forms into nanoparticles. Organisms such as bacteria, actinomycetes, fungi, yeasts, viruses, and algae are being investigated as reducing or stabilizing agents for the synthesis of metal NPs such as gold, silver, copper, cadmium, platinum, palladium, titanium, and zinc, which have a wide range of industrial and biomedical applications. As a result, nanotechnology has

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played a part in enabling the agrotechnological revolution that will transform the entire agricultural system while ensuring food security in the near future. The result is that nanoparticles are evolving into cutting-edge substances that will change contemporary agriculture forever. Numerous nanoparticle-based formulations have been investigated to control plant health and soil improvement, including nano-sized insecticides, herbicides, fungicides, fertilizers, and sensors. By thoroughly understanding the interactions between plants and nanomaterials, agricultural practices can be improved by increasing disease resistance, crop output, and nutrient absorption. Our purpose in this chapter is to outline the important issues that future agricultural research based on nanotechnology can solve to increase productivity and food security.

Keywords

Agriculture · Bacterial · Fungi · Green synthesis · Nanomaterials

Abbreviations

AgNp	Silver nanoparticles
Al_2O_3	Aluminum Oxide
Ca	Calcium
Cd	Cadmium
CeO_2	Cerium oxide
Fe	Iron
Fe_3O_2-	Ironoxidenanoparticles
FeO	Iron oxide
MtNPs	Metal nanoparticles
NPs	Nanoparticles
P	Phosphorus
Se	Selenium
TiO_2	Titanium dioxide
Zn	Zinc
ZnO	Zinc oxide

14.1 Introduction

Agriculture acts as the primary pillar of the developing economy and provides food for a better life. In the current scenario, the field of agriculture has been facing a wide range of challenges, including unpredictable climate change, contamination of soil with various harmful environmental pollutants such as fertilizers and pesticides, and majorly elevating food demands with a growing global population (Pouratashi and Iravani 2012). Agricultural nutrient balances differed noticeably with economic

growth, and especially from this surmise, the development of soil fertility is very much significant in developing countries (Campbell et al. 2014). The development of agriculture is a compulsory phenomenon for the purge of poverty and hunger which must be getting rid of from the present situation. Therefore, we should have to take one bold step for agricultural development. In this world mainstream of people are below poverty level which are being scatted in rural areas where agriculture enlargement has not so been effective.

Nanoparticles are materials that range between 10 to 100 nanometers (nm) and can be designed with unique chemical, physical, and biological properties, to be distinctively different from those of their molecular and bulk counterparts (Yang et al. 2008). Nanoparticles alone have the potential to be directly applied to plant seeds, foliage, or roots for protection against pests and pathogens, such as insects, bacteria, fungi, and viruses. Metal nanoparticles such as silver, copper, zinc oxide, and titanium dioxide have been intensively researched for their antibacterial and antifungal properties and are known for their antiviral properties (Kah and Hofmann 2014; Gogos et al. 2012; Kim et al. 2018; Prasad et al. 2016, 2018).

Recently, it has been common practice to manufacture metals and metal oxide nanoparticles (NPs) for use in a variety of biotechnological applications, including biomedical, agricultural, industrial, and the treatment of environmental contaminants. As a key component of biotechnology, the green synthesis of NPs employing biological organisms, including bacteria, actinomycetes, fungi, algae, and plants, has been established (Tsekhmistrenko et al. 2020; Prasad et al. 2016; Srivastava et al. 2021; Kisimba et al. 2023). The green approach to NP synthesis provides several benefits over traditional approaches, including ease of synthesis, economic effectiveness, environmental friendliness, and simplicity of scaling up. As a result, a better understanding of green chemistry and environmentally friendly methods for producing NPs paves the way for a wide range of biotechnological applications. Fundamentally, the production of metal or metal oxide nanoparticles (NPs) in an environmentally friendly manner has a variety of applications, including antimicrobial and antitumor activity, the management of various phytopathogens, the bioremediation process, the food and textile industries, and wastewater treatment (Grillone et al. 2017).

Nanotechnology can take an important part in the productivity through control of nutrients (Gruère 2012; Mukhopadhyay 2014), and it can also participate in the monitoring of water quality and pesticides for sustainable development of agriculture (Prasad et al. 2014; Chausali et al. 2023; Osherov et al. 2023). Nanomaterials have such diverse assets and activities that it is impossible to deliver a general assessment of their health and environmental risks (Prasad et al. 2014). Properties (other than size) of NPs that influence toxicity including chemical composition, shape, surface structure, surface charge, behavior, and the extent of particle aggregation (clumping) or disaggregation may associate with engineered NPs (Ion et al. 2010). For this reason, even nanomaterials of the same chemical composition that have different sizes or shapes can exhibit different toxicity.

The implication of nanotechnology research in the agricultural sector has become a necessary key factor for sustainable development. In the agri-food areas, pertinent

applications of nanotubes, fullerenes, biosensors, controlled delivery systems, nanofiltration, etc. were observed (Ion et al. 2010; Sabir et al. 2014). This technology proved to be as good in resource management of agricultural fields and drug delivery mechanisms in plants and helped maintain soil fertility. Moreover, it is being also evaluated steadily in the use of biomass and agricultural waste as well as in food processing and food packaging systems as well as risk assessment (Floros et al. 2010; Chausali et al. 2022). Recently, nanosensors are widely applied in agriculture due to their strengths and fast for environmental monitoring of contamination in the soils and in the water (Ion et al. 2010).

In the form of nanotransporters, nanocapsules, and nanonutrients, nanostructured fertilizers may be thought of as intelligent fertilizers that can improve the effectiveness of plant nutrient uptake, regulate nutrient release, and lower environmental pollution. But there is a pressing need to standardize and evaluate the toxicity of nanomaterials employed in agriculture; as a result, it is strongly advised to carry out comprehensive field and greenhouse studies for execution evaluation.

Several sensors based on nano-detection technology such as biosensors, electrochemical sensors, optical sensors, and devices will be the main instruments for detecting heavy metals in the trace range (Ion et al. 2010). This chapter discusses the brief overview and updates on current research reports reviews pertaining to the individual nanoparticles that already exist (Kah and Hofmann 2014; Gogos et al. 2012; Kim et al. 2018 9–11; Mishra and Singh 2015, Sadeghi et al. 2017; Malerba and Cerana 2016).

14.2 Nanomaterials in Agriculture

Studying the potential for one kind of bacterium to produce diverse elemental nanoparticles is encouraging, but it also brings up a variety of new issues and challenges. The European Union's strategy on nanotechnology is based on the idea that research into the synthesis and deployment of nanoparticles needs a thorough, safe, and responsible approach to analyzing possible health and environmental concerns (Rauscher et al. 2012). In order to increase agricultural production, it is essential to look for sustainable green antimicrobials due to the exponential development of the human population and the growing food demand. In this work, pH levels of the source precursors and growth time were controlled to accomplish hydrothermal precipitation for the synthesis of a variety of nanostructures, including nanorods (1D), nanoplatelets (2D), and multibranched flower-like particles (3D) (Rauscher et al. 2012).

Crop output must be increased to meet the world's growing food demand and improve agricultural sustainability, as the world's population is growing at an alarming rate. As active components of biofertilizers and biopesticides, plant growth-promoting microorganisms may be seen as a workable substitute technique for increasing plant production and warding off diseases. The microbial inoculums have the potential to have a positive effect on the agricultural industry, but plant selectivity, along with organic and conventional management techniques, also plays

a role in determining the structure of the rhizospheric microbiome, its coexistence, and its subsequent effects. It becomes necessary to reorganize the priorities of research toward isolating beneficial microbes and understanding the dynamics of their association with plants for improved crop productivity, quality, and agroecological sustainability because the microbial community structure in bulk and the rhizosphere region frequently differ in their composition in various plant niches. Even though microbial consortium application has certain limits, steps may be taken to get over them, such as improving the shelf-life and viable load at the time of application and having more trust in farmers to consistently use inoculants in their fields. Future research on the viability of producing inoculants on a wide scale may include synergistic microorganisms that have been shown to boost crop output in both conventional and organic farming methods.

A lot of attention has been paid to green synthesis technology recently since it provides a potentially simple, effective, clean, nontoxic, and environmentally acceptable way to synthesize metal nanoparticles (MtNPs). The efficient production of MtNPs may be accomplished using a number of microbes and plant extracts (Koch et al. 2023). Microorganisms are a more cost-effective way to create MtNPs, despite the fact that plant extracts are a simpler method of doing so. Green MtNP synthesis and its use in a variety of technologies, including agriculture, have a bright future thanks to the shifting perspectives of the global community on sustainable development, bettering environmental circumstances, and reducing hazardous man-made waste. The agriculture sector can be improved with the use of nanotechnology. The use of nanotechnology in contemporary agriculture contributes to a stronger global economy.

Agrochemicals have been used continuously to increase agricultural output, but they have contaminated topsoil, groundwater, and food (Salem and Fouda 2021). Increased agricultural growth and less pollution from vital sources are needed; however, new technologies must be developed due to ecological degradation. In this regard, nanotechnology is emerging as a popular area for the development of sustainable agriculture. Delivery of insecticides (Chang et al. 2020), biopesticides (Revie et al. 2018), fertilizers (Thakur et al. 2020), and genetic material for plant transformation all show promising results and uses already. Therefore, with the use of nanotechnology, it is possible to guarantee dosage reduction and the regulated administration of fertilizers and pesticides (Mittal et al. 2020). The basic hypothesis is that the use of NPs to stabilize biocontrol preparations will significantly reduce environmental risks. The critical problems of protecting plant development and maintaining sustainability may be handled using nanotechnology instruments. Furthermore, environmental detection, sensing, and cleanup technologies may be provided or fundamentally modernized by means of nanotechnology (Yaseen et al. 2020; Maddela et al. 2023; Saglam et al. 2021; Sarma et al. 2021; Shash et al. 2019).

The use of MtNPs in agriculture significantly aids in overcoming the harm caused by the excessive use of pesticides and artificial fertilizers for improving agricultural output, given the multiple problems faced by population increase and global climate change (Vishwakarma et al. 2020). The application and controlled release of pesticides and fertilizers included in different nanoformulations are improved,

preventing environmental damage. Various MtNPs have been successfully used in research as nanobiosensors, nanopesticides, and nanofertilizers in the agricultural industry. The adsorption potential, allowable limit, and environmental toxicity of these MtNPs are still mostly unknown (Saravanan et al. 2021). It is essential to carefully assess the toxicological effects of MtNPs on the ecosystem, regardless of whether they originated as products with a specific purpose for agriculture or whether there is a chance that mishandling of wastes containing MtNPs could have accidentally released them into the environment. Therefore, in-depth research is required to ascertain their long-term effects. If they are shown to be safe, they may be useful as alternatives to traditional agricultural goods (Bahrulolum et al. 2021). One of the key elements of sustainable agricultural growth is nanotechnology, but the promise of meaningful use of nanotechnology can only be realized if the ecotoxicity of these nanomaterials is well examined and appropriately handled (Shende et al. 2022).

The adsorption capacity, acceptable limit, and environmental toxicity of these MtNPs, however, are still poorly understood. It is essential to carefully assess the toxicological effects of MtNPs on the ecosystem, regardless of whether they originated as products with a specific purpose for agriculture or whether there is a chance they could be released into the environment due to improper handling of wastes containing MtNPs (Fariq et al. 2017). Because of this, further research is required to ascertain their long-term effects. If they are shown to be safe, they may be useful as alternatives to traditional agricultural goods (Chhipa 2017). The promise of widespread application of nanotechnology can only be realized if the ecotoxicity of these nanomaterials is thoroughly researched and effectively managed. Nanotechnology is one of the key elements of sustainable agricultural production (Raliya et al. 2018; Prasad et al. 2017a).

The use of nanostructures as agrochemicals (fertilizers or pesticides) for plant development and protection is constantly being investigated due to their distinctive physicochemical characteristics (Chen and Cui 2018). Recent sponsored studies and open requests for future research seem to be increasingly concerned with developing safer nanomaterials for efficient reactions while being ecologically benign (Vishwakarma et al. 2018). Agriculture-related nanotechnology research is still in its infancy but is developing quickly. However, in order to assure the safe use of such agrochemicals, it is necessary to better understand the modes of operation of nanofertilizers before they can be utilized on farms for ordinary agricultural practices (McGee et al. 2017).

The next breakthrough technology in agriculture is nanotechnology, which may provide traditional agricultural practices with sustainable tools in the form of nanopesticides and nanofertilizers (Pandey 2018). The site-specific and regulated release of the active component in the nanoform of traditional agri-inputs helps to decrease excess runoff, avoid eutrophication, and eliminate residual contamination (Prasad et al. 2017b). The use of metal and encapsulated nanopesticides and fertilizers has shown the potential of this technology in agriculture. As an alternative to traditional agricultural input, one may employ CNT, Fe, ZnO, TiO_2, Ag nanoparticles, and Ca and P hydroxyapatite. Before commercialization, further

study is needed to evaluate how nanotools would affect the environment (Pandey 2018).

14.3 Nanofertilizers

The use of nanomaterials in plant protection and production of food is an under-explored area in the future. It is well known that insect pests are the predominant ones in the agricultural fields and also in its products, thus NPs may have a key role in the control of insect pests and host pathogens (Khota et al. 2012) The recent development of a nanoencapsulated pesticide formulation has slow releasing properties with enhanced solubility, specificity, permeability, and stability (Bhattacharyya et al. 2016). These assets are mainly achieved through either protecting the encapsulated active ingredients from premature degradation or increasing their pest control efficacy for a longer period. Formulation of nanoencapsulated pesticides led to reduction of the dosage of pesticides and human beings' exposure to them which is environmentally friendly for crop protection (Nuruzzaman et al. 2016). So, the development of nontoxic and promising pesticide delivery systems for increasing global food production while reducing the negative environmental impacts on the ecosystem (de Oliveira et al. 2014; Kah and Hofmann 2014; Bhattacharyya et al. 2016; Grillo et al. 2016).

Nanofertilizers may contain nano zinc, silica, iron and titanium dioxide, ZnCdSe/ZnS core-shell QDs, InP/ZnS core-shell QDs, Mn/ZnSe QDs, gold nanorods, core-shell QDs, etc. as well as should endorse control release and improve its quality. Studies of the uptake, biological fate, and toxicity of several metal oxide NPs, viz., Al_2O_3, TiO_2, CeO_2, FeO, and ZnONPs, were carried out intensively in the present decade for agricultural production (Dimkpa 2014; Zhang et al. 2016). The deficiency of zinc has been documented as one of the main problems in limiting agricultural productivity in the alkaline nature of soils (Sadeghzadeh 2013).

The many functions that NPs perform in the agricultural and livestock sectors are highlighted in the current study. The use of nanotechnology in contemporary agriculture supports and develops the global economy in a variety of ways. The introduction of NPs makes a significant contribution to addressing the various problems caused by the growing population, plant and animal diseases, and climate change (Salem and Fouda 2021). However, by increasing the use of conventional pesticides and fertilizers to increase crop production, it ultimately harms the environment. In comparison to conventional resources, the efficacy and agronomic efficiency of NPs have greatly increased. Pesticides may be applied more effectively thanks to varied nanoformulations and controlled release safeguards the environment (Salem and Fouda 2021). Some nanofertilizers and herbicides are currently on the market, and many more are being developed. Understanding how NP interacts with plants is crucial to comprehending the physiological and biochemical reactions imposed by plants (Ali et al. 2020). The notion of their transformation and safety features in a complex system is provided by emerging approaches that are designed to find and measure NPs via the plant system. Nanotechnology makes use of NPs'

special characteristics to create nanosensors that can measure soil factors like pH and moisture as well as pesticide residue (Salem and Fouda 2021).

The research group (Noor et al. 2022) demonstrated the use of Fe_3O_2-NPs biofabricated from aqueous extracts of *Zingiber officinale* and *Cuminum cyminum* during drought stress produces drought tolerance in wheat plants by enhancing a variety of morphological and physiological characteristics. The effective and protective action of Fe_2O_3-NPs on wheat plants under drought stress was demonstrated at both quantities, i.e., 0.6 mM of Fe_3O_2-NPs (ginger) and 1.2 mM of Fe_3O_2-NPs (cumin seeds). By controlling photosynthetic pigments, ROS scavenging machinery, and osmoprotectants, the wheat plants exposed to Fe_3O_2-NPs demonstrated resilience. The sources of the other medicinal herbs, however, may affect the effective Fe_3O_2-NP concentrations (Jegadeesan et al. 2019; Irum et al. 2020). Therefore, nanopriming may be considered a successful method for ensuring sustainable food production, especially when used on weak soils. A plant's ability to survive once the soil becomes wet again indicates greater drought tolerance (Zia et al. 2021). In this work, they discovered that wheat plants primed with Fe_3O_2-NPs had a greater survival rate than untreated control plants under drought stress (Sreelakshmi et al. 2020). Numerous studies have shown the beneficial impacts of nanofertilizers on plants by boosting yield, enhancing biochemical characteristics, and defending against ROS under stressful situations (Babaei et al. 2017; Khalilzadeh et al. 2016; Rastogi et al. 2017; Mubeen et al. 2023).

Recent advances in nanotechnology have raised the possibility of creating NPs as a potent method for addressing issues brought on by conventional fertilizers in conventional agricultural systems. The results pertaining to nutritional components containing NPs (i.e., Fe, Cu, Se, and Co) have demonstrated strong scientific proof of their effectiveness in enhancing the micronutrients of the plant, which is reflected in improved growth parameters and notable improvements in the physiological level (i.e., chlorophyll and carotenoids, photosynthetic activity, metabolic pathways, and transpiration rate) (Ali et al. 2021). The exact dose and activity of NPs on the surface of plant targets is a significant challenge; therefore, reducing the leakage of chemical products derived from bulk materials (i.e., mineral fertilizers) has emerged as a beneficial characteristic that enables NPs' employment in the future. The function of NPs within and outside the plant as well as their impacts on the environment, however, urgently need to be determined by rigorous investigations conducted in controlled environments (Ali et al. 2021).

14.4 Nanopesticides

The existing approaches to pest management might be drastically changed by nanotechnology, which also holds promise for agricultural uses. When pesticides are developed as nanoparticles, they can have advantages that were never before possible, such as (a) improved solubility of poorly water-soluble pesticides; (b) increased bioavailability and efficacy of pesticides when loaded onto nanoparticles and reduced pesticide toxicity; (c) increased shelf-life and controlled

delivery of actives; (d) target-specific delivery of the active molecules and pH-dependent release; and (e) clever delivery of It is clear from the discussion above that nanopesticides are a promising technical advancement given their potential advantages for the environment and human health. Nevertheless, agricultural nanotechnology has not yet penetrated the market. More study is needed to ascertain the efficiency and toxicity of the nanopesticides on soil and the environment since the bulk of the manufactured nanoparticle-based pesticides is still in the early phases of development (Worrall et al. 2018).

Microbial pesticides are at the forefront of IPM systems because of the difficulties with pesticide resistance that farmers often encounter, along with their adverse effects. When compared to chemical pesticides, insect bodies build resistance to microorganisms extremely slowly and not readily. Due to their eco-friendly and host-specific characteristics, these biopesticides are being produced and used at an ever-increasing rate on a global scale (Thakur et al. 2020). Positively, more farmers would adopt biopesticides if they practiced organic farming and produced food without pesticide residue. It is crucial to popularize this modern technology (microbial pesticides) by offering quality control training to production and executive training to extension workers and local farmers (Thakur et al. 2020).

Today, environmental safety is one of our top priorities, so we must raise awareness among manufacturers, farmers, policymakers, government agencies, and the public in order to encourage the use of biopesticides for pest control. Biopesticides have the potential to achieve sustainability in global agriculture for feed and food security because they are less vulnerable to genetic differences (pesticide resistance) across plant populations (Kour et al. 2020). In comparison to other agrochemicals, microbial pesticides have much lower production costs and regulatory issues. The impact of these microbial diseases on untargeted living things is minimal. Although biopesticides have a limited shelf-life and it might be challenging to make them viable beyond 1–2 years in an ambient setting, their bulk manufacture and use are often simple and inexpensive (Yadav et al. 2020a, 2020b).

Biopesticides have shown specialized action in addition to wide-spectrum efficacy against certain insect pests at phases in the disease organisms' life cycles. The use of these microbes against certain pests also has issues. The slow killing of hosts puts its efficacy and user approval in jeopardy (Gill and Garg 2014).). Viruses may survive for up to 7 days at this time, and environmental conditions can affect how effective microbial pesticides are. The viability and pathogenicity of the microorganisms must be maintained until use. Some microbes, such as viruses and protozoa, are exceedingly challenging to cultivate, and the methods used are both expensive and time-consuming. The increased resistance of arthropods to chemical pesticides, environmental risks, and the necessity for the synthesis of novel insecticidal compounds are what is driving the fast spread of microbial pesticides now (Munoz-Leoz et al. 2011).

Major agrochemical companies have recently shown a greater interest in biopesticides, particularly microbial pesticides. However, in-depth research is required to understand the fundamentals of the connections between the host and pathogen to effectively use entomopathogens in an IPM system. To improve

accuracy in the case of entomopathogens, better knowledge of microbial control activity is needed in actual injury upgrading (Chandler et al. (2011). Additionally, it is important to understand the ecology of local microorganisms and how they contribute to the control of insect pests. Future developments will mostly focus on improving microorganisms by connecting their high productivity with ecological stability. It is necessary to conduct a comprehensive inquiry in various agroecological zones to classify naturally existing microorganisms to improve the effectiveness of microbial pesticides in IPM. It is crucial to conduct in-depth surveys on the possessions, pathogenicity, and behavior of pests (Birch et al. 2011).

As the ecological element has a significant role in the spread of illnesses and ultimately manages the population of insect pests, environmental studies are most needed on the different types of infections in insects (Tian et al. 2016). To lessen the loss of pathogen infectivity caused by photo-inactivation, the proper precautions must be taken. It is necessary to do studies on the safety of insect pests for plants, other animals, and beneficial insects. For the creation of improved IPM strategies, interactions between insects and their related bacteria should be carefully investigated. Pathogens' tendency to spread themselves over space and time would unquestionably be advantageous for sustainable agriculture (Sundari et al. 2016).

The absence of long-term studies at this point in the study on nanoparticles for plant protection is another problem. Extensive time trials have only been used in a small number of studies. For instance, Mitter et al. (2017) tested an RNAi/nanoparticle topical delivery platform called BioClay to protect plants against viruses 20 days post-spray application, and Zhao et al. (2017) studied the pesticide levels over 48 days after applying their developed nanoformulation. Yang et al. (2009) tested for insecticidal activity for 5 months after applying their formulation. An emerging technical development, nanopesticides, lacks a precise definition of what constitutes and does not constitute a nanopesticide from regulatory organizations. According to Kookana et al. (2014), the effects of nanopesticides, in contrast to traditional pesticides, may depend on the absorption, bioavailability, concentration, and toxicity of the nanoparticles as well as the ratio of the active bound to them.

14.5 Antibacterial and Antifungal

In order to increase agricultural production, it is essential to look for sustainable green antimicrobials due to the exponential development of the human population and the growing food demand. In this work, pH levels of the source precursors and growth time were controlled to accomplish hydrothermal precipitation for the synthesis of a variety of nanostructured zinc oxide (nZnO) structures, including nanorods (1D), nanoplatelets (2D), and multibranched flower-like particles (Guo et al. 2018; Tian et al. 2018), Two-dimensional (2D) (Dral and ten Elshof 2018; Zhao et al. 2019) (Agarwal et al. 2019; Sebastian et al. 2019).

Additionally, the hydrothermal process is a perfect method for creating various nZnO morphologies due to its benefits, such as straightforward operations, easy control, a relatively low temperature, a cheap cost, and environmental friendliness.

Different soil-borne plant diseases, which are significant limiting constraints in agriculture, were used to assess the antibacterial capabilities of different morphologies of nanomaterials (Servin and White 2016).

The structural characteristics of nZnOs, particularly their sizes and morphologies, are what determines their antimicrobial properties (morphology-dependent antifungal activity). The findings suggest that among the nZnOs, 3D nZnO (i.e., multi-branched flower-like particles) had the best antifungal efficacy. According to SEM findings, 3D nZnO may mechanically harm soil-borne pathogens (Yang et al. 2009). In addition to their distinct antibacterial and antifungal properties, the ZnO multi-branched flower-like particles demonstrated a remarkable capacity for photodecomposition of organic compounds in strong sunlight. Synthesized ZnO has antibacterial capabilities and may use its photodegradation abilities to eliminate chemical contaminants when sprinkled over soil (Sirelkhatim et al. 2015).

AgNPs considerably inhibited biological activity in the soil and had an impact on the bacterial and fungal community structures at very low concentrations (50 mg kg1). Additionally, it has been shown that ammonia-oxidizing microorganisms in a terrestrial setting are very susceptible to AgNP pollution, indicating that these NPs may have a deleterious influence on the soil nitrogen cycle. These findings emphasize the necessity to take into account the influence of NPs on soil microbial populations when evaluating their environmental impact, given the critical role that bacterial and fungal communities play in the preservation of healthy soils. Further research is necessary to identify the levels at which NPs adversely affect important functional groups and biological activity in natural ecosystems in order to fully comprehend the effect of these compounds (Wang et al. 2011).

According to the findings (Chang et al. 2020), the plant HA has a greater potential for producing ZnO NPs in an environmentally friendly manner without the use of hazardous materials. The prepared ZnO NPs also have a wide range of applications as powerful antimicrobials, antioxidants, and photocatalysts for destroying environmental pollutants like dyes and chemicals (Bhuyan et al. 2015; Dhiman et al. 2022, 2023; Kavitha et al. 2023). The research group demonstrated that all Gram-positive and Gram-negative bacteria tested positively and negatively for these produced ZnO nanoparticles, demonstrating remarkable antimicrobial properties. When compared to other microorganisms, those that produced ZnO NPs were more effective at suppressing *Proteus vulgaris* and *Salmonella enterica typhimurium*. The results of the photocatalytic MB dye degradation demonstrated an irreversible color shift from the original blue to colorless at basic pH with around 96% degradation, which was greater than commercial bulk ZnO powder. nZnOs are also used in agriculture as enhancers to boost plants' uptake of macronutrient fertilizers (Milani et al. 2012). Because ZnO has a broad band gap energy and can produce photogenerated holes with a strong oxidizing power, it has also been claimed to totally mineralize organic environmental contaminants and destroy them (Han et al. 2010; Hariharan et al. 2006). ZnO is a perfect photocatalytic material helpful in an antibacterial response and utilized as a UV protector in cosmetics because it has strong optical absorption in the UVA (315–400 nm) and UVB (280–315 nm) areas (Brayner et al. 2006). As

far as we are aware, this study is the first to compare the antimicrobial (i.e., antifungal, antibacterial) capabilities of diverse nZnOs and their uses in agriculture. The study's findings are anticipated to be widely used in a variety of fields, including food security and sustainable agricultural growth (Singhal et al. 2017).

14.6 Prospectus

By employing either extracellularly or intracellularly generated enzymes, fungi may create stable nanoparticles. Due to the antibacterial activity of silver nanoparticles, which has shown encouraging results, packaging materials for processed foods or post-harvest commodities may one day be manufactured with silver nanoparticles incorporated in them. In a similar vein, studies conducted in labs and greenhouses reveal that nanopesticides and nanonutrients have a fantastic potential impact on agriculture. Additional fungal systems need to be researched in order to enhance nanomaterial mycosynthesis for production at a commercial scale. Due to their expensive physical and chemical production, nanoparticles are less ideal for biological applications, which raises concerns about how hazardous they can be to the environment and human health. Microorganisms and plants have been studied for the biological synthesis of NPs with the goal of reducing the toxicity of NPs by capping or encasing them with biological molecules. Fungi have shown promise in the environmentally friendly production of eco-friendly nanomaterials. The agriculture sector is significantly impacted by the usage of nanoformulations in fertilizers and pesticides' sophisticated delivery systems. The greatest benefits to the endeavor to eliminate environmental toxins are anticipated to come from the controlled release of nanofertilizers to stabilize biocontrol preparations and their targeted administration. Nanotechnology could also be used to make packaging materials that are more durable and cheaper. This could help store food better and make it last longer. Despite these advantageous applications and potential ones, it's critical to consider how recently created nanomaterials could influence diverse systems.

Due to the dangers that NPs represent to plants, a study is required to allow the appropriate use of NPs. The impact of nanoparticles might be positive or negative depending on the kind and concentration of NPs, the length of the treatment, the stage of the plant's development, and many other factors. Since the influence of plants directly affects the environment and animal health, safety precautions are required. There is no denying that nanotechnology has enormous promise for the agriculture sector and poses minimal environmental harm. Even though several studies have shown that nanoparticles are harmful, the toxicity of nanomaterials is often concentration dependent. Contrary to what some people have said, very few nanoparticles are used in agricultural applications compared to regular fertilizers, so there is no need to be afraid of nanotechnology.

However, it is sometimes possible to demonstrate the toxicity of smaller nanoparticles that have infiltrated cells. Future research should focus on the exact mechanism, cellular and biochemical processes, large-scale synthesis, and applications of the biosynthesized nanoparticles. It has been shown that protein is

produced more abundantly by fungal synthesis than by bacterial synthesis, increasing productivity. Future studies should focus on improving the reaction conditions, strengthening the stability of the nanoparticles, and clarifying the broad microbial spectrum for nanoparticle synthesis since this is essential for the practical sustainability of biosynthesized nanomaterials.

One method for enhancing sustainability is seed nanopriming, and agriculture is one possible application area for nanotechnology. These systems have the potential to change traditional agriculture based on the use of agrochemicals into a more sustainable agriculture when they can promote plant development and give protection against biotic and abiotic problems, leading to advances in production and food quality. These factors may work together to create a system that is less harmful to farmers, consumers, and the environment by halting the continual damage that conventional agriculture does. Concerns surrounding the industrial manufacture of these technological systems and their field application need to be addressed, including scale-up, seed priming conditions, negative impacts on plants and other living things, and others. However, it is evident that using nanoparticle systems might alter crop management by lowering the need for pesticides and concerns about contamination. As a result, agricultural methods could become safer for farmers, customers, and the environment.

The principles of dosing the age of NPs, exposure length, translocation and accumulation, and mechanism of action on plants are essential for the creation of an application strategy. Secondary impacts, the accumulation of soil, air, water, and biotic organisms, and their effects on the environment, are all crucial factors in defining the exact effects of NPs. The production of nanoparticles from plant and microbial sources has advantages as a cost-effective, energy-saving, and low-cost final product. It may protect the environment and human health by producing less waste and providing safer products. Since they can avoid the time-consuming procedure of employing microorganisms and maintaining their culture, which may lose its potential throughout the process of nanoparticle biosynthesis, the usage of plant-synthesized nanoparticles may be preferable to that of other biological entities. Nanoparticles, which have significant elements of nanotechnology via unparalleled uses, may be produced by plants.

14.7 Conclusion

Future research should focus on the exact mechanism, cellular and biochemical processes, large-scale synthesis, and applications of the biosynthesized nanoparticles. It has been shown that protein is produced more abundantly by fungal synthesis than by bacterial synthesis, increasing productivity. Future studies should focus on improving reaction parameters, improving nanoparticle stability, and revealing the broad microbial spectrum for nanoparticle synthesis in order to assure the practical sustainability of biosynthesized nanomaterials. Future research should focus on the exact mechanism, cellular and biochemical processes, large-scale synthesis, and applications of the biosynthesized nanoparticles. It has been shown

that protein is produced more abundantly by fungal synthesis than by bacterial synthesis, increasing productivity. Future studies should focus on improving reaction parameters, improving nanoparticle stability, and revealing the broad microbial spectrum for nanoparticle synthesis in order to assure the practical sustainability of biosynthesized nanomaterials. Nanotechnology, one of the most recent fields, offers numerous real-world applications for challenges pertaining to the economy and the environment. To make nanoparticles, top-down and bottom-up methods are often used. The bulk of the impacts that metal nanoparticle biogenesis has on the environment is positive, such as the efficient removal of pollutants like metal ions, dyes, and biological substances from a contaminated environment. However, it is sometimes possible to detect the toxicity of smaller nanoparticles that have penetrated cells.

References

Agarwal S, Rai P, Gatell EN, Llobet E, Güell F, Kumar M, Awasthi K (2019) Gas sensing properties of ZnO nanostructures (flowers/rods) synthesized by hyrothermal method. Sensor Actuator B Chem 292:24–31

Ali A, Ahmed T, Wu W, Hossain A, Hafeez R, Masum MMI, Wang Y, An Q, Sun G, Li B (2020) Advancements in plant and microbe-based synthesis of metallic nanoparticles and their antimicrobial activity against plant pathogens. Nanomaterials (Basel) 10:1146

Ali S, Mehmood A, Khan N (2021) Uptake, translocation, and consequences of nanomaterials on plant growth and stress adaptation. J Nanomater 2021:1. https://doi.org/10.1155/2021/6677616

Babaei K, Sharifi RS, Pirzad A, Khalilzadeh R (2017) Effects of bio fertilizer and nano zn-fe oxide on physiological traits, antioxidant enzymes activity and yield of wheat (Triticum aestivum l.) under salinity stress. J Plant Interact 12(1):381–389

Bahrulolum H, Nooraei S, Javanshir N, Tarrahimofrad H, Mirbagheri VS, Easton AJ, Ahmadian G (2021) Green synthesis of metal nanoparticles using microorganisms and their application in the agrifood sector. J Nanobiotechnol 19:86. https://doi.org/10.1186/s12951-021-00834-3

Bhattacharyya A, Duraisamy P, Govindarajan M, Buhroo AA, Prasad R (2016) Nano-biofungicides: emerging trend in insect pest control. In: Prasad R (ed) Advances and applications through fungal nanobiotechnology. Springer International Publishing, Cham, pp 307–319. https://doi.org/10.1007/978-3-319-42990-8_15

Bhuyan T, Mishra K, Khanuja M, Prasad R, Varma A (2015) Biosynthesis of zinc oxide nanoparticles from *Azadirachta indica* for antibacterial and photocatalytic applications. Mater Sci Semicond Process 32:55–61

Birch E, Begg S, Squire R (2011) How agro-ecological research helps to address food security issues under new IPM and pesticide reduction policies for global crop production systems. J Exp Bot 62:3251–3261

Brayner R, Ferrari-Iliou R, Brivois N, Djediat S, Benedetti MF, Fiévet F (2006) Toxicological impact studies based on Escherichia coli bacteria in ultrafine ZnO nanoparticles colloidal medium. Nano Lett 6(4):866–870

Campbell BM, Thornton P, Zougmoré R, van Asten P, Lipper L (2014) Sustainable intensification: what is its role in climate smart agriculture? Curr Opin Environ Sustain 8:39–43

Chandler D, Bailey AS, Tatchell GM, Davidson G, Greaves J, Grant WP (2011) The development, regulation and use of biopesticides for integrated pest management. Philos Trans R Soc Lond Ser B Biol Sci 366:1987–1998

Chang T-H, Lu Y-C, Yang M-J (2020) Multibranched flower-like ZnO particles from eco-friendly hydrothermal synthesis as green antimicrobials in agriculture. J Clean Prod 262:121342. https://doi.org/10.1016/j.jclepro.2020.121342

Chausali N, Jyoti Saxena J, Prasad R (2022) Recent trends in nanotechnology applications of bio-based packaging. J Agric Food Res. https://doi.org/10.1016/j.jafr.2021.100257

Chausali N, Saxena J, Prasad R (2023) Nanotechnology as a sustainable approach for combating the environmental effects of climate change. J Agric Food Res. https://doi.org/10.1016/j.jafr.2023.100541

Chen H, Cui H (2018) Nanotechnology applications and implications of agrochemicals toward sustainable agriculture and food systems. J Agric Food Chem 66:6451–6456

Chhipa H (2017) Nanofertilizers and nanopesticides for agriculture. Environ Chem Lett 15:15–22

de Oliveira JL, Campos EV, Bakshi M, Abhilash PC, Fraceto LF (2014) Application of nanotechnology for the encapsulation of botanical insecticides for sustainable agriculture: prospects and promises. Biotechnol Adv 32:1550–1561. https://doi.org/10.1016/j.biotechadv.2014.10.010

Dhiman S, Varma A, Prasad R, Goel A (2022) Mechanistic insight of the antifungal potential of green synthesized zinc oxide nanoparticles against *Alternaria brassicae*. J Nanomater 2022:7138843, 13. https://doi.org/10.1155/2022/7138843

Dhiman S, Varma A, Rao M, Prasad R, Goel A (2023) Deciphering the fertilizing and disease suppression potential of phytofabricated zinc oxide nanoparticles on *Brassica juncea*. Environ Res. https://doi.org/10.1016/j.envres.2023.116276

Dimkpa CO (2014) Can nanotechnology deliver the promised benefits without negatively impacting soil microbial life? J Basic Microbiol 54:889–904. https://doi.org/10.1002/jobm.201400298

Dral AP, ten Elshof JE (2018) 2D metal oxide nanoflakes for sensing applications: review and perspective. Sensor Actuator B Chem 272:369–392

Fariq A, Khan T, Yasmin A (2017) Microbial synthesis of nanoparticles and their potential applications in biomedicine. J Appl Biomed 15:241. https://doi.org/10.1016/j.jab.2017.03.004

Floros JD, Newsome R, Fisher W, Barbosa-Cánovas GV, Chen H, Dunne CP et al (2010) Feeding the world today and tomorrow: the importance of food science and technology. Compr Rev Food Sci Food Saf 9:572–599. https://doi.org/10.1111/j.1541-4337.2010.00127.x

Gill HK, Garg H (2014) Pesticides: environmental impacts and management strategies. In: Larramendy ML, Soloneski S (eds) Pesticides-toxic aspects. IntechOpen. https://doi.org/10.5772/57399

Gogos A, Knauer K, Bucheli TD (2012) Nanomaterials in plant protection and fertilization: current state, foreseen applications, and research priorities. J Agric Food Chem 60:9781–9792

Grillo R, Abhilash PC, Fraceto LF (2016) Nanotechnology applied to bio-encapsulation of pesticides. J Nanosci Nanotechnol 16:1231–1234. https://doi.org/10.1016/j.tifs.2003.10.005

Grillone A, Li T, Battaglini M, Scarpellini A, Prato M, Takeoka S, Ciofani G (2017) Preparation, characterization, and preliminary in vitro testing of Nanoceria-loaded liposomes. Nanomeaterials 7(9):276

Gruère GP (2012) Implications of nanotechnology growth in food and agriculture in OECD countries. Food Policy 37:191–198. https://doi.org/10.1016/j.jhazmat.2014.05.079

Guo L, Shi Y, Liu X, Han Z, Zhao Z, Chen Y, Xie W, Li X (2018) Enhanced fluorescence detection of proteins using ZnO nanowires integrated inside microfluidic chips. Biosens Bioelectron 99:368–374

Han J, Fan F, Xu C, Lin S, Wei M, Xue D, Wang ZL (2010) ZnO nanotube-based dye-sensitized solar cell and its application in self-powered devices. Nanotechnology 21(40):405203

Hariharan S, Bhardwaj V, Bala I, Sitterberg J, Bakowsky U, Ravi Kumar MNV (2006) Design of estradiol loaded PLGA nanoparticulate formulations: a potential oral delivery system for hormone therapy. Pharm Res 23:84–195

Ion AC, Ion I, Culetu A (2010) Carbon-based nanomaterials: environmental applications. Univ Politehn Bucharest 38:129–132

Irum S, Jabeen N, Ahmad KS, Shafique S, Khan TF, Gul H, Anwaar S, Shah NI, Mehmoo A, Hussain SZ (2020) Biogenic iron oxide nanoparticles enhance callogenesis and regeneration pattern of recalcitrant Cicer arietinum L. PLoS One 15(12):e0242829

Jegadeesan GB, Srimathi K, Santosh Srinivas N, Manishkanna S, Vignesh D (2019) Green synthesis of iron oxide nanoparticles using Terminalia bellirica and Moringa oleifera fruit and leaf extracts: antioxidant, antibacterial and thermoacoustic properties. Biocatal Agric Biotechnol 21:101354

Kah M, Hofmann T (2014) Nanopesticides research: current trends and future priorities. Environ Int 63:224–235. https://doi.org/10.1016/j.envint.2013.11.015

Kavitha A, Doss A, Pole RPP, Pushpa Rani TPK, Prasad R, Satheesh S (2023) A mini review on plant-mediated zinc oxide nanoparticles and their antibacterial potency. Biocatal Agric Biotechnol. https://doi.org/10.1016/j.bcab.2023.102654

Khalilzadeh R, Sharifi RS, Jalilian J (2016) Antioxidant status and physiological responses of wheat (Triticum aestivum L.) to cycocel application and bio fertilizers under water limitation condition. J Plant Interact 11(1):130–137

Khota LR, Sankarana S, Majaa JM, Ehsania R, Schuster EW (2012) Applications of nanomaterials in agricultural production and crop protection: a review. Crop Prot 35:64–70. https://doi.org/10.1016/j.cropro.2012.01.007

Kim DY, Kadam A, Shinde S, Saratale RG, Patra J, Ghodake G (2018) Recent developments in nanotechnology transforming the agricultural sector: a transition replete with opportunities. J Sci Food Agric 98(849–864):12

Kisimba K, Krishnan A, Faya M, Byanga K, Kasumbwe K, Vijayakumar K, Prasad R (2023) Synthesis of metallic nanoparticles based on green chemistry and their medical biochemical applications: synthesis of metallic nanoparticles. J Renew Mater 11(6):2575–2591. https://doi.org/10.32604/jrm.2023.026159

Koch N, Sonowal S, Prasad R (2023) Elucidate the smart tailored biogenic nanoparticles and their applications in remediation. Biotechnol Genet Eng Rev. https://doi.org/10.1080/02648725.2023.2219942

Kour D, Rana KL, Kaur T, Singh B, Chauhan VS, Kumar A et al (2020) Extremophiles for hydrolytic enzymes productions: biodiversity and potential biotechnological applications. In: Molina G, Gupta VK, Singh B, Gathergood N (eds) Bioprocessing for biomolecules production. Wiley, Hoboken, NJ, pp 321–372

Kookana RS, Boxall AB, Reeves PT, Ashauer R, Beulke S, Chaudhry Q, Cornelis G, Fernandes TF, Gan J, Kah M, Lynch I (2014) Nanopesticides: guiding principles for regulatory evaluation of environmental risks. J Agric Food Chem 62(19):4227–4240

Maddela NR, Eller LKW, Prasad R (2023) Microbiology for cleaner production and environmental sustainability. CRC Press. (ISBN-13: 9781032496061)

Malerba M, Cerana R (2016) Chitosan effects on plant systems. Int J Mol Sci 17:996

McGee CF, Storey S, Clipson N, Doyle E (2017) Soil microbial community responses to contamination with silver, aluminiumoxide and silicon dioxide nanoparticles. Ecotoxicology 26(3):449–458. https://doi.org/10.1007/s10646-017-1776-5

Milani S, Baldelli Bombelli F, Pitek AS, Dawson KA, Radler J (2012) Reversible versus irreversible binding of transferrin to polystyrene nanoparticles: soft and hard corona. ACS Nano 6 (3):2532–2541

Mishra S, Singh H (2015) Biosynthesized silver nanoparticles as a nanoweapon against phytopathogens: exploring their scope and potential in agriculture. Appl Microbiol Biotechnol 99:1097–1107

Mittal D, Kaur G, Singh P, Yadav K, Ali SA (2020) Nanoparticle-based sustainable agriculture and food science: recent advances and future outlook. Front Nanotechnol 2:579954

Mitter N, Worrall EA, Robinson KE, Li P, Jain RG, Taochy C, Fletcher SJ, Carroll BJ, Lu G, Xu ZP (2017) Clay nanosheets for topical delivery of RNAi for sustained protection against plant viruses. Nat Plants 3:16207

Mubeen B, Hasnain A, Wang J, Zheng H, Naqvi SAH, Prasad R, Rehman AU, Sohail MA, Hassan MZ, Farhan M, Khan MA, Moustaf M (2023) Current progress and open challenges for combined toxic effects of manufactured nano-sized objects (MNO's) on soil biota and microbial community. Coatings 13:212. https://doi.org/10.3390/coatings13010212

Mukhopadhyay SS (2014) Nanotechnology in agriculture: prospects and constraints. Nanotechnol Sci Appl 7:63–71. https://doi.org/10.2147/NSA.S39409
Munoz-Leoz B, Ruiz-Romera E, Antigüedad I, Garbisu C (2011) Tebuconazole application decreases soil microbial biomass and activity. Soil Biol Biochem 43:2176–2183
Noor R, Yasmin H, Ilyas N, Nosheena A, Hassan MN, Mumtaz S, Khan N, Ahmad A, Ahmad P (2022) Comparative analysis of iron oxide nanoparticles synthesized from ginger (Zingiber officinale) and cumin seeds (Cuminum cyminum) to induce resistance in wheat against drought stress. Chemosphere 292:133201. https://doi.org/10.1016/j.chemosphere.2021.133201
Nuruzzaman M, Rahman MM, Liu Y, Naidu R (2016) Nanoencapsulation, nano-guard for pesticides: a new window for safe application. J Agric Food Chem 64:1447–1483. https://doi.org/10.1021/acs.jafc.5b05214
Osherov A, Prasad R, Chrzanowski W, New EJ, Brazaca L, Sadik O, Haynes CL, Maine E (2023) Responsible nanotechnology for a sustainable future. One Earth 6(7):763–766. https://doi.org/10.1016/j.oneear.2023.06.010
Pandey G (2018) Challenges and future prospects of Agri-nanotechnology for sustainable agriculture in India. Environ Technol Innov 11:299. https://doi.org/10.1016/j.eti.2018.06.012
Pouratashi M, Iravani H (2012) Farmers' knowledge of integrated pest management and learning style preferences: implications for information delivery. Int J Pest Manage 58:347–353
Prasad R, Kumar V, Prasad KS (2014) Nanotechnology in sustainable agriculture: present concerns and future aspects. Afr J Biotechnol 13:705–713. https://doi.org/10.5897/AJBX2013.13554
Prasad R, Pandey R, Barman I (2016) Engineering tailored nanoparticles with microbes: quo vadis. WIREs Nanomed Nanobiotechnol 8:316–330. https://doi.org/10.1002/wnan.1363
Prasad R, Kumar M, Kumar V (2017a) Nanotechnology: an agriculture paradigm. Springer Nature Singapore Pte Ltd. (ISBN: 978-981-10-4573-8)
Prasad R, Bhattacharyya A, Nguyen QD (2017b) Nanotechnology in sustainable agriculture: recent developments, challenges, and perspectives. Front Microbiol 8:1–13
Prasad R, Jha A, Prasad K (2018) Exploring the realms of nature for nanosynthesis. Springer International Publishing. (ISBN 978-3-319-99570-0) https://www.springer.com/978-3-319-99570-0
Raliya R, Saharan V, Dimkpa C, Biswas P (2018) Nanofertilizer for precision and sustainable agriculture: current state and future perspectives. J Agric Food Chem 66:6487–6503
Rastogi A, Zivcak M, Sytar O, Kalaji HM, He X, Mbarki S, Brestic M (2017) Impact of metal and metal oxide nanoparticles on plant: a critical review. Front Chem 5(October):1–16
Rauscher H, Sokull-Klüttgen B, Stamm H (2012) The European Commission's recommendation on the definition of nanomaterial makes an impact. Nanotoxicology 7:1195–1197
Revie NM, Iyer KR, Robbins N, Cowen LE (2018) Antifungal drug resistance: evolution, mechanisms and impact. Curr Opin Microbiol 45:70–76
Sabir S, Arshad M, Chaudhari SK (2014) Zinc oxide nanoparticles for revolutionizing agriculture: synthesis and applications. Sci World J 2014:8. https://doi.org/10.1155/2014/925494
Sadeghi R, Rodriguez RJ, Yao Y, Kokini JL (2017) Advances in nanotechnology as they pertain to food and agriculture: benefits and risks. Annu Rev Food Sci Technol 8:467–492
Sadeghzadeh B (2013) A review of zinc nutrition and plant breeding. J Soil Sci Plant Nutr 13:905–927. https://doi.org/10.4067/S0718-95162013005000072
Saglam N, Korkusuz F, Prasad R (2021) Nanotechnology applications in health and environmental sciences. Springer International Publishing. (ISBN: 978-3-030-64410-9) https://www.springer.com/gp/book/9783030644093
Salem SS, Fouda A (2021) Green synthesis of metallic nanoparticles and their prospective biotechnological applications: an overview. Biol Trace Elem Res 199(1):344–370. https://doi.org/10.1007/s12011-020-02138-3
Saravanan A, Kumar PSS, Karishma S, Vo DN, Jeevananthama S, Yaashikaa PR, George CS (2021) A review on biosynthesis of metal nanoparticles and its environmental applications. Chemosphere 264:128580

Sarma H, Joshi S, Prasad R, Jampilek J (2021) Biobased nanotechnology for green applications. Springer International Publishing. (ISBN 978-3-030-61985-5) https://www.springer.com/gp/book/9783030619848

Sebastian N, Yu W-C, Hu Y-C, Balram D, Yu Y-H (2019) Sonochemical synthesis of iron-graphene oxide/honeycomb-like ZnO ternary nanohybrids for sensitive electrochemical detection of antipsychotic drug chlorpromazine. Ultrason Sonochem 59:104696

Servin AD, White JC (2016) Nanotechnology in agriculture: next steps for understanding engineered nanoparticle exposure and risk. NanoImpact 1:9–12

Shash S, Ramanan VV, Prasad R (2019) Sustainable green technologies for environmental management. Springer Singapore. (ISBN: 978-981-13-2772-8) https://www.springer.com/la/book/9789811327711

Shende S, Rajput V, Gade A, Minkina T, Sushkova SN, Mandzhieva SS, Boldyreva VE (2022) Metal-based green synthesized nanoparticles: boon for sustainable agriculture and food security. IEEE Trans Nanobioscience 21:44. https://doi.org/10.1109/TNB.2021.3089773

Singhal U, Khanuja M, Prasad R, Varma A (2017) Impact of synergistic association of ZnO-nanorods and symbiotic fungus *Piriformospora indica* DSM 11827 on *Brassica oleracea* var. botrytis (Broccoli). Front Microbiol 8:1909. https://doi.org/10.3389/fmicb.2017.01909

Sirelkhatim A, Mahmud S, Seeni A, Kaus NHM, Ann LC, Bakhori SKM, Hasan H, Mohamad D (2015) Review on zinc oxide nanoparticles: antibacterial activity and toxicity mechanism. Nanomicro Lett 7:1–24

Sreelakshmi B, Induja S, Adarsh PP, Rahul HL, Arya SM, Aswana S, Vishnudasan D (2020) Drought stress amelioration in plants using green synthesise iron oxide nanoparticles. Mater Today Proc 41:723–727

Srivastava S, Usmani Z, Atanasov AG, Singh VK, Singh NP, Abdel-Azeem AM, Prasad R, Gupta G, Sharma M, Bhargava A (2021) Biological nanofactories: using living forms for metal nanoparticle synthesis. Mini-Rev Med Chem 21(2):245–265

Sundari S, Singh A, Yadava P (2016) Review of current research advances in microbial and phyto-biopesticides. Int J Biotechnol Biomed Sci 2:73–77

Thakur N, Kaur S, Tomar P, Thakur S, Yadav AN (2020) Microbial biopesticides: current status and advancement for sustainable agriculture and environment. In: New and future developments in microbial biotechnology and bioengineering. Elsevier, Amsterdam. https://doi.org/10.1016/B978-0-12-820526-6.00016-6

Tian T, Sun B, Li H, Li Y, Gao T, Li Y et al (2016) Commercialization and regulatory requirements of biopesticides in China. In: Singh H, Sarma B, Keswani C (eds) Agriculturally important microorganisms. Springer, Singapore, pp 237–254

Tian H, Fan H, Ma J, Liu Z, Ma L, Lei S, Fang J, Long C (2018) Ptdecorated zinc oxide nanorod arrays with graphitic carbon nitride nanosheets for highly efficient dual-functional gas sensing. J Hazard Mater 341:102–111

Tsekhmistrenko SI, Bityutskyy VS, Tsekhmistrenko OS, Horalskyi LP, Tymoshok NO, Spivak MY (2020) Bacterial synthesis of nanoparticles: a green approach. Biosyst Divers 28(1):9–17

Vishwakarma K, Upadhyay N, Kumar N, Tripathi DK, Chauhan DK, Sharma S, Sahi S (2018) Potential applications and avenues of nanotechnology in sustainable agriculture. In: Nanomaterials in plants, algae, and microorganisms. https://doi.org/10.1016/B978-0-12-811487-2.00021-9

Vishwakarma K, Kumar N, Shandilya C, Mohapatra S, Bhayana S, Varma A (2020) Revisiting plant–microbe interactions and microbial consortia application for enhancing sustainable agriculture: a review. Front Microbiol 11:560406. https://doi.org/10.3389/fmicb.2020.560406

Wang H, Xie J, Yan K, Duan M (2011) Growth mechanism of different mor- phologies of ZnO crystals prepared by hydrothermal method. J Mater Sci Technol 27:153–158

Worrall EA, Hamid A, Mody KT, Mitter N, Pappu HR (2018) Nanotechnology for plant disease management. Agronomy 8:285. https://doi.org/10.3390/agronomy8120285

Yadav AN, Singh J, Rastegari AA, Yadav N (2020a) Plant microbiomes for sustainable agriculture. Springer, Cham, pp 475–482

Yadav AN, Rastegari AA, Yadav N, Kour D (2020b) Advances in plant microbiome and sustainable agriculture, Diversity and bio-technological applications, vol 1. Springer, Singapore

Yang W, Peters JI, Williams RO (2008) Inhaled nanoparticles a current review. Int J Pharm 356: 239–2479

Yang H, Liu C, Yang D, Zhang H, Xi Z (2009) Comparative study of cytotoxicity, oxidative stress and genotoxicity induced by four typical nanomaterials: the role of particle size, shape and composition. J Appl Toxicol 29:69–78

Yaseen R, Ahmed AIS, Omer AM, Agha MKM, Emam TM (2020) Nano-fertilizers: bio-fabrication, application and biosafety. Novel Res Microbiol J 4(4):884–900

Zhang Q, Han L, Jing H, Blom DA, Lin Y, Xin HL et al (2016) Facet control of gold nanorods. ACS Nano 10:2960–2974. https://doi.org/10.1021/acsnano.6b00258

Zhao P, Cao L, Ma D, Zhou Z, Huang Q, Pan C (2017) Synthesis of Pyrimethanil-loaded mesoporous silica nanoparticles and its distribution and dissipation in cucumber plants. Molecules 22:817

Zhao F, Zhou X, Deng W, Liu Z (2019) Entrapping lithium deposition in lithiophilic reservoir constructed by vertically aligned ZnO nanosheets for dendrite-free Li metal anodes. Nano Energy 62:55–63

Zia R, Nawaz MS, Siddique MJ, Hakim S, Imran A (2021) Plant survival under drought stress: implications, adaptive responses, and integrated rhizosphere management strategy for stress mitigation. Microbiol Res 242:126626

Applications of Microbially Synthesized Nanoparticles to Food Science

15

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Abstract

Food plays a major role in the life of plants, animals, and human beings. When a man has become stationary and started farming, storage of food has become an essential issue. In the olden days, food used to be preserved by adding vinegar, honey, and salts and even by sun drying or heat. Due to limited preservation techniques, food wastage has become a major problem. The emergence of technology has evolved in engineering food processing. Many processes have improved by using nanotechnology-based applications, resulting in nanofood. With the application of nanotechnology in the processing, production, security, and packaging of food, the shelf life of food has been improved. Microbially synthesised nanoparticles were found advantageous compared to plant-based nanoparticles. These green synthesised nanoparticles have been widely used in food science to enhance the shelf life of food to meet the growing needs of the population. As few studies are being done on microbially synthesised nanoparticles in food science, this attempt is made to compile the relevance of nanoparticles in the food industry.

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Keywords

Nanoparticles · Shelf life · Nanotechnology · Green synthesis · Food nanotechnology

15.1 Introduction

Food is a substance that includes normally eaten or drunk. It is the main source of energy and nutrition for animals and humans, originating either from plants or animals. The Institute of Food Technologists defines food science as "The discipline in which the engineering, biological, and physical sciences are used to study the nature of foods, the causes of deterioration, the principles underlying food processing, and the improvement of foods for the consuming public" (Heldman 2006). The textbook *Food Science* defines food science in simpler terms as "the application of basic sciences and engineering to study the physical, chemical, and biochemical nature of foods and the principles of food processing" (Potter and Hotchkiss 1998). From the ages, food is preserved by holding in vinegar, honey, salts, and even some foods were dried either in the sun or heat. Food science has become a legitimate profession following World War II, before that the vast majority of foods in the world were prepared locally, and consumers had no choice but to visit butchers, bakeries, dairies, green groceries, and other purveyors close to their homes and purchase mainly unbranded goods.

Food wastage leads to major issues in the food industry. The Food and Agriculture Organization of the United Nations reported that more than 1.3 billion metric tons of consumable food are lost during the food supply chain due to poor postharvest technologies available resulting in food wastage during storage, transport, and marketing (Tricco et al. 2019). Apart from increasing the food production rate, it's important to control food wastage to meet the demands of the increasing population. The major cause of food wastage is bacterial contamination which reduces food quality and security, reduces the shelf life of food products, and increases the risk of foodborne diseases (Sperber and Doyle 2009).

15.1.1 Nanotechnology

Technology developed in the early and middle twentieth century allowed the manufacturer to produce canned, chilled, frozen foods, and packaged foods and made them available to consumers. Advanced usage of science results in technology and the use of scientific innovations for the advancements of industry (differencebetween.com). Technologies are used after the point of harvesting crops until the point of consumption belongs to the food technology. Some of the technologies used in food preservation are sterilization and pasteurization. Specific technological applications can be called techniques that include analytical, separation, vacuum packaging, and modified atmospheric techniques.

The term "nano" a prefix meaning "one billionth" is derived from the ancient Greek language. In 1974, the word "nanotechnology" was coined for the first time in the scientific world by Taniguchi (1974) at the International Conference on Industrial Production in Tokyo. He was a professor at the Tokyo University of Science. Nanoscience is the study of nanometre size materials that are below 1 micrometre (1 μm) in size. The nanoscale is measured in nanometres (10^{-9} m). In recent years, nanotechnology is the most active research field as it can control and manipulate matter in the nano-size.

Nanoscience and nanotechnology are new frontiers of this century and food nanotechnology is an emerging technology. Their applications to the agriculture and food sector are relatively recent compared with their use in drug delivery and pharmaceuticals. Many scientists and engineers have recognized well the potential of nanotechnology to lead all the food industries in the twenty-first century. In the food engineering field, two major applications related to nanotechnology, that is, food nanosensing and food nano-structured ingredients, are being expected. In the former field, better food quality and safety evaluation can be achieved by using nanotechnology. Advances in technologies, such as DNA microarrays, microelectromechanical systems, and microfluidics, will enable the realization of the potential of nanotechnology for food applications. In the latter, food processing can be largely improved in the aspects of smart delivery of nutrients, bioseparation of proteins, rapid sampling of biological and chemical contaminants, nanoencapsulation of nutraceuticals, solubilization, delivery, and colour in food systems.

Nanotechnology is the technology applied in the manipulation of nanomaterials for several purposes, which plays a crucial role in the food and agriculture sectors, contributes to improving crops, enhances food quality and safety, and promotes human health through novel and innovative approaches (Duncan et al. 2007).

Nanotechnology is a key advanced technology enabling contribution, development, and sustainable impact on the food, medicine, and agriculture sectors. Nanomaterials have the potential to lead to qualitative and quantitative production of healthier, safer, and high-quality functional foods which are perishable or semi-perishable. Nanotechnologies are superior to conventional food processing technologies with an increased shelf life of food products, preventing contamination, and production of enhanced food quality (Nile et al. 2020) Nanotechnology-enhanced food packaging improves the shelf life of food products by its antibacterial activity over conventional packaging by detection of food toxins, flavours, colours, and formations (Sekhon 2009; Karlo et al. 2023; Chausali et al. 2023). Nanotechnology-based intelligent systems provide localization, sensing, reporting, and remote control of food items with improved efficiency and security. Further, it also improves the neutraceutical value of the food components.

Nanomaterials are tiny particles ranging from 1 to 100 nm in size, insoluble or bio-persistent, synthesized through various routes, and used in numerous fields including medicine, electronics, agriculture, and food industries. Different-sized nanoparticles are used in nanotechnologies of food science for the potential production and processing of healthier, safer, and high-quality foods (Duncan et al. 2007).

15.1.2 Synthesis of Nanoparticles (Fig. 15.1)

Various methods have been used to obtain silica particles are employed such as plasma synthesis, chemical vapor deposition, microemulsion processing, combustion synthesis, sol-gel processing, and hydrothermal techniques (Singh et al. 2011). These methods can be categorized into three main approaches: top-down and bottom-up. Top-down is characterized by reducing the dimension of the original size by utilizing special size reduction techniques (physical approach). The bottom-up or chemical approach involves a common route used to produce nanoparticles from an atomic or molecular scale. In biological synthesis (green nanotechnology), the synthesis of nanoparticles (NPs) micro-organisms is used (Prasad et al. 2016). It is well known that many microorganisms aggregate inorganic material within or outside the cell to form NPs. While a large number of microbial species are capable of producing metal NPs, the mechanism of NP biosynthesis is very important. Microbial synthesis of NPs is a green chemistry approach that interconnects nanotechnology and microbial biotechnology.

Various physical and chemical methods are broadly used for the synthesis of nanoparticles. Dry processing (milling/grinding materials are physically broken down into coarse particles using mechanical energy), high-pressure homogenization (decreasing fat globule size to enhance emulsion stability), or mico-fluidization (type of homogeneity wherein supplementary compartments are used to reduce the size and generate emulsions, improving texture, and mouthfeel) and ultrasonic emulsification (employing high-intensity ultrasonic pulse capable of changing the characteristics of treated materials owing to cavitation's intense shear forces, pressure, and temperature) are the techniques used in the top-down method to prepare nanoparticles (Pathakoti et al. 2017). Its usage has benefited the making of salad

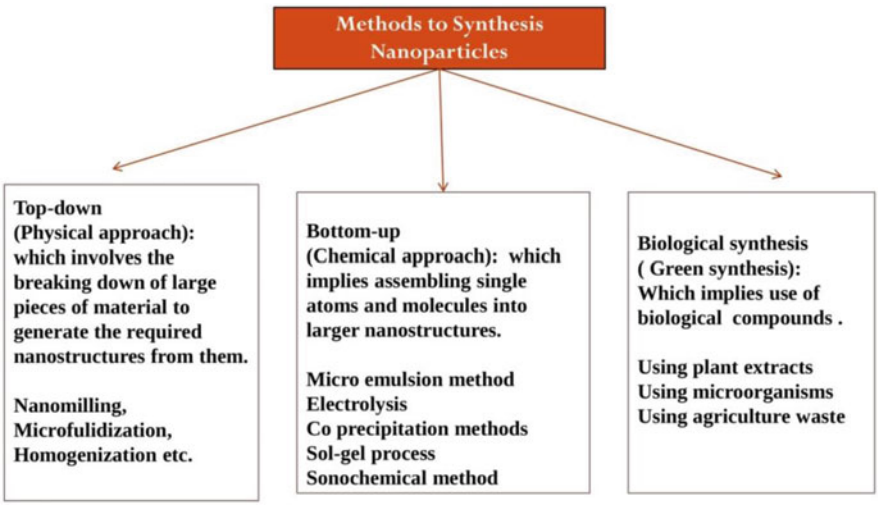

Fig. 15.1 Nanoparticle synthesis methods

dressings, yoghurts, creams, chocolate, syrups, and malted beverages, as well as fillings, flavour oil emulsions, and icings (Kentish et al. 2008).

Though these approaches offer higher production rates and better size control over the synthesized nanoparticles, they are considered unfavourable due to high capital cost, energy requirements, anaerobic conditions, use of toxic reagents, and the generation of hazardous wastes. Moreover, the chemically synthesized nanoparticles are less biocompatible (Hosseini and Sarvi 2015), and the use of toxic chemicals for synthesis and lack of stability has limited their use in clinical applications. Therefore, the development of environmentally safe, economical, and biocompatible procedures for the synthesis of nanoparticles is desired.

15.2 Microbial Synthesis of Nanoparticles

One of nanotechnology's primary objectives is to establish an eco-friendly production process that can provide low-toxicity nanoparticles. Several investigators have focused their interest on biological methods of synthesizing metal nanoparticles to achieve this objective, as these are fast, cost-effective, and eco-friendly. For this reason, the biological synthesis of nanoparticles includes a vast range of species in nature, such as viruses, bacteria, fungi, algae, and plants (using their enzymes, proteins, DNA, lipids, carbohydrates, etc.) (Prasad 2016, 2017, 2019; Eftekhari et al. 2023; Srivastava et al. 2021; Koch et al. 2023). Bacteria that reduce metals are found environmental-friendly catalysts for bioremediation as well as materials synthesis. Microbes may help in the synthesis of diverse metal oxides through respiration processes (Kim et al. 2018). Electrons can be moved from reduced organic to oxidized inorganic compounds through microbial dissimilatory anaerobic respiration, thus promoting the formation of crystal/nanoparticles along with bioremediation processes. It is well-documented that the genus *Shewanella* can the oxidation of organic acids as electron donors and reduction of inorganic metals as electron acceptors (Heidelberg et al. 2002; Harris et al. 2018). Further, the mechanism for detoxifying the immediate cell environment has been developed by microorganisms such as bacteria by reducing toxic metal species into metal nanoparticles (Deplanche and Macaskie 2008; Murray et al. 2017). Also, biomolecules secreted by bacteria were used as capping as well as stabilizing agents of nanoparticle synthesis. The nanoparticle synthesis by the microbial process is depicted in Fig. 15.2. The nanoparticles are usually formed following the way where metal ions are first trapped on the surface or inside of the microbial cells. The trapped metal ions are then reduced to nanoparticles in the presence of enzymes. In general, microorganisms impact mineral formation in two distinct ways. They can modify the composition of the solution so that it becomes supersaturated or more supersaturated than it previously was concerning a specific phase. A second means by which microorganisms can impact mineral formation is through the production of organic polymers, which can impact nucleation by favouring (or inhibiting) the stabilization of the very first mineral seeds. Microbes, which are regarded as potent eco-friendly green nano-factories, have the potential to control the size and shape of biological

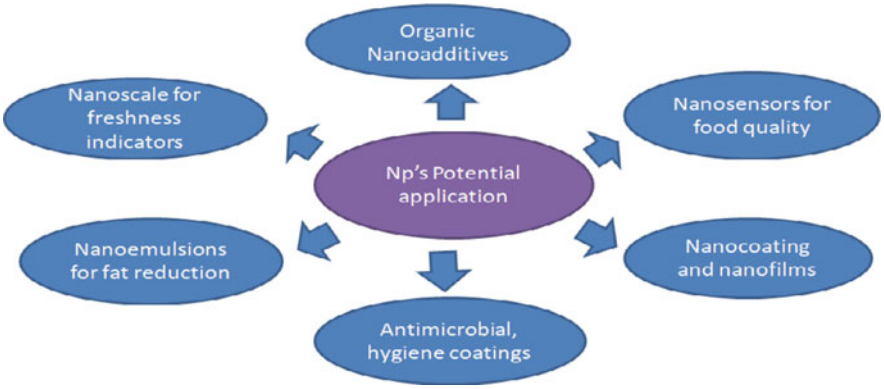

Fig. 15.2 Applications of nanoparticles in food processing

nanoparticles. Even though plant-extract-based nanoparticle synthesis is a well-known biological nano-synthesis platform, nanoparticles synthesized this way may become polydisperse due to the presence of phytochemicals as well as have a difference in yield due to seasonal variations (Mishra et al. 2013, 2016; Ovais et al. 2018; Sadaf et al. 2020; Ahmad et al. 2021). Thus, these are the distinct advantages of the synthesis of nanoparticles by microbes as compared to plants. Therefore, many microorganisms are considered to be potential candidates for the synthesis of nanoparticles (Priyadarshini et al. 2013).

Synthesis of nanoparticles by biological means offers a cheap, nontoxic, and eco-friendly alternative to their counter-physical and chemical methods (Ahmed et al. 2016). Microbes are found to be tiny nano-factories, and microbial synthesis of nanoparticles has merged biotechnology, microbiology, and nanotechnology into a new field of nano-biotechnology (Narayanan and Sakthivel 2010). Biosynthesis of gold, silver, gold–silver alloy, selenium, tellurium, platinum, palladium, silica, titania, zirconia, quantum dots (QDs), magnetite, and uraninite NPs by bacteria, actinomycetes, fungi, yeasts, and viruses have been reported. Silver nanoparticles (Ag NPs) have become one of the most commonly used nanomaterials in consumer products (104 out of 502 nanoproducts) surveyed (Maynard and Michelson 2005). Microbes may interact with nanomaterials or in certain instances produce nanostructured materials (Shankar et al. 2003). This is because of their excellent performance, selective adsorption of metal ions, operation over a broad range of ecological conditions (pH, ionic strength, temperature), low cost, free availability, regeneration, and high biosorption capacity and the fact that large quantities can be obtained (Rai et al. 2009) (Table 15.1).

15.2.1 Nanotechnology in Food Processing

Food processing involves different types of numerous unit operations from raw materials to finished products, particularly key processing, preservation, packaging,

Table 15.1 Microbially synthesized nanoparticles and applications

Species	Nanoparticle	size (nm)	Application	Reference
Bacteria				
Bacillus subtilis	TiO_2	10–30	Photocatalytic effect	Dhandapani et al. (2012)
Lactobacillus sp.		50–100	Antibacterial activity, immobilization, and refolding of enzymes	Ahmad et al. (2014)
Escherichia coli	Ag	5–50	Antibacterial activity	Saeed et al. (2020)
Thermophilic *Bacillus* sp. Az1	Ag	32	Antimicrobial activity	Saeed et al. (2020)
Lactobacillus kimchicus DCY51	Au	5–30	Antioxidant activity	Markus et al. (2016)
Lactobacillus fermentum	Iron oxide	10–15		Park et al. (2014)
Bacillus licheniformis	Cadmium sulphide	20–40	Antibacterial activity	Shivashankarappa and Sanjay (2015)
Fungus				
Penicillium sp.	Ag	25–30	Antibacterial	Singh et al. (2014)
Aspergillus niger	Ag	13.2–600	Antifungal activity	Gursoy (2020)
Trichoderma harzianum	Au	32–44	Antibacterial activity	Tripathi et al. (2018)
Aspergillus flavus	TiO_2	62–74	Antimicrobial activity	Rajakumar et al. (2012)
Yeast				
Yarrowia lipolytica	Ag	2–10	Antimicrobial and activity against *E. coli*	Apte et al. (2013), Bolbanabad et al. (2020)
Saccharomyces cerevisiae	TiO_2	7	Antibacterial activity	Jha et al. (2009)
Baker's yeast	Fe_2O_3	2–10	Detection of H2O2 and glucose	Mishra et al. (2015)

transportation, distribution, and storage where the major purpose is the inactivation of different pathogens/microorganisms and enzymatic activity, removal of toxic substances, nutrient enrichment (fortification-nutrition supplements) and so on activities implementation. As a result, many processes might be considerably improved by using nanotechnology-based applications. Nanofood refers to the food generated by using nanotechnology in the processing, production, security, and packaging of food (Powers et al. 2006). Based on process technology, packaging, antimicrobials, and food components are some of the potential usages of nanotechnology in foodstuffs that may be characterized as either "direct" (Karlo et al. 2023; Chausali et al. 2023) or "indirect". Direct usages include the direct integration of nanostructured materials into the food matrix, as well as the indication

of their presence other usages also involving including preservatives, aromas, antioxidants, colouring agents, and bioactive constituents like polyphenols, omega-3 fatty acids, vitamins, and various types of food components. Indirect usages include the nanostructured particles using smart packaging techniques (McClements and Xiao 2012), for the hydration of lipids, or the employment of expertly nanostructured catalyzers (Moraru et al. 2009). Nanotechnology advances in food processing are primarily focused on improving food texture, encapsulating food additives or ingredients, generating novel tastes and sensations, regulating flavour release, and enhancing the bioavailability of nutrient content (Abbas et al. 2009). Nanotechnology is used to innovate and improve foodstuffs and commodities throughout food processing and production (Reddy et al. 2022). Antioxidants, antimicrobials, vitamins, flavouring agents, colouring agents, and preservatives are among many functional elements utilized in the food industry. These materials are available in a variety of physical and molecular forms (physical states and molecular weights and polarities) (Chau et al. 2007). During food processing, storage, and use, these functional components should be preserved from degradation. A delivery method for nutrients and supplements is an essential component that influences the effectiveness of food ingredients in the food industry (Abbas et al. 2009). The delivery method serves a variety of functions in transportation, including transporting functional materials to the intended action location. The functional components have also been shielded against chemical or biological deterioration in the delivery system to keep them active. Aside from that, the delivery method may be able to manage the delivery of the functioning substance, including the pace at which it is released and the precise environmental circumstances that cause it to be delivered. Additionally, the distribution strategy must be in line with the other components of the process as well as the physicochemical characteristics of the finished product, such as its appearance, texture, taste, and shelf life. Because functional materials are so significant in delivery methods, delivery methods have been implemented to encapsulate them, such as simple solutions, emulsions, colloids, biopolymer matrices, and some others (Chau et al. 2007). Self-assembled nanotubes made from hydrolyzed milk protein like α-lactalbumin may provide a novel naturally produced provider for nanoencapsulation of vitamins, nutrition, and drugs (Graveland and De Kruif 2006). Encapsulation of food ingredients and additives is among the most prevalent applications of nanotechnology. Consumers may customize nano-encapsulated foods to match their nutritional requirements and interests. Nano-encapsulated food ingredients and additives/supplements provide protective barriers, taste and aroma concealment, sustained discharge, and enhanced dispensability for water-insoluble food components and supplements/additives (Abbas et al. 2009). To provide nutrients, nanocapsules can be introduced to foodstuffs. Higher nutrient absorption may be achieved by adding nanoparticles to present foods. Another key use is the use of additives that are readily absorbed into the body and prolongs the shelf life of commodities. Nanoparticle's colloids, emulsions, and packed nanocapsules do not settle, resulting in a longer product life and storage life.

In the food industry, nanotechnology is applied to all practices like food production, processing, storage, and distribution. It provides enhanced security by using nanosensors to detect any pathogens or containments in food. Nanotechnology-enhanced food packaging offers an improvement over conventional packaging that uses plastic barriers, and at the same time, its functional components such as antimicrobial activities provide increased shelf life to the food products. It is also involved in the detection of food toxins, flavour production, and colour formation (Sekhon 2010). Edible nano-coating thin coatings can be used in meat cheese, fast foods, bakery and confectionary goods, fruits, and vegetables in which they act as gas and moisture barriers.

15.2.2 Prospects of Nanotechnology in Industry (Fig. 15.3)

Applications of nanotechnology in food science are going to impact the vital aspects of food and related industries from food safety to the molecular synthesis of new food products and ingredients. The unique properties of these nanostructures and nanomaterials including physical, chemical, and biological properties are considerably different from their bulk counterparts and alter the understanding of biological and physical occurrence in food systems. Several recent reports and reviews have identified potential applications of nanotechnology for the food sector to improve food safety, enhance packaging, and lead to improved processing and nutrition (Dasgupta et al. 2015). Increasing the shelf life of the food (preservation), food safety, colouring, flavouring, and nutritional additives, and using antimicrobial

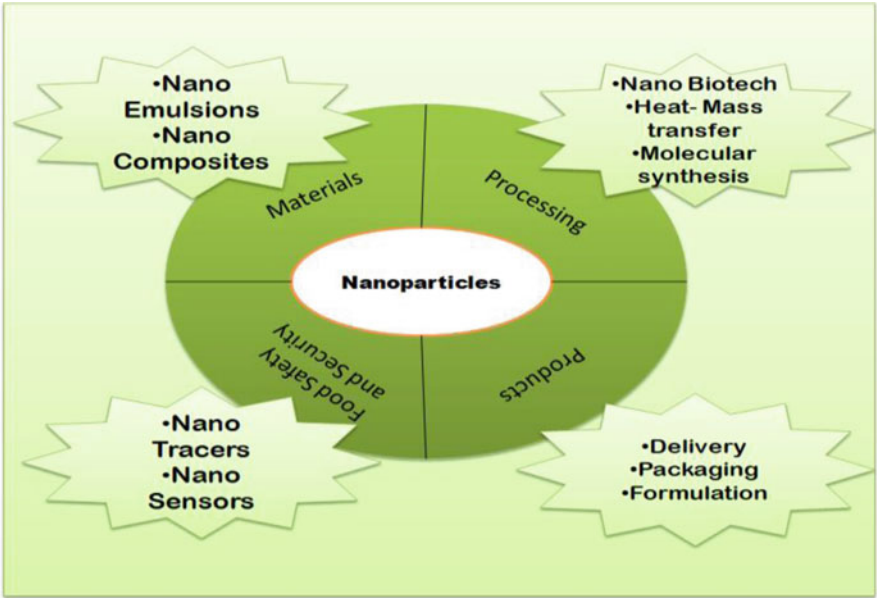

Fig. 15.3 Nanoparticles in the food industry

Table 15.2 Applications of nanoparticles in the food industry

S. no.	Nanomaterials	Type of nanomaterials	Applications in food industry
1	Nanoparticles	Ag, ZnO, Mg, SiO_2	Food packaging antibacterial and oxidation of contaminate
2	Nanosieves	Specific nanoparticles	Removal of pathogens and unwanted materials
3	Nanocapsules	Bioactive compounds	Control release, increased efficacy, and solubility property
4	Nano-emulsions	Gum, modified starch, soy, spans	Food encapsulation, food processing, food storage, antimicrobial
5	Nanospheres	Starch nanosphere	Synthetic adhesives
6	Nanocochleates	Coiled nanoparticles	Antioxidant, food protection, nutritional enhancement
7	Nanomicelles	Novasol	Liquid carrier, enhanced solubility
8	Nanosensors	Aptasensors	Food microbial detection, food spoilage control

ingredients for food packaging are some of the important applications of nanotechnology in the food industry (Chaudhry et al. 2008; Prasad et al. 2017a, b; Prasad et al. 2020). It is commonly distinguished between two forms of nanofood applications: food additives (nano inside) and food packaging (nano outside). Nanoscale food additives may, for example, be used to influence product shelf life, texture, flavour, and nutrient composition, or even detect food pathogens and provide functions as food quality indicators. In the context of food packaging, nanotechnologies are mainly considered to be of use to increase product shelf life, indicate spoilt ingredients, or generally increase product quality, e.g., by preventing gas flow across product packaging (Nickols-Richardson and Piehowski 2008; Thangadurai et al. 2020). Nanotechnology has major advantages in its usage for packaging in comparison with the conventional ways using polymers, which may include merits such as enhanced barrier and mechanical and heat-resistant properties, along with biodegradability (de Azeredo 2009). In addition to enhanced antimicrobial effects, nanomaterials can be used for the detection of food spoilage through nanosensors (McClements 2012). Although nanotechnology has great potential to fabricate innovative products and processes in the food sector, there are many challenges to overcome in food science and technology. The major challenges are to produce edible delivery systems using economic processing operations with effective formulation for human consumption and safety (Osherov et al. 2023).

According to Sasaki et al. (2011), curcumin dispersed with colloidal NPs found to have higher absorption efficacy than natural curcumin powder. A study revealed that the colour degradation rate of beta-carotene dissolved in nano-emulsions was much slower in the presence of a chemical inhibitor because of its attraction to chelate transition elements (such as Fe^{2+}) that usually favour oxidation (Qian et al. 2012). Moreover, the oral bioavailability of curcumin can be nine folds higher when administered with (piperine) absorption enhancer (Shaikh et al. 2009; Haq et al. 2020) (Table 15.2).

Yadav (2017) proposed the low bioavailability, stability, and solubility of bioactive molecules can be improved with the assistance of nanotechnology, especially with nano-formulations (Prasad et al. 2019). Many biologically active particles utilized in dealing with diseases are hydrophobic with limited bioavailability. Nanotechnology-based delivery systems are formulated to improve the targeted delivery of such nutrients. NPs are also prepared from natural food-grade macroingredients such as proteins, polysaccharides, lipids, and phospholipids, thus delivering no toxic effects. Nano-emulsions are identified as numerous combinations of food-grade ingredients such as lipid core along with protein shell (Kumar 2000).

The breakdowns of a micronutrient present in a food product significantly rely on its physicochemical and molecular properties, as well as the food composition and storage conditions. Micronutrients may be vulnerable to enzymatic, physical, and chemical instability within a food product. Chemical variability includes changes in the molecular arrangement which may lead to considerable variation in nutritional attributes and physicochemical properties of the bioactive component. Oxidation, hydrolysis, isomerization, and reduction are the common causes of the chemical breakdown of micronutrients, and these reactions can be carried out by enzymes present within the food products (McClements 2015; McClements et al. 2009). Physical instability is considered an alteration in the locality of micronutrients such as phase variations (e.g., crystallization, polymorphic transitions, or melting), gravitational separation, and aggregation, whereas principal degradation mechanisms and key factors (i.e., pH, temperature, and water activity) are critically significant to recognize for a specific micronutrient (Joye et al. 2014; Manzoor et al. 2019).

NPs may be layered with materials that inhibit the dissemination of one or more reactants into the particles. According to Matalanis et al. (2011), the degree of lipid oxidation in oil-in-water suspensions can be decreased by embedding the lipid molecules within a microgel surrounded by protein molecules (Matalanis et al. 2011; Zhang et al. 2013). For example, the rate of lipid oxidation is lower in fish oil droplets captured within casein pectin microgels as compared to their free form (Zhang et al. 2013). These microgels may limit oxidation via several mechanisms such as antioxidant activity, chelating transition metals, and inhibiting dissemination of reactants (McClements 2015).

Biopolymer NPs and microgels prepared by dietary fibres may be capable of delivering not only several lipophilic bioactive components into the lumen but also remaining intact within GIT. However, it may be essential to design a biopolymer NP that protects the micronutrient within the food product. When designing biopolymer NPs for controlled release systems, it is necessary to investigate them by using *in vitro* virtual GIT models and practical *in vivo* animal studies along with human trials (McClements 2015).

Nanoscale thymoquinone (Khader and Eckl 2014) which was found to improve the anticancer roles of doxorubicin by upregulation of P53 and down-regulation of Bcl2 and potentiate paclitaxel's apoptosis in MCF-7 breast cancer cells, could protect also against diabetes, inflammation, central nervous system, and hepatotoxicity primarily by enhancing the antioxidant status of organs and could be considered

as a promising nutraceutical for human health (El-Far et al. 2018). Recent findings concerning the use of cellulosic nanomaterials for food and nutraceutical needs were summarized by Khan et al. (2018). The addition of cellulose nanocrystals and lecithin into alginate microbeads improved the viability of encapsulated probiotic (*Lactobacillus rhamnosus* ATCC 9595) during gastric passage and storage, and at 25 and 4 °C storage conditions, a decrease in the viability of *L. rhamnosus* by 1.23 and 1.08 log, respectively, was estimated, while at encapsulation of the probiotic with alginate microbeads, a 3.17 and 1.93 log reduction, respectively, was observed (Huq et al. 2017).

Protein–lipid composite NPs having a three-layered structure (barley protein layer, α-tocopherol layer, and phospholipid layer) and an inner aqueous compartment to load the hydrophilic nutraceutical vitamin B12 exhibited controlled release behaviour in simulated GI media, and in an *in vivo* experiment, the NPs loaded with vitamin B12 increased serum vitamin B12 levels in rats upon their oral administration and reduced the level of methylmalonic acid more efficiently than the free vitamin B12 form without any toxicity of the formulation observed during 14 days. These NPs could be used for increasing vitamin B12 absorption upon oral administration.

15.2.3 Applications (Relevance of Nanoparticles in Food Science)

Some food products contain ingredients that are nanosized and different from synthetically manufactured nanomaterials. Many food proteins are of globular structures between 10 nm and 100 nm in size, and others include the majority of polysaccharides and lipids, which are linear polymers of <1 nm in thickness (one-dimensional, nanostructures). Milk and milk products, such as milk proteins and casein, are also natural nanostructures. The most significant synthetic nanostructured systems in food are polymeric NPs, liposomes, nanoemulsions, and microemulsions. These materials enhance solubility, improve bioavailability, facilitate controlled release, and protect bioactive components during manufacture and storage (Chang and Chen 2005).

Carbon nanotubes are cylinders with nanoscale diameters that can be used in food packaging to improve their mechanical properties. In addition, it was recently discovered that they may also exert powerful antimicrobial effects. *Escherichia coli* died immediately upon direct contact with aggregates of carbon nanotubes. Presumably, the long, thin nanotubes punctured the *E. coli* cells, causing cellular damage. Single-walled carbon nanotubes may eventually serve as building blocks for antimicrobial materials (Kang et al. 2007).

Nano-wheels were also recently developed to improve food packaging. Inorganic alumina platelets have been self-assembled into wagon wheel-shaped structures that are incorporated into plastics to improve their barrier and mechanical properties. This was the first time large wheel-shaped molecules had been formed (Mossinger et al. 2007).

The addition of nanosensors to food packages is also anticipated in the future. Nanosensors could be used to detect chemicals, pathogens, and toxins in foods. Numerous research reports describe detection methods for bacteria, viruses, toxins, and allergens using nanotechnology. For example, adhering antibodies to *Staphylococcus enterotoxin* B onto poly (dimethyl-siloxane) chips formed biosensors that have a detection limit of 0.5 ng/mL. Nanovesicles have been developed to simultaneously detect *E. coli* 0157:H7, *Salmonella* spp., and *Listeria monocytogenes*. Liposome nanovesicles have been devised to detect peanut allergen proteins (Doyle 2006). In addition, AgroMicron has developed a nanobioluminescence detection spray containing a luminescent protein that has been engineered to bind to the surface of microbes such as *Salmonella* and *E. coli*. When bound, it emits a visible glow that varies in intensity according to the amount of bacterial contamination. This product is being marketed under the name BioMark (Joseph and Morrison 2006).

Nanosensors Inc. is another company pursuing this potential. Through a license agreement with Michigan State University, a nanoporous silicon-based biosensor has been developed to detect *Salmonella* and *E. coli*. A prototype nanobiosensor was recently tested to detect *Bacillus cereus* and *E. coli* and was found to be able to detect multiple pathogens faster and more accurately than current devices (Liu et al. 2007). Finally, Mahadevan Iyer and his colleagues at Georgia Institute of Technology are experimenting with integrating nanocomponents in ultrathin polymer substrates for RFID chips containing biosensors that can detect foodborne pathogens or sense the temperature or moisture of a product (Nachay 2007).

Silver-based nanoparticles improve barrier and mechanical characteristics; yellowness, poor transparency, and heat stability; higher antioxidant activity; and the antibacterial activity that is effective against Gram-positive and Gram-negative bacteria which helps in active packaging for food preservation in prolonging the food shelf-life and to control the pathogenic and spoilage microorganism/bacteria (Arfat et al. 2017; Jafari et al. 2016; Ramachandraiah et al. 2017; Aziz et al. 2014, 2015, 2016, 2019).

Zinc oxide nanoparticles showed powerful antibacterial properties; irradiation with UV-A had no influence on the mechanical characteristics of the nanomaterial produced; activated oxygen scavenging materials are used to prevent oxygen flow within packing containers packaging highlights for food preservation emphasizing its antimicrobial impact and are utilized to extend the shelf life of fresh foodstuffs with inhibited foodstuffs from adhering together(Esmailzadeh et al. 2016; Mizielinska et al. 2018; Bhuyan et al. 2015; Dhiman et al. 2023; Kavitha et al. 2023).

Copper-based nanoparticles help to prevent bacteria, viruses, and fungi from growing and due to their large surface area; they were able to interface with cell membranes and show antimicrobial activity. They help in the permeation of water vapour and act as barrier characteristics, UV rays, and heat resistance. So they are used in packaging for food preservation in prolonging the food shelf-life and to control the pathogenic and spoilage microorganisms/bacteria (Almasi et al. 2018; Lomate et al. 2018; Shankar et al. 2017; Yadav et al. 2017; Gaba et al. 2023).

Nanoparticles of titanium dioxide offer several benefits. Being inexpensive, nontoxic, and photo-stable renders gaining traction as a better photocatalyst particle for economical and power applications (water splitting, air or gas and water decontamination, antibacterial, and surfaces that clean themselves) (Jassal et al. 2022). It acts as an antibacterial agent. As polymer nanocomposites' titanium dioxide mechanical characteristics have been enhanced, milk, cheese, and other various products are used as food whiteners. Active packaging for food preservation in prolonging the food shelf-life and controls the pathogenic and spoilage microorganisms/bacteria (Roilo et al. 2018; Xing et al. 2012; Yadav et al. 2016).

Gold nanoparticles as smart colourimetric sensors conform to the requirement of modern analysis, such as high selectivity, sensitivity, simplicity, celerity, and portability. Thus, they have great potential to be applied as power-sensing tools for food safety screening (Chen et al. 2018).

Silicon dioxide nanoparticles exhibit hygroscopic applicability by absorbing water molecules in food by which moisture leakage is decreased. It serves as a food colouring, drying, and anti-caking agent, typical particle size, large surface area, stability, biocompatibility, low toxicity, poor heat conductivity, and superlative insulation (Jones et al. 2008; Mallakpour and Nazari 2018).

Nano-clay and silicate increased overall volatiles, antioxidant activity, organic acids, and antibacterial activity in active packaging for food preservation in prolonging the food shelf-life and controlling the pathogenic and spoilage microorganisms/bacteria (Lopez-Rubio et al. 2019).

Metal sulphide nanoparticles have recently attracted much attention due to their unique physical and functional properties. Metal sulphide nanoparticles used as optoelectronic and biomedical materials in the past decades are promising for making functional nanocomposite films due to their low toxicity and strong antibacterial activity. Recently, copper sulphide and zinc sulphide nanomaterials have been used to produce food packaging films for active packaging. Metal sulphide nanoparticles added as nanofillers are attracting attention in packaging applications due to their excellent potential to improve mechanical, barrier properties, and antibacterial activity. This review covers the fabrication process and important applications of metal sulphide nanoparticles. The development of metal sulphides reinforcing mainly copper sulphide and zinc sulphide nanomaterials as multifunctional nanofillers in bio-based films for active packaging applications has been comprehensively reviewed. As the recognition of metal sulphide nanoparticles as a functional filler increases, the development and application potential of active packaging films using them is expected to increase (Roy et al. 2022). In addition, they provide flavour, colour, enzyme antioxidants, anti-browning compounds, and prolonged shelf life to the manufactured products.

Nanofilters have been used to remove the colour from beetroot juice while retaining its flavour and even in red wine. These are also used to remove lactose from milk so that it can be substituted with other sugars that are suitable for lactose-intolerant patients. Nanofilters also help in the elimination of bacterial species from mills and water without boiling.

It was reported that silicon dioxide (SiO_2) and TiO_2 were used in bulk as food additives. The shelf life of tomatoes has been increased by the bionanoencapsulated quercetin nanogreen tea neosinocapsule, canola active oil, aquanova (micelle to enhance the solubility of vitamins (A, C, D, E, and K), beta-carotene, and omega fatty acids), nutralease are the common commercial nanoproducts available in the market. Similarly, products like fortified fruits juices, oat nutritional drinks, nano-teas, nanocapsules containing tuna fish oil in bread, nanoceutical slim shakes, and a few commercially available nano-processed foods are available in the market (Gilligan 2008; Pocas et al. 2008). Food technology is regarded as one of the industry sectors where nanotechnology will play an important role in the future (The Eleventh ASEAN Food Conference; 21–23 October 2009; Bandar Seri Begawan, Brunei Darussalam).

15.2.4 Effects of Nanoparticles

Besides many significant applications of nanotechnology, some toxicities are associated with NPs (Ibrahim 2013). The benefits of NPs include small size, great capacity, and high reactivity, which may be fatal by causing cellular lethal effects. NPs may cause the potential for adverse human effects due to their early appreciation of biotechnology via extended exposure to GIT. One of the common NPs toxicities is the ability to gather nearby protein concentrations that can be influenced by particle size, shape, and surface. Due to this unique binding capability, some nano-materials produce adverse biotic consequences via protein fibrillation, unfolding, loss of enzymatic activity, and thiol crosslinking (Bahadar et al. 2016). Moreover, NPs are readily bioavailable but their increased surface area can result in different toxicities. The discharge of lethal ions is another premise when the thermodynamic characteristics of substances may favour NP discharge in a biological system (Xia et al. 2008). Moreover, nano-structures established for curative tenacities are in very primary stages and the lasting adverse effects on human health need advanced research.

15.3 Conclusion

Ever since the use of nanoparticles came into light, NPs are being used in different fields like painting, farming, pharmacology, biotechnology, and food processing industry. The NP production from green synthesis has enhanced the usage of NPs in food science consistent with analysis, production, processing, preservation, packaging, storage, and production of quality and safe food production. Even though successful applications of nanotechnology to foods are still limited, the tremendous use of NPs in food science has been widespread. However, a few numbers of studies are being done to decrease the toxicity of synthesized nanostructures but still, there are crucial concerns regarding the potential of NPs (Agrawal 2016; Lambadi 2015). The production, handling, and storage of nano-structures may result in a loss of

efficacy and increase the risk of toxicities which are necessary to be investigated in detail. Since the adverse effects of NPs are fatal, more research in the future needs to be focused on this.

References

Abbas K, Saleh A, Mohamed A, MohdAzhan N (2009) The recent advances in nanotechnology and its applications in food processing: a review. Food Agric Environ 7(3–4):14–17

Agrawal P (2016) Potential prospects of future medicine: nanomedicine. J Pharm 4(1):1000–1149. https://doi.org/10.4172/2329-6887.1000e149

Ahmad R, Khatoon N, Sardar M (2014) Antibacterial effect of green synthesized TiO2 nanoparticles. Adv Sci Lett 20:1616–1620. https://doi.org/10.1166/asl.2014.5563

Ahmad R, Srivastava S, Ghosh S, Khare SK (2021) Phytochemical delivery through nanocarriers: a review. Colloids Surf B Biointerfaces 197:111389. https://doi.org/10.1016/j.colsurfb.2020.111389

Ahmed S, Annu SI, Yudha SS (2016) Biosynthesis of gold nanoparticles: a green approach. J Photochem Photobiol B Biol 161:141–153

Almasi H, Jafarzadeh P, Mehryar L (2018) Fabrication of novel nanohybrids by impregnation of CuO nanoparticles into bacterial cellulose and chitosan nanofibers: characterization, antimicrobial and release properties. Carbohydr Polym 186:273–281

Apte M, Sambre D, Gaikawad S, Joshi S, Bankar A, Kumar AR et al (2013) Psychrotrophic yeast Yarrowia lipolytica NCYC 789 mediates the synthesis of antimicrobial silver nanoparticles via cell-associated melanin. AMB Express 3:32. https://doi.org/10.1186/2191-0855-3-32

Arfat YA, Ahmed J, Hiremath N, Auras R, Joseph A (2017) Thermo-mechanical, rheological, structural and antimicrobial properties of bionanocomposite films based on fish skin gelatin and silver-copper nanoparticles. Food Hydrocoll 62:191–202

Aziz N, Fatma T, Varma A, Prasad R (2014) Biogenic synthesis of silver nanoparticles using Scenedesmus abundans and evaluation of their antibacterial activity. J Nanoparticles 2014:689419. https://doi.org/10.1155/2014/689419

Aziz N, Faraz M, Pandey R, Sakir M, Fatma T, Varma A, Barman I, Prasad R (2015) Facile algae-derived route to biogenic silver nanoparticles: synthesis, antibacterial and photocatalytic properties. Langmuir 31:11605–11612. https://doi.org/10.1021/acs.langmuir.5b03081

Aziz N, Pandey R, Barman I, Prasad R (2016) Leveraging the attributes of Mucor hiemalis-derived silver nanoparticles for a synergistic broad-spectrum antimicrobial platform. Front Microbiol 7:1984. https://doi.org/10.3389/fmicb.2016.01984

Aziz N, Faraz M, Sherwani MA, Fatma T, Prasad R (2019) Illuminating the anticancerous efficacy of a new fungal chassis for silver nanoparticle synthesis. Front Chem 7:65. https://doi.org/10.3389/fchem.2019.00065

Bahadar H, Maqbool F, Niaz K, Abdollahi M (2016) Toxicity of nanoparticles and an overview of current experimental models. Iran Biomed J 20:1–11. https://doi.org/10.7508/obj.2016.01.001

Bhuyan T, Mishra K, Khanuja M, Prasad R, Varma A (2015) Biosynthesis of zinc oxide nanoparticles from *Azadirachta indica* for antibacterial and photocatalytic applications. Mater Sci Semicond Process 32:55–61

Bolbanabad EM, Ashengroph M, Darvishi F (2020) Development and evaluation of different strategies for the clean synthesis of silver nanoparticles using Yarrowia lipolytica and their antibacterial activity. Process Biochem 94:319–328. https://doi.org/10.1016/j.procbio.2020.03.024

Chang YC, Chen DH (2005) Adsorption kinetics and thermodynamics of acid dyes on a carboxymethylated chitosan-conjugated magnetic nano-adsorbent. Macromol Biosci 5(3):254–261

Chau C-F, Wu S-H, Yen G-C (2007) The development of regulations for food nanotechnology. Trends Food Sci Technol 18(5):269–280

Chaudhry Q, Scotter M, Blackburn J, Ross B, Boxall A, Castle L, Aitken R, Watkins R (2008) Applications and implications of nanotechnologies for the food sector. Food Addit Contam Part A Chem Anal Control Expo Risk Assess 25:241–258

Chausali N, Saxena J, Prasad R (2023) Nanotechnology as a sustainable approach for combating the environmental effects of climate change. J Agric Food Res. https://doi.org/10.1016/j.jafr.2023.100541

Chen H, Weiss J, Shahidi F (2006) Nanotechnology in nutraceuticals and functional foods. Food Technol 60:30–36

Chen H, Zhou K, Zhao G (2018) Gold nanoparticles: from synthesis, properties to their potential application as colourimetric sensors in food safety screening. Trends Food Sci Technol 78:83–94

Dasgupta N, Ranjan S, Mundekkad D, Ramalingam C, Shanker R, Kumar A (2015) Nanotechnology in agro-food: from field to plate. Food Res Int 69:381–400

de Azeredo HMC (2009) Nanocomposites for food packaging applications. Food Res Int 42:1240–1253

Deplanche K, Macaskie LE (2008) Biorecovery of gold by Escherichia coli and Desulfovibrio desulfuricans. Biotechnol Bioeng 99:1055–1064. https://doi.org/10.1002/bit.21688

Dhandapani P, Maruthamuthu S, Rajagopal G (2012) Bio-mediated synthesis of TiO2 nanoparticles and its photocatalytic effect on aquatic biofilm. J Photochem Photobiol B Biol 110:43–49. https://doi.org/10.1016/j.jphotobiol.2012.03.003

Dhiman S, Varma A, Rao M, Prasad R, Goel A (2023) Deciphering the fertilizing and disease suppression potential of phytofabricated zinc oxide nanoparticles on *Brassica juncea*. Environ Res. https://doi.org/10.1016/j.envres.2023.116276

Doyle ME (2006) Nanotechnology: a brief literature review. Food Research Institute Briefings

Duncan LG, Douglas Coatsworth J, Greenberg MT (2007) A model of mindful parenting: implications for parent–child relationships and prevention research. Clin Child Fam Psychol Rev 12(3):255–270

Duncan TV (2011a) Applications of nanotechnology in food packaging and food safety: barrier materials, antimicrobials and sensors. Curr Opin Colloid Interface Sci 363:1–24. https://doi.org/10.1016/J.JCIS.2011.07.017

Duncan TV (2011b) The communication challenges presented by nano foods. Nat Nanotechnol 6:683–688. https://doi.org/10.1038/nnano.2011.193

El-Far AH, Al Jaouni SK, Li WK, Mousa SA (2018) Protective roles of thymoquinone nanoformulations: potential nano nutraceuticals in human diseases. Nutrients 10:1369. https://doi.org/10.3390/nu10101369

Eftekhari A, Khalilov R, Kavetskyy T, Keskin C, Prasad R, Rosic GL (2023) Biological/chemical-based metallic nanoparticles synthesis, characterization, and environmental applications. Front Chem 11:1191659. https://doi.org/10.3389/fchem.2023.1191659

Esmailzadeh H, Sangpour P, Shahraz F, Hejazi J, Khaksar R (2016) Effect of nanocomposite packaging containing ZnO on the growth of Bacillus subtilis and for improved oral bioavailability. Biol Pharm Bull 34(5):660–665. https://doi.org/10.1248/bpb.34.660

Gaba S, Prasad L, Varma A, Rai AK, Prasad R, Goel A (2023) Leveraging of mycogenic copper oxide nanostructures for disease management of Alternaria blight of *Brassica juncea*. Green Processing Synth 12:20230015. https://doi.org/10.1515/gps-2023-0015

Gilligan BK (2008) Nanny, Nano, Boo, Boo Food? http://www.towerofbabel.com/blog/2008/08/28/nanny-nano-boo-boo-food/

Graveland-Bikker J, De Kruif C (2006) Unique milk protein-based nanotubes: food and nanotechnology meet. Trends Food Sci Technol 17(5):196–203

Gursoy N (2020) Fungus-mediated synthesis of silver nanoparticles (AgNP) and inhibitory effect on Aspergillus spp. in combination with an antifungal agent. Cumhuriyet Sci J 41:311–318. https://doi.org/10.17776/csj.653627

Harris HW, Sanchez-Andrea I, Mclean JS, Salas EC, Tran W, El-Naggar MY et al (2018) Redox sensing within the genus Shewanella. Front Microbiol 8:2568. https://doi.org/10.3389/fmicb.2017.02568

Heidelberg JF, Paulsen IT, Nelson KE, Gaidos EJ, Nelson WC, Read TD et al (2002) Genome sequence of the dissimilatory metal ion-reducing bacterium Shewanella oneidensis. Nat Biotechnol 2006(20):1118–1123. https://doi.org/10.1038/nbt749

Heldman DR (2006) IFT and the food science profession. Food Technol 60(10)

Hosseini MR, Sarvi MN (2015) Recent achievements in the microbial synthesis of semiconductor metal sulfide nanoparticles. Mater Sci Semicond Process 40:293–301

Huq T, Fraschini C, Khan A, Riedl B, Bouchard J, Lacroix M (2017) Alginate based nanocomposite for microencapsulation of probiotic: effect of cellulose nanocrystal (CNC) and lecithin. Carbohydr Polym 168:61–69. https://doi.org/10.1016/j.carbpol.2017.03.032

Haq I, Mazumder P, Kalamdhad AS (2020) Recent advances in removal of lignin from paper industry wastewater and its industrial applications–a review. Bioresour Technol:123636

Ibrahim KS (2013) Carbon nanotubes-properties and applications: a review. Carbon Lett 14:131–144. https://doi.org/10.5714/CL.2013.14.3.131

Jafari H, Pirouzifard M, Khaledabad MA, Almasi H (2016) Effect of chitin nanofiber on the morphological and physical properties of chitosan/silver nanoparticle nanocomposite films. Int J Biol Macromol 92:461–466

Jassal PS, Kaur D, Prasad R, Singh J (2022) Green synthesis of titanium dioxide nanoparticles: development and applications. J Agric Food Res 10:100361. https://doi.org/10.1016/j.jafr.2022.100361

Jha AK, Prasad K, Prasad K (2009) Green low-cost biosynthesis of Sb2O3 nanoparticles. Biochem Eng J 43:303–306. https://doi.org/10.1016/j.bej.2008.10.016

Jones N, Ray B, Ranjit KT, Manna AC (2008) Antibacterial activity of ZnO nanoparticle suspensions on a broad spectrum of microorganisms. FEMS Microbiol Lett 279(1):71–76

Joseph T, Morrison M (2006) Nanotechnology in agriculture and food. A nano forum report. pp 1–14

Joye IJ, Davidov-Pardo G, McClements DJ (2014) Nanotechnology for increased micronutrient bioavailability. Trends Food Sci Technol 40(2):168–182. https://doi.org/10.1016/j.tifs.2014.08.006

Kang S, Pinault M, Pfefferle LD, Elimelech M (2007) Single-walled carbon nanotubes exhibit strong antimicrobial activity. Langmuir 23(17):8670–8673

Karlo J, Prasad R, Singh SP (2023) Biophotonics in food technology: quo vadis? J Agric Food Res. https://doi.org/10.1016/j.jafr.2022.100482

Kavitha A, Doss A, Pole RPP, Pushpa Rani TPK, Prasad R, Satheesh S (2023) A mini review on plant-mediated zinc oxide nanoparticles and their antibacterial potency. Biocatal Agric Biotechnol. https://doi.org/10.1016/j.bcab.2023.102654

Kentish S, Wooster TJ, Ashokkumar M, Balachandran S, Mawson R, Simons L (2008) The use of ultrasonics for nanoemulsion preparation. Innov Food Sci Emerg Technol 9:170–175

Khader M, Eckl PM (2014) Thymoquinone: an emerging natural drug with a wide range of medical applications. Iran J Basic Med Sci 17:950–957

Khan A, Wen YB, Huq T, Ni YH (2018) Cellulosic nanomaterials in food and nutraceutical applications: a review. J Agric Food Chem 66:8–19. https://doi.org/10.1021/acs.jafc.7b04204

Kim T-Y, Kim MG, Lee J-H, Hur H-G (2018) Biosynthesis of nanomaterials by Shewanella species for application in lithium-ion batteries. Front Microbiol 9:2817. https://doi.org/10.3389/fmicb.2018.02817

Koch N, Sonowal S, Prasad R (2023) Elucidate the smart tailored biogenic nanoparticles and their applications in remediation. Biotechnol Genet Eng Rev. https://doi.org/10.1080/02648725.2023.2219942

Kulkarni SK (2015) Synthesis of nanomaterials—I (Physical methods). In: Nanotechnology: principles and practices. Springer, pp 55–76

Kumar MNR (2000) Nano and microparticles as controlled drug delivery devices. J Pharm Pharm Sci 3(2):234–258

Lambadi PR (2015) Facilebiofunctionalization of silver nanoparticles for enhanced antibacterial properties, endotoxin removal, and biofilm control. Int J Nanomedicine 10:2155–2171. https://doi.org/10.2147/IJN.S72923

Liu Y, Chakrabartty S, Alocilja E (2007) Fundamental building blocks for molecular wire-based forward error-correcting biosensors. Nanotechnology 18:1–6

Lomate GB, Dandi B, Mishra S (2018) Development of antimicrobial LDPE/Cu nanocomposite food packaging film for the extended shelf life of peda. Food Packag Shelf Life 16:211–219

Lopez-Rubio A, Fabra MJ, Martínez-Sanz M (2019) Food packaging based on nanomaterials. Multidisciplinary Digital Publishing Institute, Basel

Mallakpour S, Nazari HY (2018) The influence of bovine serum albumin-modified silica on the physicochemical properties of poly (vinyl alcohol) nanocomposites synthesized by ultrasonication technique. Ultrason Sonochem 41:1–10

Manzoor MF, Ahmad N, Ahmed Z, Siddique R, Zeng X-A, Rahaman A, Muhammad Aadil R, Wahab A (2019) Novel extraction techniques and pharmaceutical activities of luteolin and its derivatives. J Food Biochem 43(9):e12974. https://doi.org/10.1111/jfbc.12974

Markus J, Mathiyalagan R, Kim Y-J, Abbai R, Singh P, Ahn S et al (2016) Intracellular synthesis of gold nanoparticles with antioxidant activity by probiotic Lactobacillus kimchi-cus DCY51T isolated from Korean kimchi. Enzym Microb Technol 95:85–93. https://doi.org/10.1016/j.enzmictec.2016.08.018

Matalan A, Jones OG, McClements DJ (2011) Structured biopolymer-based delivery systems for encapsulation, protection, and release of lipophilic compounds. Food Hydrocoll 25:1865–1880. https://doi.org/10.1016/j.foodhyd.2011.04.014

Matalanis A, Jones OG, McClements DJ (2011) Structured biopolymer-based delivery systems for encapsulation, protection, and release of lipophilic compounds. Food Hydrocoll 25:1865–1880. https://doi.org/10.1016/j.foodhyd.2011.04.014

Maynard AD, Michelson E (2005) The nanotechnology consumer product inventory. Woodrow Wilson International Center for Scholars, Washington, DC. http://www.nanotechprojectorg/44S

McClements DJ (2012) Advances in the fabrication of emulsions with enhanced functionality using structural design principles. Curr Opin Colloid Interface Sci 17:235–245. https://doi.org/10.1016/j.cocis.2012.06.002

McClements DJ (2015) Encapsulation, protection, and release of hydrophilic active components: potential and limitations of colloidal delivery systems. Adv Colloid Interf Sci 219:27–53

McClements DJ, Xiao H (2012) Potential biological fate of ingested nanoemulsions: influence of particle characteristics. Food Funct 3:202–220

McClements DJ, Decker EA, Park Y, Weiss J (2009) Structural design principles for delivery of bioactive components in nutraceuticals and functional foods. Crit Rev Food Sci Nutr 49(6):577–606

Mishra A, Ahmad R, Singh V, Gupta MN, Sardar M (2013) Preparation, characterization and biocatalytic activity of a nanoconjugate of alpha-amylase and silver nanoparticles. J Nanosci Nanotechnol 13:5028–5033. https://doi.org/10.1166/jnn.2013.7593

Mishra A, Ahmad R, Sardar M (2015) Biosynthesized iron oxide nanoparticles mimicking peroxidase activity: application for biocatalysis and biosensing. J Nanoeng Nanomanufacturing 5:37–42. https://doi.org/10.1166/jnan.2015.1220

Mishra A, Ahmad R, Perwez M, Sardar M (2016) Reusable green synthesized biomimetic magnetic nanoparticles for glucose and H2O2 detection. Bionanoscience 6:93–102. https://doi.org/10.1007/s12668-016-0197-x

Mizielinska M, Kowalska U, Jarosz M, Suminska P (2018) A comparison of the effects of packaging containing nano ZnO or polylysine on the microbial purity and texture of cod (Gadus morhua) fillets. Nanomaterials (Basel) 8(3):158

Moraru CI, Huang Q, Takhistov P, Dogan H, Kokini JL (2009) Food nanotechnology: current developments and prospects. Global Issues Food Sci Technol 21:369–399

Mossinger D, Hornung J, Lei S, De Feyter S, Hoger S (2007) Molecularly defined shape persistent 2D oligomers: the covalent-template approach to molecular spoked wheels. Angew Chem Int Ed 46:6802–6806

Murray AJ, Zhu J, Wood J, Macaskie LE (2017) A novel biorefinery: recovery of precious metals from spent automotive catalyst leachates into new catalysts effective in the metal reduction and the hydrogenation of 2-pentyne. Miner Eng 113:102–108. https://doi.org/10.1016/j.mineng.2017.08.011

Nachay K (2007) Analyzing nanotechnology. Food Tech 61:34–36

Narayanan KB, Sakthivel N (2010) Biological synthesis of metal nanoparticles by microbes. Adv Colloid Interface Sci 156:1–13

Nickols-Richardson SM, Piehowski KE (2008) Nanotechnology in nutritional sciences. Minerva Biotechnol 20:176

Nile SH, Baskar V, Selvaraj D, Nile A, Xiao J, Kai G (2020) Nanotechnologies in food science: applications, recent trends, and future perspectives. Nanomicro Lett 12:45

Ojha S, Kumar B (2018) A review on nanotechnology-based innovations in diagnosis and treatment of multiple sclerosis. J Cell Immunother 4(2):56–64

Osherov A, Prasad R, Chrzanowski W, New EJ, Brazaca L, Sadik O, Haynes CL, Maine E (2023) Responsible nanotechnology for a sustainable future. One Earth 6(7):763–766. https://doi.org/10.1016/j.oneear.2023.06.010

Ovais M, Khalil AT, Ayaz M, Ahmad I, Nethi SK, Mukherjee S (2018) Biosynthesis of metal nanoparticles via microbial enzymes: a mechanistic approach. Int J Mol Sci 19:4100. https://doi.org/10.3390/ijms19124100

Park K-Y, Jeong J-K, Lee Y-E, Daily Iii JW (2014) Health benefits of kimchi (Korean fermented vegetables) as a probiotic food. J Med Food 17:6–20. https://doi.org/10.1089/jmf.2013.3083

Pathakoti K, Morrow S, Han C, Pelaez M, He X, Dionysiou DD, Hwang H-M (2013) Photoinactivation of Escherichia coli by sulfur-doped and nitrogen–fluorine codoped TiO2 nanoparticles under solar simulated light and visible light irradiation. Environ Sci Technol 47(17):9988–9996

Pathakoti K, Manubolu M, Hwang H-M (2017) Nanostructures: current uses and future applications in food science. J Food Drug Anal 25:245. https://doi.org/10.1016/j.jfda.2017.02.004

Pocas MFF, Delgado TF, Oliveira FAR (2008) Smart packaging technologies for fruits and vegetables. In: Kerry J, Butler P (eds) Smart packaging technologies for fast moving consumer goods. Wiley, Chichester. https://doi.org/10.1002/9780470753699.ch9

Potter NN, Hotchkiss JH (1998) Food science. Food science texts series, 5th edn. Springer

Powers KW, Brown SC, Krishna VB, Wasdo SC, Moudgil BM, Roberts SM (2006) Research strategies for safety evaluation of nanomaterials. Part VI. Characterization of nanoscale particles for toxicological evaluation. Toxicol Sci 90(2):296–303

Priyadarshini S, Gopinath V, Meera Priyadharsshini N, MubarakAli D, Velusamy P (2013) Synthesis of anisotropic silver nanoparticles using novel strain, Bacillus flexus and its biomedical application. Colloids Surf B: Biointerfaces 102:232–237

Prasad R (2016) Advances and applications through fungal nanobiotechnology. Springer, International Publishing Switzerland. (ISBN: 978-3-319-42989-2)

Prasad R (2017) Fungal nanotechnology: applications in agriculture, industry, and medicine. Springer Nature Singapore Pte Ltd. (ISBN 978-3-319-68423-9)

Prasad R (2019) Microbial nanobionics: basic research and applications. Springer International Publishing. (ISBN 978-3-030-16534-5) https://www.springer.com/gp/book/9783030165338

Prasad R, Pandey R, Barman I (2016) Engineering tailored nanoparticles with microbes: quo vadis. WIREs Nanomed Nanobiotechnol 8:316–330. https://doi.org/10.1002/wnan.1363

Prasad R, Kumar M, Kumar V (2017a) Nanotechnology: an agriculture paradigm. Springer Nature Singapore Pte Ltd. (ISBN: 978-981-10-4573-8)

Prasad R, Kumar V, Kumar M (2017b) Nanotechnology: food and environmental paradigm. Springer Nature Singapore Pte Ltd. (ISBN 978-981-10-4678-0)

Prasad R, Kumar V, Kumar M, Choudhary D (2019) Nanobiotechnology in bioformulations. Springer International Publishing. (ISBN 978-3-030-17061-5) https://www.springer.com/gp/book/9783030170608

Prasad R, Siddhardha B, Dyavaiah M (2020) Nanostructures for antimicrobial and antibiofilm applications. Springer International Publishing. (ISBN 978-3-030-40336-2) https://www.springer.com/gp/book/9783030403362

Qian C, Decker EA, Xiao H, McClements DJ (2012) Inhibition of beta-carotene degradation in oil-in-water nanoemulsions: influence of oil-soluble and water-soluble antioxidants. Food Chem 135(3):1036–1043

Rai M, Yadav A, Gade A (2009) Silver nanoparticles as a new generation of antimicrobials. Biotechnol Adv. 2009;27:76–83] 27:76

Rajakumar G, Rahuman AA, Roopan SM, Khanna VG, Elango G, Kamaraj C (2012) Fungus-mediated biosynthesis and characterization of TiO2 nanoparticles and their activity against pathogenic bacteria. Spectrochim Acta A Mol Biomol Spectrosc 91:23–29. https://doi.org/10.1016/j.saa.2012.01.011

Ramachandraiah K, Gnoc NTB, Chin KB (2017) Biosynthesis of silver nanoparticles from persimmon byproducts and incorporation in biodegradable sodium alginate thin film. J Food Sci 82(10):2329–2336

Reddy BL, Jatav HS, Rajput VD, Minkina T, Ranjan A, Harikrishnan A, Veena VK, Chauhan A, Kumar S, Prakash A, Prasad R (2022) Nanomaterials based monitoring of food- and water-borne pathogens. J Nanomater 2022:9543532, 13. https://doi.org/10.1155/2022/9543532

Roilo D, Maestri CA, Scarpa M, Bettotti P, Checchetto R (2018) Gas barrier and optical properties of cellulose nanofiber coatings with dispersed TiO2 nanoparticles. Surf Coating Technol 343:131–137

Roy S, Ezati P, Priyadarshi R, Biswas D, Rhim J-W (2022) Review on Recent advances in metal sulfide nanoparticle-added bio-nanocomposite films for food packaging applications. Crit Rev Food Sci Nutr:1–14. https://doi.org/10.1080/10408398.2022.2144794

Sadaf A, Ahmad R, Ghorbal A, Elfalleh W, Khare SK (2020) Synthesis of cost-effective magnetic nano-biocomposites mimicking peroxidase activity for remediation of dyes. Environ Sci Pollut Res 27:27211–27220. https://doi.org/10.1007/s11356-019-05270-3

Saeed S, Iqbal A, Ashraf MA (2020) Bacterial-mediated synthesis of silver nanoparticles and their significant effect against pathogens. Environ Sci Pollut Res 27:37347–37356. https://doi.org/10.1007/s11356-020-07610-0

Sasaki S, Kriener M, Segawa K, Yada K, Tanaka Y, Sato M, Ando Y (2011) Topological superconductivity in cu x bi 2 se 3. Phys Rev Lett 107(21):217001

Satyanarayana T, Reddy SS (2018) A review of chemical and physical synthesis methods of nanomaterials. Int J Res Appl Sci Eng Technol 6(1):2885

Sekhon JS (2009) Opiates for the matches: matching methods for causal inference. Annu Rev Polit Sci 12:487–508

Sekhon BS (2010) Food nanotechnology-an overview. Nanotechnol Sci Appl 3:1–15. https://doi.org/10.2147/NSA.S8677

Shaikh J, Ankola D, Beniwal V, Singh D, Kumar MR (2009) Nanoparticle encapsulation improves the oral bioavailability of curcumin by at least 9-fold when compared to curcumin administered with piperine as an absorption enhancer. Eur J Pharm Sci 37(3–4):223–230

Shankar SS, Ahmad A, Pasricha R, Sastry M (2003) Bioreduction of chloroauric ions by geranium leaves and its endophytic fungus yields gold nanoparticles of different shapes. J Mater Chem 13:1822–1826

Shankar S, Wang L-F, Rhim J-W (2017) Preparation and properties of carbohydrate-based composite films incorporated with CuO nanoparticles. Carbohydr Polym 169:264–271

Shivashankarappa A, Sanjay KR (2015) Study on biological synthesis of cadmium sulfide nanoparticles by Bacillus licheniformis and its antimicrobial properties against food-borne pathogens. Nanosci Nanotechnol Res 3:6–15

Singh LP, Agarwal SK, Bhattacharyya SK, Sharma U, Ahalawat S (2011) Preparation of silica nanoparticles and its beneficial role in cementitious materials, Intech Open Access, vol 1, no 1, 44–51

Singh D, Rathod V, Ninganagouda S, Hiremath J, Singh AK, Mathew J (2014) Optimization and characterization of silver nanoparticle by endophytic fungi Penicillium sp. isolated from Curcuma longa (turmeric) and application studies against MDR E. coli and S. aureus. Bioinorg Chem Appl 2014:408021. https://doi.org/10.1155/2014/408021

Sperber WH, Doyle MP (2009) Introduction to the microbiological spoilage of foods and beverages, in Compendium of the microbiological spoilage of foods and beverages, vol 2009. Springer, New York, pp 1–40

Srivastava S, Usmani Z, Atanasov AG, Singh VK, Singh NP, Abdel-Azeem AM, Prasad R, Gupta G, Sharma M, Bhargava A (2021) Biological nanofactories: using living forms for metal nanoparticle synthesis. Mini-Rev Med Chem 21(2):245–265

Taniguchi N (1974) On the basic concept of nanotechnology. In: Proceedings of the international conference on production engineering, Tokyo, pp 18–23

Thangadurai D, Sangeetha J, Prasad R (2020) Nanotechnology for food, agriculture, and environment. Springer International Publishing. (ISBN 978-3-030-31937-3) https://www.springer.com/gp/book/9783030319373

Tricco AC, Ashoor HM, Antony J, Bouck Z, Rodrigues M et al (2019) Essential Medicines List (EML) 2019 Application for the inclusion of long-acting insulin analogues including biosimilar in the WHO Model List of Essential Medicines, as treatments used for patients with diabetes type 1

Tripathi RM, Shrivastav BR, Shrivastav A (2018) The antibacterial and catalytic activity of biogenic gold nanoparticles synthesised by Trichoderma harzianum. IET Nanobiotechnol 12: 509–513. https://doi.org/10.1049/iet-nbt.2017.0105

Wang YX, Jacobs RL, Donna V, Lavasanifar A (2018) Novel protein-lipid composite nanoparticles with an inner aqueous compartment as delivery systems of hydrophilic nutraceutical compounds. Nanoscale 10:10629–10640. https://doi.org/10.1039/C8NR01009A

Xia T, Kovochich M, Liong M, Mädler L, Gilbert B, Shi H, Yeh JI, Zink JI, Nel AE (2008) Comparison of the mechanism of toxicity of zinc oxide and cerium oxide nanoparticles based on dissolution and oxidative stress properties. ACS Nano 2:2121–2134. https://doi.org/10.1021/nn800511k

Xing Y, Li X, Zhang L, Xu Q, Che Z, Li W, Bai Y, Li K (2012) Effect of TiO2 nanoparticles on the antibacterial and physical properties of the polyethylene-based film. Prog Org Coating 73(2–3): 219–224

Yadav SK (2017) Tissue science & engineering realizing the potential of nanotechnology for agriculture and food technology. J Tissue Sci Eng 8:8–11. https://doi.org/10.4172/2157-7552.1000195

Yadav HM, Kim J-S, Pawar SH (2016) Developments in photocatalytic antibacterial activity of nano TiO2: a review. Korean J Chem Eng 33(7):1989–1998

Yadav L, Tripathi RM, Prasad R, Pudake RN, Mittal J (2017) Antibacterial activity of Cu nanoparticles against *E. coli*, *Staphylococcus aureus* and *Pseudomonas aeruginosa*. Nano Biomed Eng 9(1):9–14. https://doi.org/10.5101/nbe.v9i1.p9-14

Zhang R, McClements DJ (2016) Enhancing nutraceutical bioavailability by controlling the composition and structure of gastrointestinal contents: emulsion-based delivery and excipient systems. Food Struct 10:21–36. https://doi.org/10.1016/J.FOOSTR.2016.07.006

Zhang XP, Le Y, Wang JX, Zhao H, Chen JF (2013) Resveratrol nanodispersion with high stability and dissolution rate. Lwt Food Sci Technol 50:622–628. https://doi.org/10.1016/j.lwt.2012.07.041

Biotechnological Implications of Extracellular Vesicles

16

Ricardo David Avellán-Llaguno, Liting Zhu, Haining Huang, Xueli Xu, and Qiansheng Huang

Abstract

The need for new biotechnological tools has forced researchers to explore other options that allow them to perform their processes effectively, and for that, the extracellular vesicles (EVs) are a promising option. Most organisms, including bacteria, produce the EVs, complying with various biological and environmental functions. Multiple technologies are used for isolation and characterization, but their technical requirement can restrict their use. As for biotechnological applications, these are very encouraging, however, to some extent, today only limited to specific cases. Studies focus mainly on biomedicine, including therapy against AIDS, oncology, diagnosis, and treatment of diverse pathologies, as well as genetic engineering. Also, EVs has been used in the cosmetics and food industry. In this chapter, we made a compendium of the current progress regarding the origin, functions, techniques of analysis, and biotechnological applications of the EVs.

Keywords

Extracellular vesicle · Exosome · Biotechnology · Biomedicine

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16.1 General Conceptions

The growth and reproduction of cells require a lot of organic and inorganic substances. There is a great diversity of substances involved in these processes, including paracrine and autocrine pathways. Recent studies have found that these chemical substances can also be encapsulated in structures called EVs, which have a phospholipid bilayer structure. As a means of transportation of these biochemical molecules, the EVs have functions such as information transmission and material exchange, increasing researchers' attention on the source and function of EVs.

16.1.1 The History of EVs

In the 1960s, EVs were first observed in Gram-negative bacteria using electron microscopy, which at that time had no specific names (Bayer and Anderson 1965; Chatterjee and Das 1967; Toyofuku et al. 2015). In the 1970s and 1980s, different researchers called them differently: "platelet-dust" (Wolf 1967), or "matrix vesicles" (Anderson 1969), "microparticles" (Crawfo 1971), "microvesicles" (Dalton 1975; Trams et al. 1981), "membrane fragments" (Castagna et al. 1980), and "membrane vesicles" (Pan et al. 1985; Poutsiaka et al. 1985). The term exosomes (EXOs) appeared in 1981, specifically of mammalian origin, and its physiological functions have attracted attention since then. In particular, EXOs have become the most widely studied and known EVs population for their potential clinical application (Trams et al. 1981; Willms et al. 2018). With the development and deepening of research on EVs, such as biology, functions, therapeutics, and biomarkers, their approach has been unified. EVs derived from archaea and Gram-positive bacteria are called membrane vesicles (MVs), and EVs derived from Gram-negative bacteria are called outer membrane vesicles (OMVs), EVs derived from mammalian cells can be divided into EXOs, cell microvesicles (CMVs), and apoptotic bodies (ABs) (Mathivanan et al. 2010). Because they are secreted outside the cell, they are collectively referred to as EVs (林华 2019). The International Society for Extracellular Vesicles (ISEV) recommends EVs as a collective term for "particles naturally released from the cell that is delimited by a lipid bilayer and cannot replicate" (Thery et al. 2018).

16.1.2 Size, Morphology, and Contents of EVs

At present, EVs have been found in almost all areas of life, such as animals, plants, parasites, fungi, and microorganisms (Gill et al. 2019). The EVs come from different sources and have different sizes, typically between 50 nm and 5 μm, depending on the type and origin (Doyle and Wang 2019; Zabeo et al. 2017). The morphology of most EVs is spherical, but there are also elliptical, small, thin tubular, and irregular shapes, which are different because of their sources and the effect of extracellular milieu.

EVs are phospholipid bilayer enclosed particles that can deliver lipids, proteins, nucleic acids, adhesions, toxins, lipopolysaccharides, carbohydrates, and metabolites to both neighboring and distant cells. The composition, source, function, and destination of these cargoes' secretion via EVs to extracellular milieu, recently he has caught the attention of many researchers. The DNA, RNA, miRNA, and other nucleic acids in EVs are similar to the EVs derived cells. Genomic analysis and comparative studies on them can explain the origin of EVs to a certain extent. Analyzing the proteomics of EVs can find the protein markers, which become the marker proteins for EVs identification, such as CD9, CD81 for exosome from human cells. Comparing the proteomics of EVs and EVs derived cells and their metabolomics analysis also explain the origin and formation of vesicles to a certain extent.

16.1.3 Database on EVs

There are many open access resources for EVs on the Internet: The official journal of the International Society for Extracellular Vesicles (ISEV, official website: https://www.isev.org/), "Journal of Extracellular Vesicles" (official website: https://www.tandfonline.com/), among others. Published open access research on EVs, including microvesicles, EXOs, extracellular bodies, and apoptotic bodies. Some of these databases are given in Table 16.1.

Table 16.1 The database of EVs

Database	Contents	Website
RBase	EVs' long RNAs (long RNAs, exLRs) repository	http://www.exoRBase.org
Evpedia	Proteins, mRNA, miRNA, lipids, and metabolites found in EVs from different sources	https://ngdc.cncb.ac.cn/databasecommons/database/id/4354
Vesiclepedia	A library of manual search tools for EVs molecular data (lipid, RNA, and protein)	http://www.microvesicles.org/
ExoCarta	Mainly a manual database about exosomal protein, RNA, liposome	http://www.exocarta.org/
Urinary Exosome Protein	The database contains protein identification of human urinary EXOs using two different mass spectrometers, with a great level of detail	https://hpcwebapps.cit.nih.gov/ESBL/Database/Exosome/
EVmiRNA	Comprehensive miRNA expression profile, miRNA regulation pathway, miRNA function, miRNA biomarker in EVs	http://bioinfo.life.hust.edu.cn/EVmiRNA
EV-TRACK	Record the experimental data of EXOs, and gather the original data for the separation and characterization of EVs	http://www.evtrack.org/
ExRNA Atlas	The database information includes small RNA sequencing of human and mouse biological fluids and exRNA maps derived from qPCR	http://exrna–atlas.org/exat

16.2 Types and Origins of EVs

The diversity of organisms that produce EVs also results in a diversity of these. The following are the different types of EVs reported so far.

16.2.1 Vesicles of Prokaryotic Origin

The research on prokaryotic EVs mainly focuses on some model strains, such as *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and others. EVs derived from Gram-negative bacteria are the most studied compared to that from Gram-positive types. In addition, a tiny part involves vesicles derived from archaea in extreme environments.

The composition of the cell wall of Gram-positive bacteria and Gram-negative bacteria is very different. The cell wall of Gram-negative bacteria is composed of an inner membrane layer, a peptidoglycan layer, and an outer membrane layer. In contrast, the outer membrane is absent in Gram-positive bacteria. Gram-positive bacteria have a much thicker peptidoglycan layer compared to the Gram-negative bacteria. This will make a big difference in the formation process of EVs and the composition and structure of EVs. Published works suggest mechanisms of differential biogenesis of EVs between Gram-negative bacteria and Gram-positive bacteria (Toyofuku et al. 2019), as shown in Fig. 16.1.

16.2.1.1 Bacteria

OMVs can be out of the bubble, first, due to the different expansion speeds between the cell wall and the outer membrane of the bacteria, relaxation occurs in the part of the cell wall-OMV interaction (Fig. 16.2: Model 1) (Mashburn-Warren and Whiteley 2006). Then, peptidoglycan accumulates in the periplasmic space. Subsequently, the OMVs are bent to form vesicles and are released (Fig. 16.2: Model 2) (Berleman and Auer 2013). Finally, the OMVs can isolate divalent cations (Mg^{2+} and Ca^{2+}) and then repel anions, resulting in instability of the outer membrane. This instability causes the outer membrane to bend, thereby releasing OMVs (Fig. 16.2: Model 3) (Mashburn and Whiteley 2005; 林华 2019).

In the case of MVs, at first, it was thought that they cannot produce vesicles because of their thicker cell walls. However, with the development and in-depth study of vesicles, in 1990, researchers provided the first evidence for the emergence of MVs (Dorward and Garon 1990). The MVs are derived directly from the cytoplasmic membrane (Yu et al. 2018) (Fig. 16.3), being a complex process due the existence of a thick peptidoglycan(PGN) barrier. This process is possible through the presence of degrading enzymes and surfactant proteins to facilitate MVs to escape from the thick cell walls (Bose et al. 2020). For example, PGN degrading enzymes in *Staphylococcus aureus* can remodel the cell wall, facilitating that the MVS to transit across the cell wall (Lee et al. 2009). The genesis of MVs in mycobacteria is thought to be due to the action of remodeling enzymatic and structural molecules, the same as what happens in the MVs biogenesis of *S. aureus*

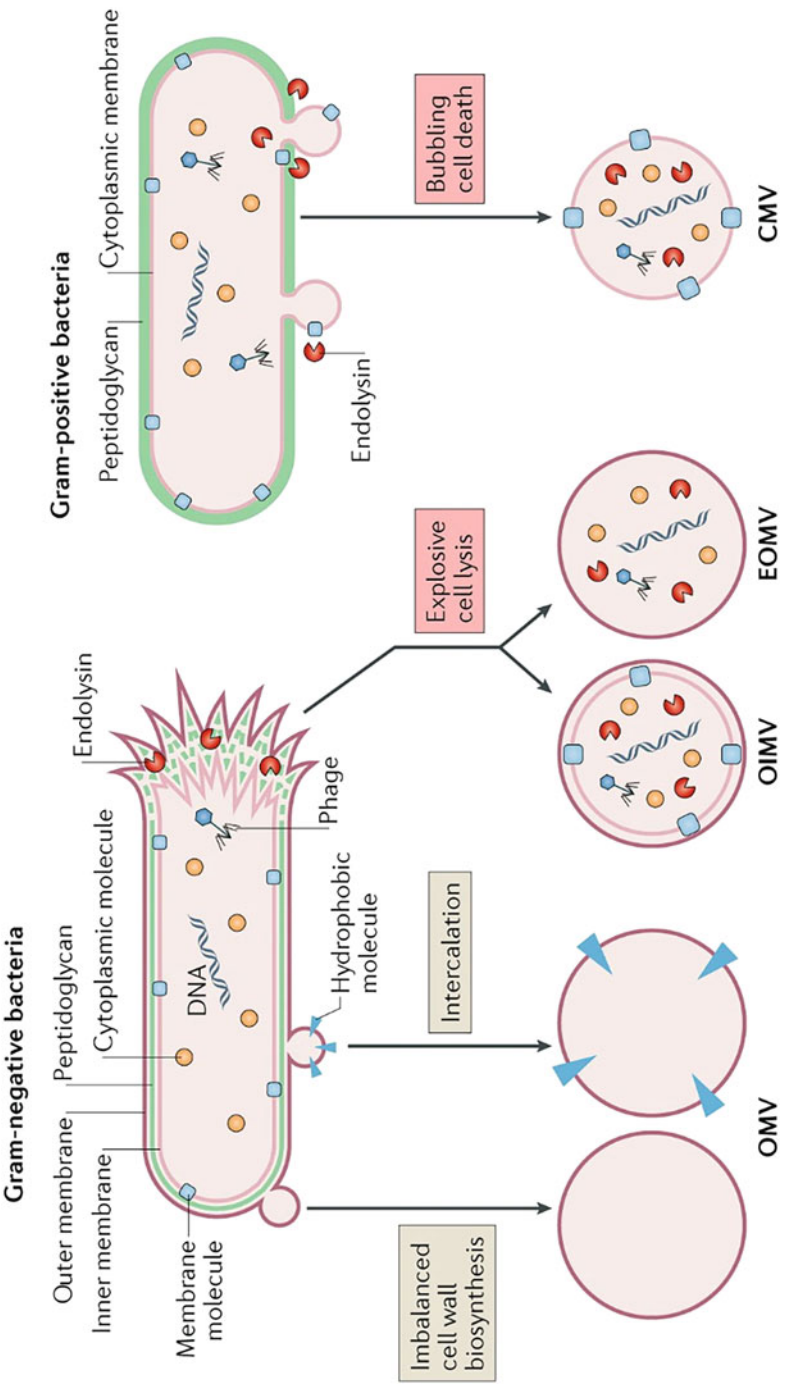

Fig. 16.1 The types and origins of Gram-positive bacteria and Gram-negative bacteria vesicles. OMVs; OIMVs: outer–inner membrane vesicles; EOMVs: explosive outer membrane vesicles; CMVs: cytoplasmic membrane vesicles. (Taken from (Toyofuku et al. 2019))

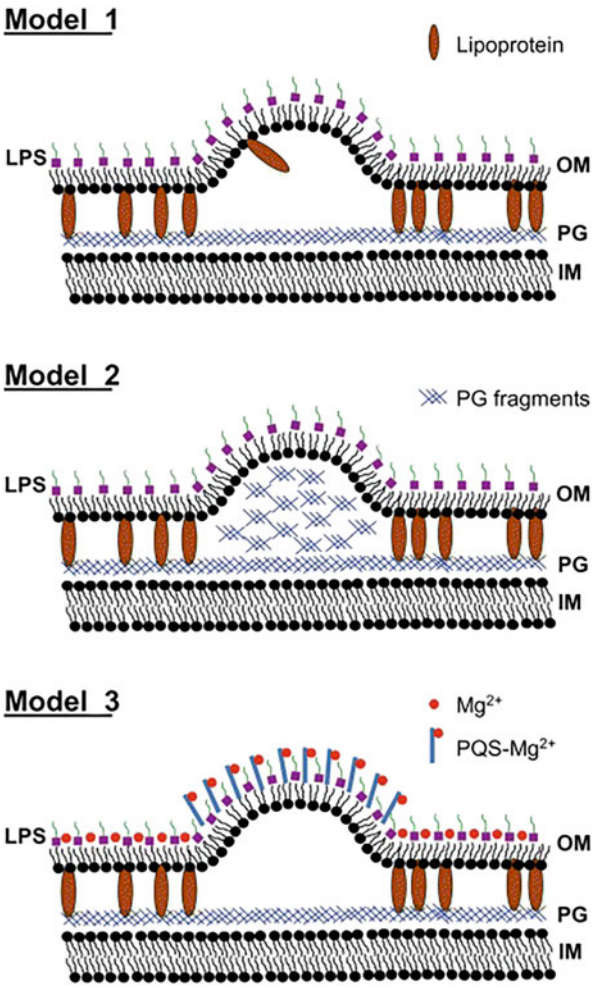

Fig. 16.2 Proposed models for OMVs formation. *LPS* lipopolysaccharide, *OM* outer membrane, *PG* peptidoglycan, *IM* inner membrane. (Taken from (Mashburn-Warren and Whiteley 2006))

(Alderwick et al. 2015; Wang et al. 2018). In *Bacillus subtilis*, a phage-encoded endolysin, which promotes the pore formation in PGN layers of the cell wall, facilitates the release of the MVs (Toyofuku et al. 2017). It is important to delve into the research to determine the involvement of autolysin in the formation of MVs. A summary of the morphology and composition of OMVs and MVs is given in Table 16.2 (Bose et al. 2020).

16.2.1.2 Archaea

An increasing number of archaea species has been reported to release EVs, such as the thermophilic archaea on *Aciduliprofundum boonei* isolated from hydrothermal deep-sea vents (Reysenbach et al. 2006), and *Sulfolobus* (Ellen et al. 2009). EVs released by *Sulfolobus* species range from 90 to 230 nm in diameter and contain

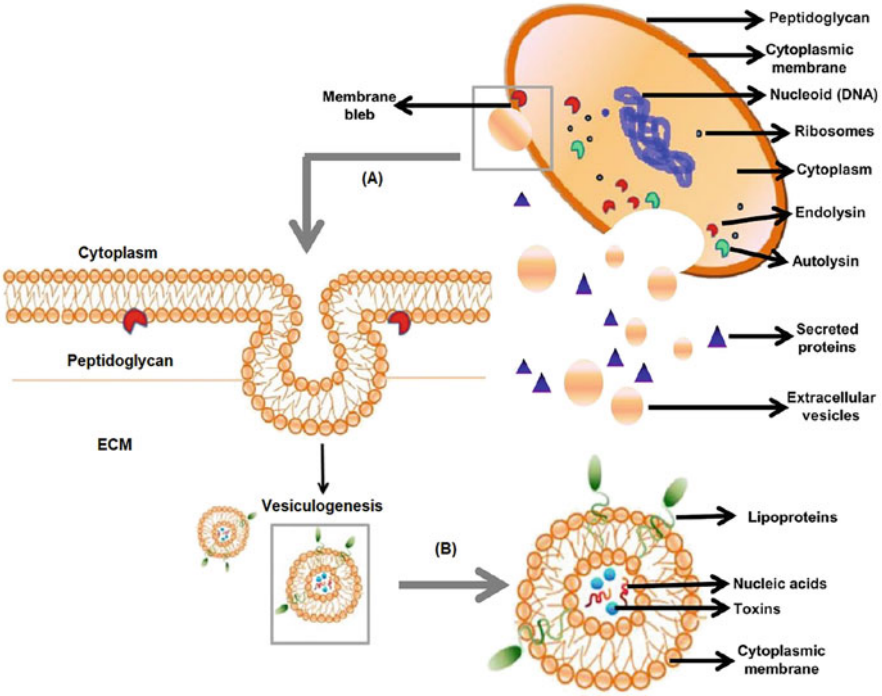

Fig. 16.3 Origin and composition of MVs. (**a**) The release of MVs involves diversified events depending on the cell lytic enzyme viz. PGN degradation followed by cytoplasmic membrane bleb protrusion via endolysins and PGN remodeling via hydrolyzing enzyme autolysins. (**b**) The internal structure of MVs comprising of nucleic acids, virulence factors, and intracellular proteins. (Taken from (Bose et al. 2020))

membrane lipids and S-layer proteins derived from the cell wall (Ellen et al. 2009). It is still unclear how archaea secrete EVs, one hypothesis is that the EVs emerge from the cytoplasmic membrane through an outward budding event similar to the inward budding of vesicles in the endosomal compartment of eukaryotes (Fig. 16.4) (Ellen et al. 2010).

16.2.2 EVs of Eukaryotic Origin

Eukaryotic cells have multiple types of EVs with complex formation mechanisms. Microvesicles (MVs), alternatively designated as microparticles or shedding vesicles or ectosomes, are usually intermediate-sized vesicles (~100–1000 nm). They are shed from the cell surface by outward budding of the plasma membrane. Large vesicles with a diameter >1 μm can be produced during apoptosis (in which case they are referred to as apoptotic bodies, APOs). During the study of mature sheep reticulocytes, researchers proposed the process of formation of EXOs (Pan and

Table 16.2 Comparison between OMVs and MVs. Taken from (Bose et al. 2020)

Features	OMVs	MVs
Origin	Outer membrane	Cytoplasmic membrane
Size	10–300 nm	20–400 nm
Components	Outer membrane proteins, periplasmic proteins, virulence factors, cytoplasmic proteins, inner membrane proteins, lipopolysaccharides, phospholipids, and peptidoglycan (10–20%)	Cytoplasmic proteins, membrane-associated proteins, lipoteichoic acid (LTA), peptidoglycan (>50%)
Genetic cargo	sRNA, mRNA, miRNA, luminal, and surface associated DNA	sRNA, extracellular, and chromosomal DNA
Proteins	Outer membrane: OmpA, OmpC, OmpF, lipoprotein (Lpp), periplasmic: Alkaline phosphatase and AcrA	Single lipid membrane proteins: penicillin-binding, immunoglobulin G-binding (protein A), staphopain A, α-hemolysins, heat shock protein
Lipids	Glycerophopholipids, phosphatidyleth-anolamine, phophotidylglycerol, and cardiolipin	Phosphatidylglycerol, myristic, and palmitic acids
Coagulation	E-selectin, P-selectin, thrombomodulin	Fibronectin binding protein, staphylocoagulase precursor, Vonwillebrand factor binding protein
Antibiotic resistance	β- lactamase, enzyme L5, multidrug efflux protein (Mtr, Mex, TolC)	β-lactamase, Penicillin-binding proteins: PBP1, PBP2, PBP2a, PBP3, and PBP4
Virulence factor delivery	Enzymes: phospholipase C, esterase lipase, alkaline phosphatase, serine protease Toxins: adenylatecyclase, cholera, cytolethal distending, PagJ, PagK1, VacA	InIB, LLO, IgG binding protein SbI, protective antigen, lethal factor, edema toxin, anthrolysin
Bacterial survival	Hemin- binding protein, TonB-dependent receptors	B-lactamase protein
Adhesion and invasion	Adhesin/invasin, OmpA	Plasma binding proteins, staphopain A
Immune evasion	Cytotoxic necrotizing factor 1, Us-pA1/A2	Coagulation, antibody degradation and sequestering, complement inhibition factors
Host-cell modulation	Cytolysin A, VacA toxin, CNF1, heatliable enterotoxin, shigatoxin, Cif, flagellin, α-haemolysin	Proteolysin, β2 toxin
Killing competing bacteria	Endopeptidase L5, murein hydrolase (Mtl, Slt), peptidoglycan hydrolase	N-aetylmuramoyl, L-alanine amidase

Johnstone 1983; Pan et al. 1985). The EXOs are released from cells during exocytosis of multivesicular bodies (MVBs) into the extracellular space. EXOs typically represent the smallest sized (30–100 nm) EVs (Osteikoetxea et al. 2015). EXOs biogenesis has been linked to the protein complex endosomal sorting complexes required for transport (ESCRT) machinery. The ESCRT complex is needed for both

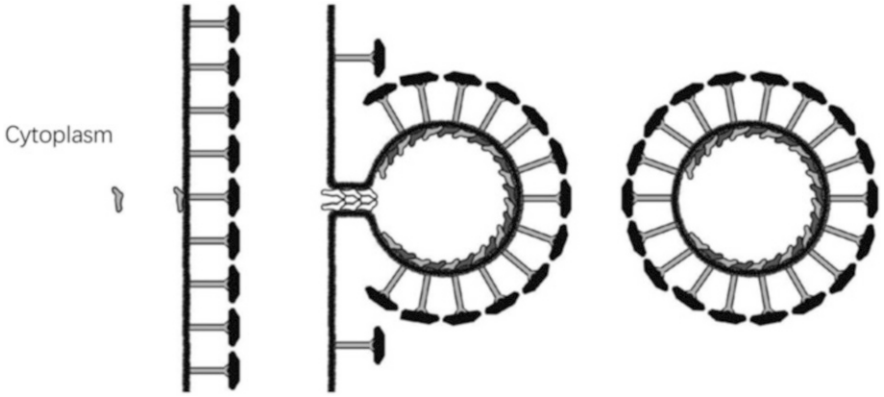

Fig. 16.4 A schematic diagram of model for EVs budding in Crenarchaea. The EVs is formed through an outwardly growing bud which is covered by S-layer protein. (Taken from (Ellen et al. 2010))

the formation of MVBs and the sorting of endosomal cargoes into these vesicles (Simpson et al. 2008). Typically, the cell membrane is sunken to form a multivesicular endosome, the lumen of multivesicular endosomes contains intraluminal vesicles (ILVs). After the ILVs mature, they are either digested by intracellular lysosomes or are released from the cell, which is called EXOs (van Niel et al. 2018). Recently, ESCRT-independent mechanisms for sorting of proteins into ILVs within MVBs have been identified that are regulated by ceramide-mediated budding of exosome vesicles into multivesicular endosomes (Simpson et al. 2008). Table 16.3 explains the types of eukaryotic EVs.

The appearance of vesicles has been reported in fungi which are typical eukaryotic organisms, such as *Cryptococcus neoformans*. They use traditional pathways to produce vesicles, which are post-Golgi vesicles that fuse with the cytoplasmic membrane and then transport cargoes (Casadevall et al. 2009; Panepinto et al. 2009; Wickner and Schekman 2005). *Saccharomyces cerevisiae* is a typical eukaryotic model organism. Characterization of the EVs it produces and related analysis of its source pathways revealed that: in the secretion of vesicles, the Golgi-derived secretory pathway in the trans-cell wall traffic in yeast cells plays a crucial role (Oliveira et al. 2010). EVs have been identified in several human body fluids, such as blood, follicular fluid, breast milk, and ejaculate, and also in human tissues, including tumors. The EVs also appear in some animal milk, such as cow's milk and goat's milk.

In addition, plants produce EVs as a kind of physiological activity, what some researchers named plant-derived EVs "exosome-like" because of their similar morphology and density compared to mammalian EXOs (Ju et al. 2013; Woith and Melzig 2019), which can be abbreviated as PEVs. The research methods and ideas of PEVs are like those of mammalian and bacterial-derived EVs.

Table 16.3 Types of EVs of eukaryotic origin

	EVs types			
Parameter	EXOs	ABs	CMV	PEVs
Diameter (nm)	30–100	50–500	100–1000	20–500
Density (g/mL)	1.10–1.21	1.16–1.28	1.14–1.18	–
Morphology/ Shap	Cup, homogeneous	Variable, heterogeneous	Irregular, variable	–
Composition	Proteins, miRNA, mRNA	Proteins, DNA miRNA, mRNA	Proteins, miRNA, mRNA	–
Markers	Tetraspanins (CD63, CD9), TNFR1, ALIX, TSG101, miRNA, HSC70, CD81	Phosphatidylserine, histones, DNA, RNA	CD40 ligand, integrins, MMPs, phosphatidylserine, Annexin 2, caspases, FGF2	Patellins 1-3, Penetration 1, Clathrin heavy chain, heat shock proteins
Site of generation	Multivesicular bodies	Plasma membrane, cytoplasm, nuclei	Plasma membrane	–
Mechanism of generation	Budding, exocytosis of multivesicular bodies	Cell shrinkage and death, release from cells undergoing apoptosis	Budding of plasma membrane	–

NOTE: ALIX= apoptosis-linked-gene-2-interacting protein X; TSG101= tumor susceptibility gene 101

16.3 Roles of EVs

16.3.1 Biological Roles

EVs were initially perceived as a way of eliminating unneeded compounds from the cell (Johnstone et al. 1987). However, the work in the late 1990s indicated that EVs could serve an intercellular communication purpose, like in immune responses and cancer (Raposo et al. 1996; Wolfers et al. 2001). EVs have been proved to be extensively involved in exchanging components between cells, including nucleic acids, lipids, and proteins. The exchange of molecules acts as signaling transmission during normal cellular homeostatic processes and pathological development (Chahar et al. 2015; Colombo et al. 2014; Kalluri and LeBleu 2020; van Niel et al. 2018). EVs and surface molecules on the cell membrane can through interaction to trigger intracellular signal cascade, but also through direct fusion with the cell membrane, phagocytosis or through a variety of internal swallowing pathways (Jarrige et al. 2021).

EVs transmits information between cells, organs, and even organisms and are present in a variety of body fluids such as blood, urine, cerebrospinal fluid, breast milk, and saliva (Kalluri and LeBleu 2020). For example, in breast milk, EVs seem to promote postnatal health and growth, with particular proteomic profiles that

provide them with specific functional characteristics (Zonneveld et al. 2021). In addition, breast milk EVs contain miRNAs with immune-related functions (Foster et al. 2016). Most EVs in circulation are platelet-derived or megakaryocyte-derived, indicating a role in blood-related processes. These EVs interact with other cells through ligand presentation or membrane fusion (van der Meijden and Heemskerk 2019). Platelet EVs have been found to participate in a variety of critical biological and pathological processes (Tao et al. 2017), such as enhancing the vasoregenerative potential of angiogenic early outgrowth cells after vascular injury (Mause et al. 2010).

Plants are also known to produce EVs, particularly in response to pathogen infection. It has been revealed that these are made up of a wide variety of proteins involved in the response to biotic and abiotic stress (Rutter and Innes 2017). The amoeba cells release EVs that transmit RNA to *Botrytis cinerea*, and this RNA silences genes that are important in the fungal ability to infect plants (Cai et al. 2018).

It has been proven that intestinal microbes also secrete EVS. Some reports revealed that EVs containing gut microbial DNA can penetrate damaged intestinal barriers in obese patients; CRIg (complement receptor of the immunoglobulin superfamily)-positive dead-no cells help the liver remove EV-containing gut microbial DNA; and obesity leads to a reduction in the number of CRIg-positive dead-no cells, which in turn promotes the spread of microbial DNA-containing EVs to various metabolic tissues, exacerbating tissue inflammation and metabolic disorders (Luo et al. 2021). Also, the healthy people's feces contain more *Akkermansia muciniphila*-derived EVs (AmEV) than those with type 2 diabetes to improve the metabolic function of high-fat mice by regulating the integrity of the intestinal barrier (Chelakkot et al. 2018).

In addition, it has been found that many viruses use EVS in the infection process. Herpesviruses incorporate genome expression products and direct cellular products into EXOs cargoes (Liu et al. 2017). Moreover, EVs changed in patients at different temporal stages of COVID-19 related to the severity of the disease (Lam et al. 2021). Other EVs biological roles are shown in Fig. 16.5.

16.3.2 Environmental Roles

Diverse microbes release EVs into the surrounding environment. Recent studies confirmed the existence of EVs in sewage, hot spring, seawater, and dust (Abe et al. 2020; Biller et al. 2017, 2014; Dinh et al. 2020; Liu et al. 2021; Maestre-Carballa et al. 2019), highlighting the importance of further studies on the origin, cargoes, and function of EVs in the environment. It has been shown that the horizontal gene transfer (HGT) process is involved in the spread of antibiotic resistance genes (ARGs) and other functional genes (Nolivos et al. 2019), process that is enhanced with the continuous intensification of industrial activity around the world (Groussin et al. 2021). EVs were proposed to be the fourth way for gene transfer, as well as mediators for intercellular interaction (Soler and Forterre 2020; Toyofuku et al. 2019).

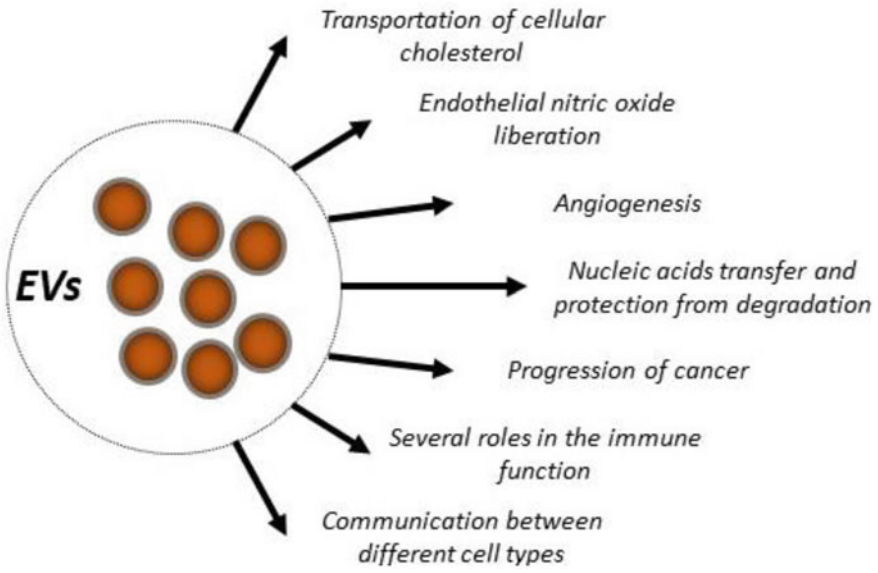

Fig. 16.5 Main reported biological roles of EVs, with common functions in several organisms

A variety of active substances encapsulated in vesicles mediate the realization of various functions in vitro, thus enhancing the adaptability of cells to environmental disturbances (Wang et al. 2021b). EVs are suitable for packing multi-molecule complexes and for delivering across long distances and therefore play critical roles in stress response, nutrition acquisition, host survival, and microbial interactions (Orench-Rivera and Kuehn 2016). For example, EVs from *E. coli* under envelope stress contain multiple misfolded proteins, whose release enhances bacterial survival (McBroom and Kuehn 2007). *Fibrobacter succinogenes* releases OMVs packed with carbohydrate-active enzymes to primarily digest insoluble cellulose (Arntzen et al. 2017). In addition, due to their lipidic nature, OMVs are highly suitable for the delivery of hydrophobic signal molecules between cells, such as the quorum-sensing compound homoserine lactone (Mashburn and Whiteley 2005). Recently, researchers reported that EVs bind to hemoglobin in an extracellular environment, passed as a common substance to DQ12-45-1b and other microorganisms to promote their growth (Wang et al. 2021b).

16.4 Analytical Techniques Applied to EVs

16.4.1 Isolation Methods Applied to EVs

Currently, guidelines for the isolation and characterization of EVs from eukaryotic cells have been published (Thery et al. 2018) and these guidelines cover the process from sample collection to isolation and characterization. In contrast, there is no

standard protocol for the isolation of EVs from prokaryotes. Some popular methods for EVs separation include ultracentrifugation, gradient density ultracentrifugation, size exclusion chromatography, and affinity chromatography.

16.4.1.1 Ultracentrifugation

Ultracentrifugation is the most used method for the isolation and extraction of EVs. The main principle is that different centrifugal forces are applied depending on the size and density of the particles, and the purification is obtained by decantation. In general, bacteria are cultured under optimal growth conditions until the late logarithmic phase (OD600=0.9-=–1.2), and EVs are obtained by centrifugation, filtration, followed by concentration techniques to reduce the volume of the sample and finally ultracentrifugation (40,000–200,000 g). Centrifugation conditions, such as rotor type, speed, and centrifugation time, can affect the availability of EVs (Balhuizen et al. 2021). Remarkably, protein aggregates and other non-EVs particles can be present in the EVs fraction obtained by ultracentrifugation.

16.4.1.2 Gradient Density Ultracentrifugation

The density gradient method usually refers to sucrose or iodixanol density gradients. The density gradient method is used to improve the efficiency of particle separation based on density. It is considered one of the best methods for the separation and purification of EVs. The crude EVs sample is usually mixed with the high-density solution and overlaid with different low-density gradient solutions on top. During centrifugation, the EVs migrate and equilibrate to a position according to their density. After centrifugation, individual fractions from either the top or bottom are collected and each particular fraction is identified and analyzed to determine the EVs fraction (Klimentova and Stulik 2015). The EVs obtained by the density gradient method are of a higher purity than those prepared by the classical ultracentrifugation method. It should be noted that this purification method can increase the purity of the target EVs while reducing their number.

16.4.1.3 Size Exclusion Chromatography (SEC)

The isolation is based on various sizes of particles eluting differently from each other through the porous polymer profile. A column is filled with this type of polymer, also known as gel filtration matrix or resin. Small particles like proteins can enter the pores of the polymer, causing a slower movement of smaller particles through the tube, so they elute later than EVs. EVs have larger pores than polymers and move faster through the column and therefore elute first (EV-TRACK Consortium et al. 2017; Potschka 1987). The SEC method preserves the structure, integrity, and biological activity of EVs and has been widely used to isolate EVs from prokaryotes and eukaryotes (Collins et al. 2021; Monguio-Tortajada et al. 2019; Reshi et al. 2021; Takov et al. 2019).

16.4.1.4 Affinity Chromatography

Affinity chromatography is based on how the target molecule interacts with an immobilized ligand to isolate the particles from the mixture. EVs, which express a specific ligand, are adsorbed by the binding resin, and the complete EVs are obtained

by elution. For example, OMVs containing mutant OmpA-His6 were purified directly from *E. coli* culture media on an immobilized metal affinity chromatography Ni-NTA resin (Alves et al. 2017).

16.4.1.5 Other Isolation Methods

Accompanying the further investigation of EVs, new techniques and methods such as ultrafiltration, polymerization precipitation, microfluidics, and capillary zone electrophoresis are used to separate EVs (Dziomba et al. 2021; Hong et al. 2019; Konoshenko et al. 2018).

16.4.2 Methods to Characterize EVs

Following the isolation of EVs, it is also necessary to characterize them and determine their concentration in the sample (defined as the number of vesicles per unit volume of liquid), their size and size distribution, shape, and other information. There are many methods to characterize EVs, however, nearly two types of approaches are used in every publication: visualization techniques and EVs concentration (Klimentova and Stulik 2015). Besides, specific protein markers in EVs are also used to characterize their existence.

16.4.2.1 Particle Visualization

Due to the small size (30–200 nm) and low resolution of EVs, it is not possible to observe them with light microscopy. Electron microscopy (EM) is widely used to characterize and visualize a wide range of biological samples. Transmission electron microscopy (TEM) is the method of choice for demonstrating the presence of EVs as it can describe the size, shape, and overall appearance of the EVs and also identify whether it is contaminated with non-EVs materials such as flagella and protein polymers. EVs can usually be observed under TEM after a stain by uranyl acetate or Phosphotungstic acid. Immobilization of the specimen with glutaraldehyde, formaldehyde, or sodium tetroxide is optional (Biller et al. 2014; Thery et al. 2006; Tulkens et al. 2020). In addition, cryo-Transmission electron microscopy (cryo-TEM) is also frequently used to characterize EVs (Baumgarten et al. 2012; Zabeo et al. 2017). The sample can be imaged by cryo-TEM without adding any heavy metals or fixatives, and the sample is rapidly frozen, so the original structure is preserved (Emelyanov et al. 2020; Szatanek et al. 2017). Other methods, such as scanning electron microscopy (SEM) and atomic force microscopy (AFM), are also used for characterization of EVs (Biller et al. 2014; Piacenza et al. 2018). Figure 16.6 shows the description of EVs using different electron microscopy approaches.

16.4.2.2 Particles Size and Concentration

Dynamic light scattering (DLS) is used to measure the hydrodynamic size distribution of nanoparticles (1 nm–6 μm) in solution (Stetefeld et al. 2016). Samples containing nanoparticles are illuminated by laser beams and all illuminated vesicles scatter incident light diffracted in all directions. Particle size distribution can be acquired by analyzing fluctuations in scattered light intensity with time (Hassan et al.

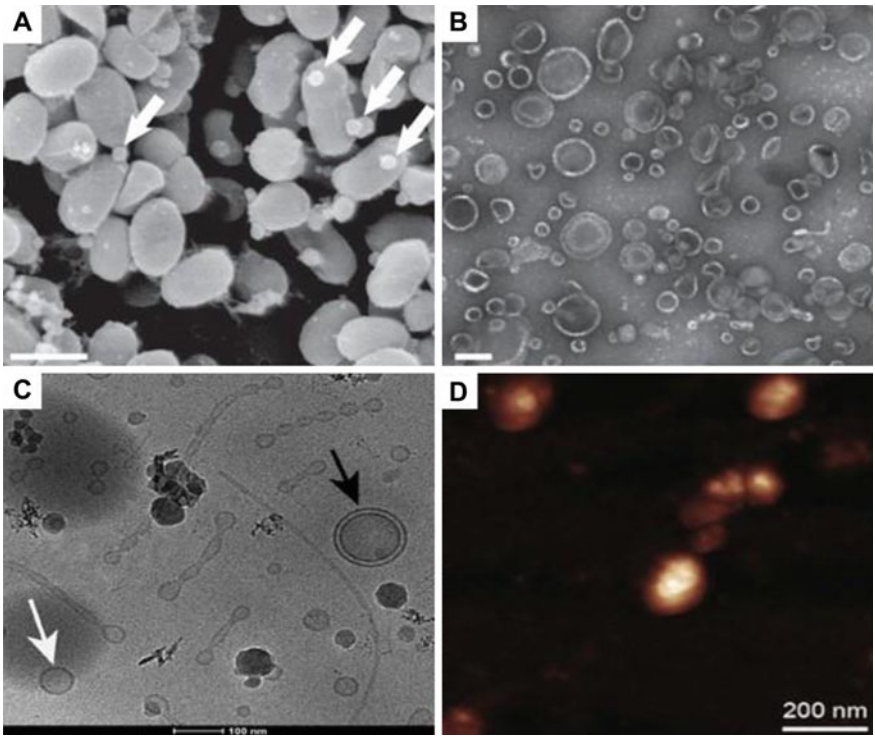

Fig. 16.6 EVs characterization using different electron microscopy approaches. (**a**) SEM of *Prochlorococcus* strain MIT9313 shows the presence of numerous small spherical features (vesicles, indicated by arrows) near the cells. Scale bar, 1 μm. (**b**) Purified *Prochlorococcus* vesicles as seen by negative-stain TEM. Scale bar, 100 nm (Biller et al. 2014). (**c**) Isolated OMVs from *S. vesiculosa* $M7^T$ observed by cryo-TEM. Two types of OMVs can be seen. Most vesicles have a single membrane (white arrow), but occasionally vesicles with two membranes are observed (black arrow). Bar, 100 nm (Perez-Cruz et al. 2013). (**d**) Exosomes imaged by AFM. AFM height image of exosomes obtained in semi-contact mode in 1 μm. Scale bar, 200 nm. (Taken from (Piacenza et al. 2018))

2015). DLS is a high throughput and sensitive technique, which requires very small sample volumes to measure particle size. However, the method can only obtain the particle size distribution of the sample without the concentration of the sample and is susceptible to interference from some factors (color, impurities) (Shpacovitch and Hergenroder 2018).

Nanoparticle tracking analysis (NTA) is one of the most frequently used methods to characterize the size and number of particles. The physical properties (size and concentration) of EVs are usually measured directly by NTA (Gardiner et al. 2016). This method harnesses the principles of light scattering and Brownian motion to determine the size and number of nanoparticles. The NTA can be performed in static mode by measuring the particles trapped in the chamber and inflow mode by slowly allowing the nanoparticle sample to flow through the chamber (Gerritzen et al. 2017). However, NTA has a minimum detection limit of 70–90 nm and a large

number of EVs are smaller than 70 nm, making it hard to reveal the complete picture of all sizes of EVs (Tian et al. 2018; van der Pol et al. 2014; H. Zhang et al. 2018).

16.4.2.3 EVs specific protein markers

Due that the EVs can encapsulated some proteins during their production, it is possible to characterize the presence of EVs by some proteins, also known as marker proteins. CD63, as well as CD9 and CD81, are proteins of the transmembrane protein family. These transmembrane proteins are usually found in EXOs and tend to be enriched in them compared to cell lysates. Therefore, these marker proteins are widely employed to characterize EXOs using Western Blot (Qin et al. 2021; Tian et al. 2020; Yu et al. 2019). The abundance of outer membrane proteins (OmpA, OmpC, and OmpF) and virulence factors in the outer membrane vesicles of Gram-negative bacteria has been revealed by biochemical analysis, including polyacrylamide gel electrophoresis with protein staining and western blot with internal antibodies (Kim et al. 2015; Lee et al. 2008).

16.5 Biotechnological Approaches of EVs

The constant need for biotechnological tools that allow to efficiently execute processes of interest in different areas obliges researchers to explore new strategies or those underexploited. In this context, EVs are shown as an appropriate option for these purposes (Mencher et al. 2020). This alternative entails several challenges in the design and transformation of the EVs for the chosen purposes, so it is crucial to establish clear protocols and join efforts (Wang et al. 2021a), popularizing the science for the common good and not only as a personal benefit tool.

16.5.1 In Vitro Design and Elaboration of the EVs

The design and preparation of the EVs require a casuistic analysis in the plane of theranostic applications. There are several ways to design and modify the EVs for biotechnological applications. The surface modification is essential for these purposes (Fig. 16.7), within which we can appoint the addition of antibodies, ligands, aptamers, and other molecules that allow the specific addressing of these EVs (Adriano et al. 2021).

In this way, with the surface modification in the EVs, it will be achieved that they work better in the host environment in which they will be inoculated (Hood 2016). This step is what we could call post-isolation modification and may be addressed in different ways. Here, EVs were isolated from mouse aortic primary endothelial cells and was analyzed the uptake efficiency of EVs derived from endothelial cells in this same cell type. The samples were subjected to electroporation to load them with a marker, confirming the capacity of this type of cells to accept and release small nucleic acid sequences (Banizs et al. 2014). On the other hand, using the mouse B16-F10 melanoma cells, by electroporation, the EVs were transformed with SPION5 (superparamagnetic iron oxide nanoparticles), a theranostic strategy to

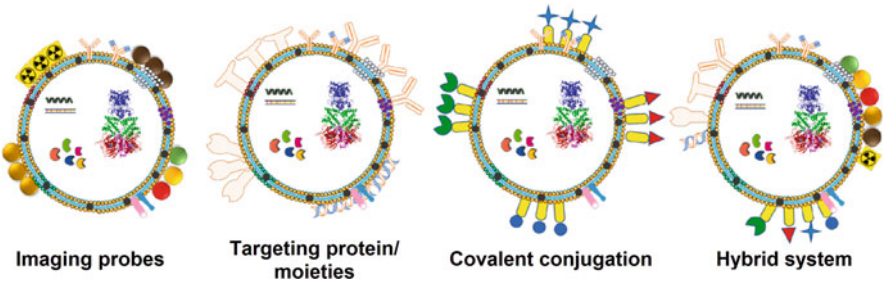

Fig. 16.7 Different strategies explored for the engineering of exosome surface with imaging probe (radioisotope/radiotracer, magnetic nanoparticles, gold, quantum dots, and labeling fluorescent probes), targeting moieties (monoclonal/polyclonal antibodies, aptamer, fragmented antibodies, and other bio-macromolecules), conjugating small, biological, macro-/bio-macromolecules (reporter agents and other molecules), and hybrid nanosystems. (Taken from (Adriano et al. 2021))

track them in the lymph nodes by MRI (Magnetic Resonance Imaging). In this way, in vivo monitoring of the EVs was achieved using a C57BL/6 mouse model (Hu et al. 2015).

Also, there is a wide variety of ways to modify the EVs cargo (Fig. 16.8), within which we can highlight those that are based on incubation processes, transfection, physical treatments, and on-site assembly and synthesis (Fu et al. 2020). In the same context, we can say that in the EVs, the encapsulation of cargo can be achieved passively (incubation with EXOs, incubation with donor cells) or actively (sonication, extrusion, thermal shock, electroporation, incubation with permeabilizing membranes, chemical methods for direct conjugation, antibodies directed to the membrane). Within the main potential applications of the EVs designed is the transport of therapeutic drugs, nucleic acids, and proteins (Luan et al. 2017). With regard to the inclusion of genetic material in EVs, this provides extended stability over time for the nucleic acid, being especially advantageous in the case of RNAs. A work that evaluated the stability of RNAs stored at −20 °C and −80 °C, finding greater integrity when placed in EVs than those held in solutions (Ge et al. 2014). Nowadays, the establishment of complex constructs added to the EVs, which can increase its functionality, is possible thanks to the synergy of several avant-garde techniques currently available. The ability to interconnect internal and surface elements in the EVs for better operation of the construct has been reported (van den Berg van Saparoea et al. 2020).

Regarding nucleic acids cargo, we know that the EVs naturally transport ARNs, indirectly regulating the abundance of these and consequently their protein translation (Eirin et al. 2014). To increase the inclusion efficiency of the cargo, EVs derived from human embryonic kidney cells (HEK293T) cells were subjected to a specific protocol (Fig. 16.9a) to create a pH gradient that can enhance the load capacity of the EVs, mainly reduced-sized nucleic acids. This enhanced capacity practically did not promote some alteration in the functioning of the EVs or significant toxic effect on wild-type (C57BL/6J) mice (Jeyaram et al. 2020). As for the cargo and transport of

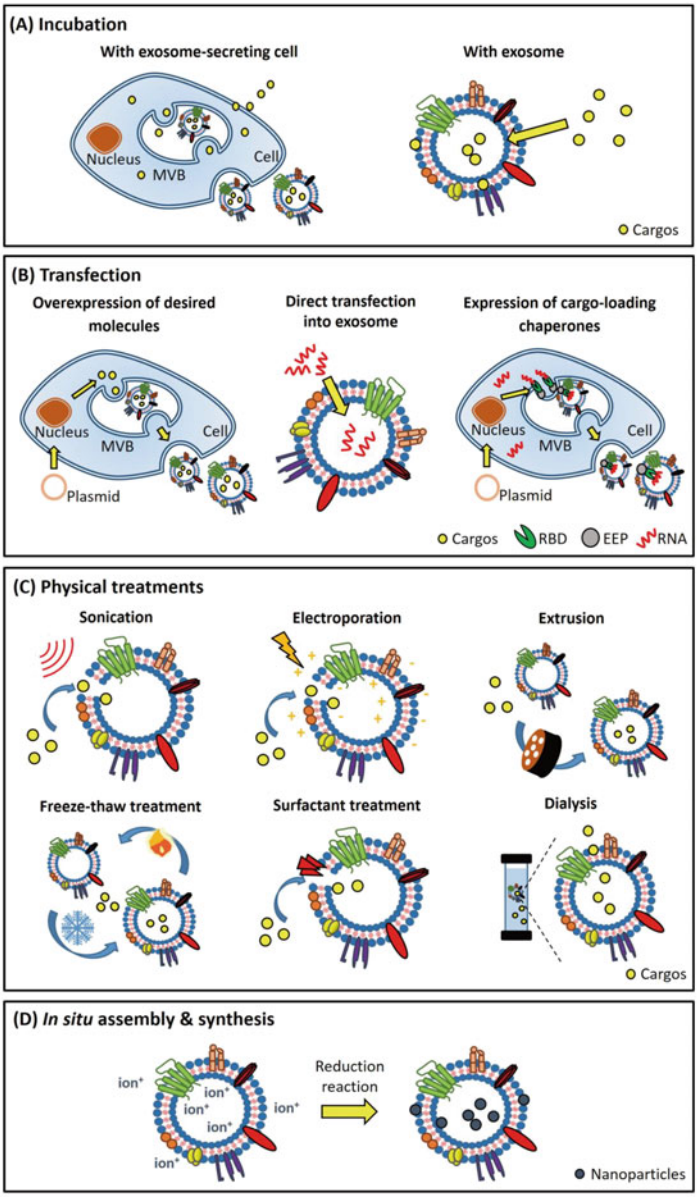

Fig. 16.8 Strategies for modification of the EVs cargo. (**a**) Exosome-secreting cells or EXOs are incubated with desired cargos. Cargos diffuse across cell and exosomal membrane, therefore packaged within EXOs. (**b**) Desired nucleic acids can be loaded into EXOs via transfection-based strategy. Transfected with vectors, the donor cell generates RNAs/proteins and packages these products into EXOs using endogenous expression and sorting machinery of donor cell, respectively. EXOs can be directly transfected with small RNAs for cargo loading purposes. (**c**) Cargos can be loaded into EXOs directly through physical treatments. Electroporation, sonication, and surfactant

drugs, the superficial manipulation of the EVs can be effectively performed. A work shows the incorporation of doxorubicin (Dox) and cholesterol-modified miRNA21 inhibitor (miR-21i) in the lipid bilayer (Fig. 16.9b). Likewise, magnetic molecules and endosomolytic peptides L17E can be associated with the EVs membrane through the link of the ligand-receptor and electrostatic interactions, respectively (Zhan et al. 2020). This allowed a specific addressing of the EVs to tumors. Therefore, a more efficient treatment is possible against these ailments.

Faced with the structural manipulation strategies of the EVs, although they are a good option and have helped the contribution in science, they may have several limitations in some instances. The design that implies biological similarity concerning the host constitutes a strategy to evade complications that may exist for the use of them, is here where the conception of artificial EVs appears as a valid option (Farooqi et al. 2018; Jang and Gho 2014). Engineered EVs can lead to obtaining more pure and homogeneous solutions, which allow better control of the experimental conditions (Nasiri Kenari et al. 2019). In this group, we can name the artificial fully exosome-like nanoparticles (Fig. 16.10a), which result from the mixture of each of its components to form a construct that resembles an EV, but with an integral control of its system. It is also possible to highlight hybrid exosome-like nanovesicles (Fig. 16.10b), constituted by an EV and another element that can be synthetic, in the same way allowing greater control of the construction of the construct (Lu and Huang 2020).

Despite the promising prospects that show the EVs in several processes, the understanding of its duality will increase the chances of success in the proposed objectives. For example, using EVs derived from cancer cells could be counterproductive if it is desired to be used as therapeutic agents on this same type of condition. Then technologies such as genetic or protein engineering will adapt the EVs under the selected therapeutic guidelines (Santos and Almeida 2021). This same fact is referenced to the emerging EVs applications for the fight against Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) (Machhi et al. 2021). If the aforementioned care is not followed, this strategy can be a double-edged weapon in most cases (Xia et al. 2021).

16.5.2 Biomedical Applications

The nanobiotechnological approach of the EVs is broad, which in the last two decades has been a target of a great effort of the scientific community. However, clear guidelines must still be established in all their performance. Under this precept,

Fig. 16.8 (continued) treatment generate pores on exosomal membrane that facilitate cargo loading. Freeze-thaw treatment, extrusion, and dialysis enhance cargo loading into EXOs during membrane recombination processes. (**d**) In situ assembly and synthesis promotes metal nanoparticles loading through reducing metal ions into nanoparticles within EXOs. (Taken from (Fu et al. 2020))

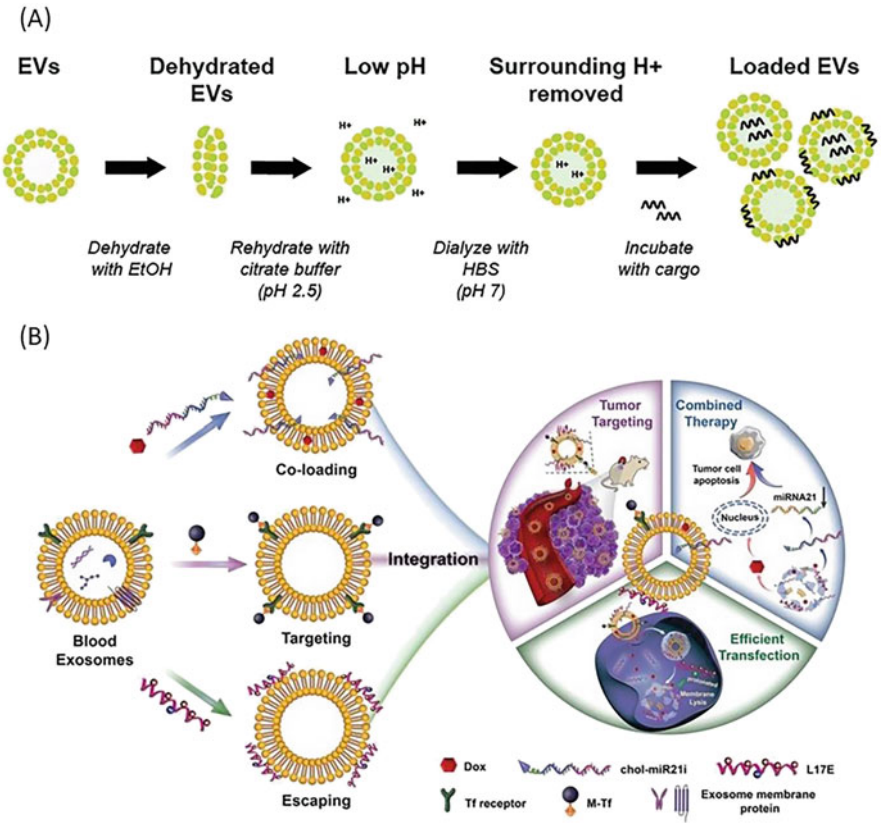

Fig. 16.9 Other technologies for the incorporation of EVs cargo. (**a**) Schematic describing the steps to prepare and load pH-EVs. Taken and modified from (Jeyaram et al. 2020). (**b**) Schematic representation of engineered blood EXOs for effective gene/chemo combined antitumor therapy. Taking full use of the structure and properties of the exosome membrane, such blood exosome-based co-delivery nanosystem tactfully integrates three moieties: co-loading of drugs and nucleic acids with high-payloads, tumor targeting, and endosomal escaping. After intravenous injection, the engineered EXOs can accumulate at the tumor site with high-efficiency under an external magnetic field, following cellular uptake, the presence of endosomolytic peptide facilitates the effective release of therapeutic RNAs and chemotherapeutic drugs, resulting in a significantly improved gene/chemo combination antitumor effect. (Taken and modified from (Zhan et al. 2020))

the minimal information for studies of extracellular vesicles 2018 (MISEV2018) suggests minimum guidelines for preanalytical, analytical, and scientific dissemination of the EVs research works (Théry et al. 2018). As mentioned in previous lines, the EVs are potential theranostic platforms highly suitable for several applications against the intensification of constant and growing demand for new services and biotechnological products (Yang et al. 2019). Next, some of these nanobiotechnological applications of the EVs will be exposed in order to have a more profound knowledge of the real potential of this technology.

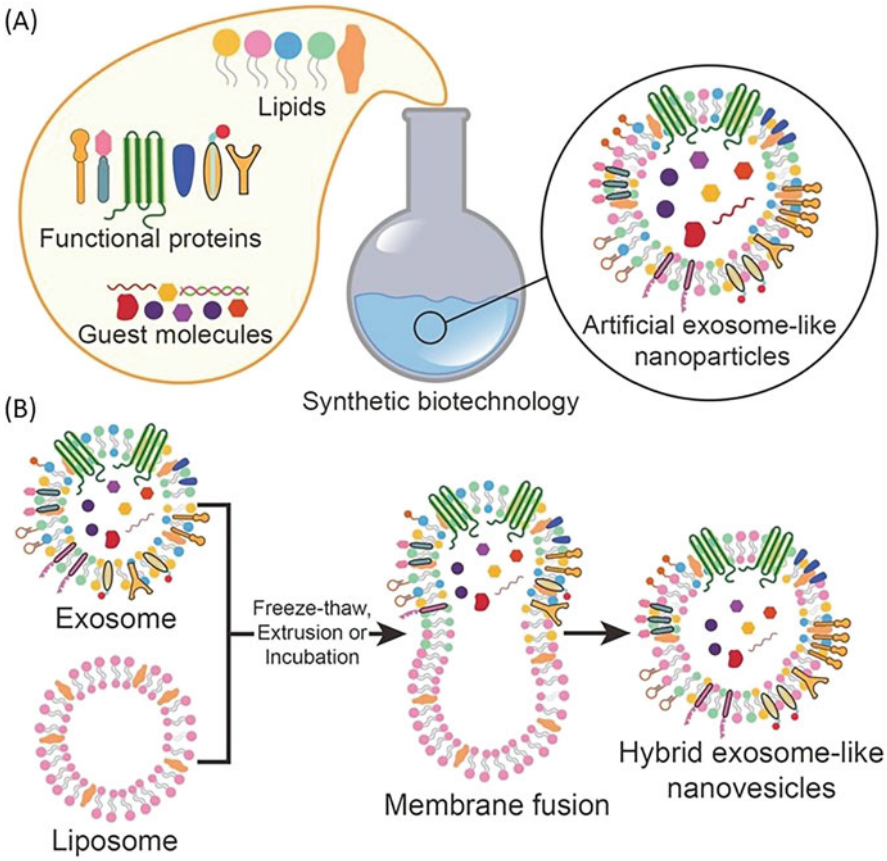

Fig. 16.10 Engineered EVs options. (**a**) Schematic illustration of the typical design route for fully artificial exosome-like nanoparticles by bottom-up approaches. In vitro synthesis is performed in a mild reaction chamber containing specific lipids and functional membrane proteins of natural EXOs, and guest molecules to direct the assembly of exosome-mimicking lipid bilayers, drug encapsulation, and membrane integration of functional proteins. (**b**) Schematic representing the hybridization of EXOs and synthetic liposomes to form hybrid exosome-like nanovesicles through freeze-thaw method, membrane extrusion, or simple incubation. (Taken and modified from (Lu and Huang 2020))

As we know, the origin of the EVs is very diverse, it is crucial to emphasize again that they are not organisms, therefore, they cannot be self-sustained or independently reproduced. As indicated in previous lines, they have biological and environmental roles, nowadays they are considered as excellent emerging biotechnological tools. Some of the applications are focused on many fields of human health (Watanabe 2016). Before applying EVs for therapeutic purposes, it must be borne in mind that EVs inoculation can trigger the recognition of these as foreign agents and initiate an inflammatory response. For this reason, understanding the structure of the EVs and

their effect within the body of interest will be a fundamental step for a successful biotechnological application (Lee et al. 2018).

16.5.2.1 Cancer

In the case of EVs of bacterial origin, their study for clinical purposes is widely addressed. The capacity attributed so that the bacterial EVs are distributed throughout the system of an organism provides determining implications to that body's microbiome. Then, for example, dysbiosis in the intestinal microbiome could not only involve alterations in digestive processes but also in other more distant organs. In this way, pathologies such as cancer could be detected by analysis systems of bacterial EVs and their associated markers (Chronopoulos and Kalluri 2020).

The use of artificial EVs, called Synthetic Bacterial Vesicles (SyBV) (Fig. 16.11), significantly reduced the acute toxic response by its inoculation at RAW 264.7 cells. SyBV also did not trigger a systemic pro-inflammatory reaction, as when the naturally released bacterial EVs are used. The joint inoculation of SyBV and melanoma EVs achieved tumor regression in Melanoma-Bearing Mice. The described therapeutic activity was enhanced by the anti-PD-1 inhibitor (Park et al. 2021). By bioengineering, bacterial EVs were developed that exhibited different tumor antigens, having the ability to stop metastasis in lung melanoma and inhibit subcutaneous colorectal cancer in mouse models. The presentation of antigens was carried out directly in the tumor, demonstrating a significative antigenic specificity and desired response. This strategy is undoubtedly feasible in the field of personalized medicine (Cheng et al. 2021).

EVs of non-bacterial origin have also been reported as potential therapeutic agents, considering that there are research works with encouraging results in the

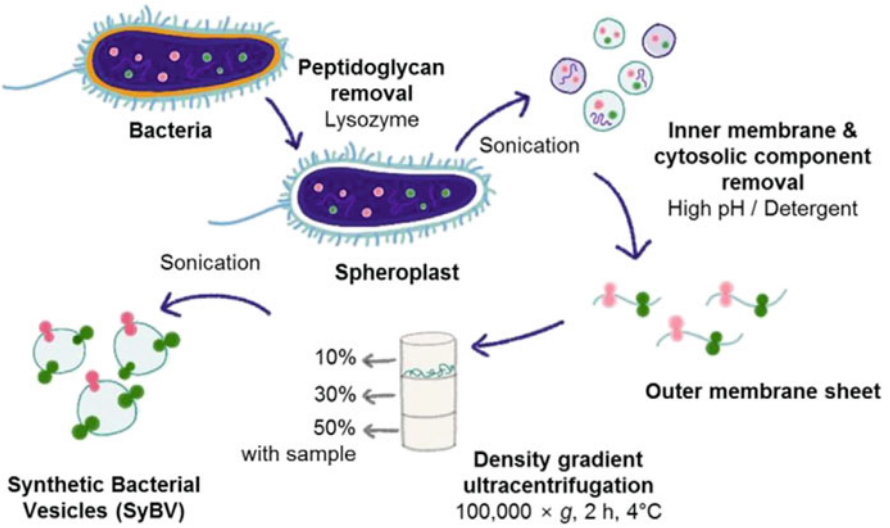

Fig. 16.11 Schematic diagram of the isolation of bacterial SyBV. (Taken and modified from (Park et al. 2021))

treatment against various types of cancer, although many are made in animal models and not in humans (Gilligan and Dwyer 2017). In a study carried out in rats, the intraperitoneal administration of EXOs derived from mesenchymal stem cells (MSCs) demonstrated a pro-angiogenic and anti-inflammatory effect. This allowed alleviating broncho-pulmonary dysplasia in the model organisms in vitro (Braun et al. 2018). The capacity of the EVs in oncology is not only in the therapeutic field but also in the field of diagnosis. The potentiality of EVs as biomarkers for different pathological processes is evident. Such is the case of renal cell carcinoma (RCC), where were have characterized specific effectors transported by the EVs at the origin and progression of this type of cancer (Grange et al. 2019). The capacity of the EVs as a tool to monitor cancerous processes lies in its ability to transport specific markers of a pathology (Cufaro et al. 2019).

A particular case is exemplified with celastrol (CEL), a compound derived from plants, has a promising therapeutic effect to treat cancer due to its ability to inhibit Hsp90 and NF-κB signal pathways. CEL has poor bioavailability and undesired side effects. In this context, EXOs derived from bovine and artificially loaded with CEL, demonstrated to increase their bioavailability, thus inhibiting the proliferation of cell lines A549 and H1299 NSCLC. In a mouse model, these preparations had a significant inhibitory capacity in tumor growth (Aqil et al. 2016).

The therapeutic capacity of the EVs has also been successfully tested in clinical trials. In patients with non-small cell lung cancer (NSCLC), it was inoculated some dendritic cell (DC)-derived EXOs (Dex) that had a cargo of the MAGE (Melanoma Antigen Gene) tumor antigens. This preparation was well tolerated in patients inoculated and with promising results in the field of oncology therapy (Morse et al. 2005). Also, Dex demonstrated enhancing natural killer cells (NKCs) antitumor activity in patients in an advanced stage of non-small cell lung cancer (NSCLC). The results were more favorable for improving the clinical panorama by using the second generation of Dex (IFN-g-Dex), designed to enhance the response of NKC and T lymphocytes (Besse et al. 2016).

16.5.2.2 Immunological Applications

In the regulation of the immune system, EVs also have relevant applications to review, like the reference as potential tools for the study of the progression of allergic reactions (Hovhannisyan et al. 2021). In the case of the EXOs derived from MSCs, they have the ability to over-regulate IL-10 and TGF-β1 of peripheral blood cells (PBMCs) in asthmatic patients. In this way, the capacity and function of regulatory T Cells would benefit, thus exercising an efficient immunosuppressive role. According to this, the administration of EXOs derived from MSCs is shown as a potential therapeutic strategy in patients with asthmatic symptoms (Du et al. 2018). For its part, EXOs have also been described as effective enhancers of MSCS immunomodulatory capacity in inflammatory processes, thanks to the transportation of IL-1β (Song et al. 2017).

The EVs are also being considered as tools for the fight against COVID-19. EVs from *Salmonella typhimurium* were transformed with mammalian cell culture-derived Spike receptor-binding domain (RBD). This construct was inoculated in

Golden Syrian hamsters (*Mesocricetus auratus*). The results were a high degree of anti-RBD IgG and mucosal immunity in treated individuals against SARS-CoV-2 (Jiang et al. 2021). Apart from the approach to SARS-CoV-2, EVs of bacterial origin have also been applied for other immunization processes. A study used EVs derived from genetically modified *S. aureus* to express detoxified cytolysins. When these EVs were inoculated in mice, it was possible to detect cytolysin-neutralizing antibodies (Wang et al. 2018).

16.5.2.3 Other Potential Therapeutic Biomedical Applications

Also, in regenerative medicine, the EVS is shown as promising tools within biomedicine. The EVs derived from adipose MSCs (ADSC) demonstrated having a protective capacity of the skin flap during ischemia reperfusion (I/R). This protective level was possible through the neovascularization and diminution of inflammation. Interestingly, pre-conditioned preparations with hydrogen peroxide had better results than those EXOs without this treatment (Bai et al. 2018). In another study, a decrease was obtained at the time of healing of wounds in diabetic patients after administration of EVs loaded with LncRNA-H19. Additional evidence allowed relating to long noncoding RNA (LncRNA)-H19 as a pro-angiogenesis agent (Tao et al. 2018). In rats' models, it was shown that bone marrow MSC-derived EVs (BMSC-EVs), alone or enriched with microRNA-233 (miR-233), had a protective effect against damage produced during autoimmune hepatitis. In the same way, the inhibition of miR-233 suppressed the beneficial effects of the aforementioned treatments (Chen et al. 2018). Additionally, there are EVs derived from MSCs that are used in craniofacial regeneration; however, the design and manipulation part of the EVs still needs to be optimized (Cooper et al. 2020).

Also, EVs derived from rat milk and from rats (ileon) were administered in intestinal epithelial cells (IEC-18). This treatment resulted in the IEC viability increase, contrary to treatment without EVs. This strategy could be an alternative treatment for necrotizing enterocolitis (NEC) in human patients (Hock et al. 2017). On the other hand, in mouse models, the curcumin transport enhancer capacity was demonstrated in EVs, contrary to the traditionally curcumin administration and the EVs without curcumin (Sun et al. 2010). In another similar study, the administration in rats of embryonic stem cell EXOs (MESC-exo^{cur}) charged with curcumin managed to decrease damage caused by ischemia reperfusion (IR) injury. Likewise, in healthy specimens, the treatment with MESC-exo^{cur} resulted in a decrease in inflammation markers (Kalani et al. 2016).

In spinal cord injuries, EVS has also been used successfully, with good potential for their application in humans. BMSC-EVs demonstrated having a potential therapeutic capacity for the treatment of spinal cord injury (SCI). In rat's models, the administration of BMSC-EVs allowed motor function recovery. It was also possible to observe the deregulation of the NF-kB p65 signaling pathway downward in Pericytes (Lu et al. 2019). In an SCI rat model, it was noted that BMSC-EVs could accelerate SCI recovery through TIMP2/MMP signaling pathway (Xin et al. 2021). In addition to the bacterial-derived EVS, those derivatives from MSCs are essential to highlight (Fig. 16.12). Other clinical studies are given in Table 16.4.

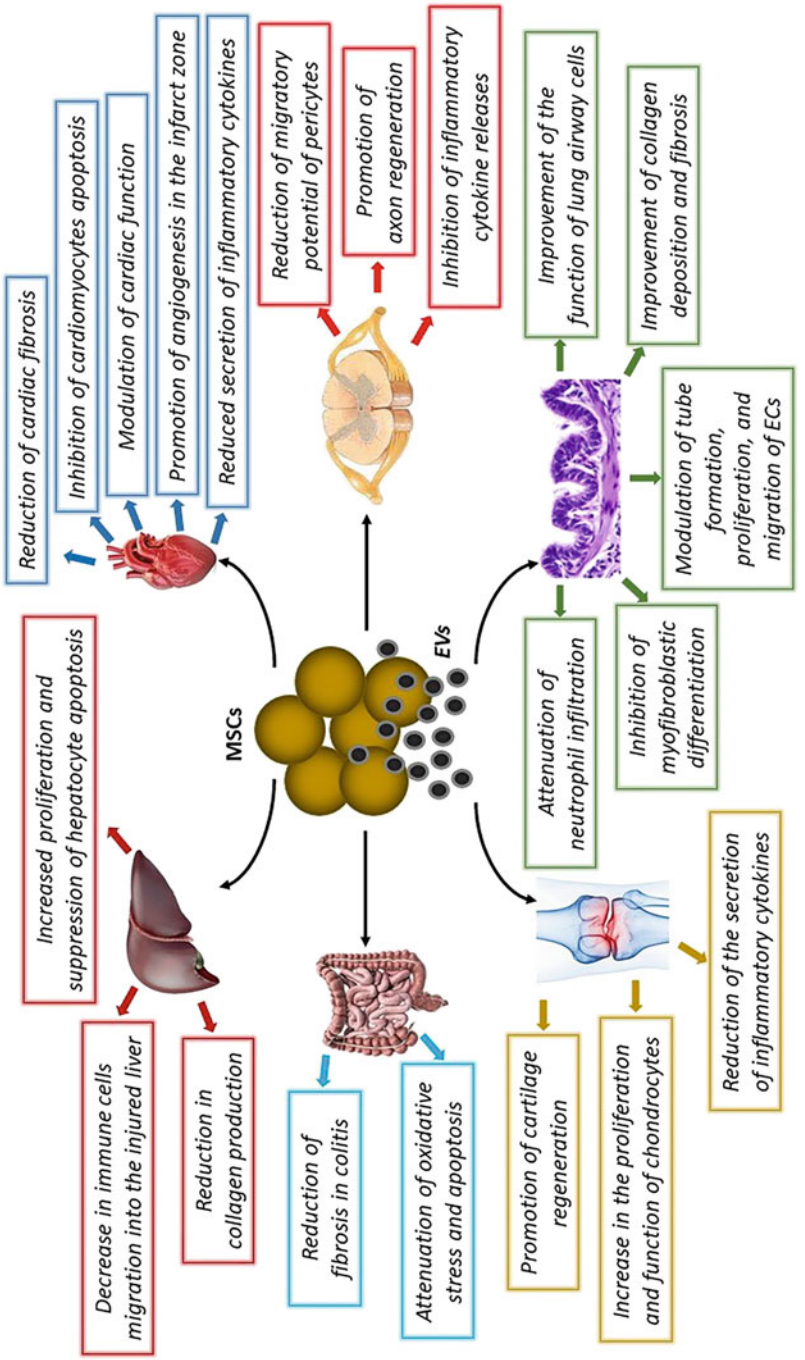

Fig. 16.12 Role of MSC-derived EVs in the regeneration of different tissues. (Taken and modified from (Ghafouri-Fard et al. 2021))

Table 16.4 Additional references of biomedical applications of the EVs.

Outcomes	Application	Reference
EVs from *L. crispatus* and *L. gasseri* had a protective capacity against HIV-1 infection in tissues ex vivo and isolated cells	Therapy against HIV	Ñahui Palomino et al. (2019)
Improvement of cardiac functions by administration of EVs derived from cardiosphere-derived cells (CDCS) in a porcine model with cardiomyopathy	Biomedicine	Hirai et al. (2020)
Engineered EVs (small RNA and anticancer drug) showed protection properties and lower drug resistance in laboratory models (cell lines and mouse) for colorectal cancer (CRC)	Improvement of cancer treatment	Liang et al. (2020)
EVs loaded with the CRISPR-CAS9 system achieved a more efficiently delivery of its transgene on target cells	Improve in the delivery system of a transgen	Ye et al. (2020)
Echogenic EVs derived from bovine milk demonstrated a competitive contrast level compared to traditional systems	New effective contrast element in imaging	Osborn et al. (2020)
Recovery of the epidermal barrier in atopic dermatitis (AD) on mouse models by treatment with EVs derived from mesenchymal stem cells (ASC)	Therapeutic strategy for AD	Shin et al. (2020)
Detection of the variable molecular profile in EVs extracted from patients in oncological treatment process	Analysis of cancer progression	Theodoraki et al. (2021)
Analysis of the variable expression profile of EVs miRNA in patients with different stage of development of prostate cancer	Predictive marker of metastasis in prostate cancer	Shin et al. (2021)
MIR-1246 detection (oncological marker) in blood samples using EVS transformed with specific probes	Less invasive system for cancer detection	Chen et al. (2021)
Determination that epithelial contactin—from Evs plays a critical role in asthma pathology	Therapeutic strategy for airway allergy	Zhang et al. (2021)
Epigenetic regression of HIV in a mouse model mediated by transformed EVs	HIV treatment	Shrivastava et al. (2021)
The SARS-COV-2 Spike Protein S2 was detected in symptomatic and asymptomatic patients during active infection	Potential diagnostic tool for SARS-CoV-2	Bansal et al. (2021)

16.6 Perspectives

As we have seen in this chapter, the EVS has several origins, functions, and possible therapeutic applications. Even though its use is beginning to spread in a practical way, the application should still be strictly regulated and validated, mainly in humans. This can be a short-term limitation, so efforts in this field must be widely collaborative to timely achieve each proposed objective.

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References

Abe K, Nomura N, Suzuki S (2020) Biofilms: hot spots of horizontal gene transfer (HGT) in aquatic environments, with a focus on a new HGT mechanism. FEMS Microbiol Ecol 96(5):fiaa031. https://doi.org/10.1093/femsec/fiaa031

Adriano B, Cotto NM, Chauhan N, Jaggi M, Chauhan SC, Yallapu MM (2021) Milk exosomes: nature's abundant nanoplatform for theranostic applications. Bioact Mater 6(8):2479–2490. https://doi.org/10.1016/j.bioactmat.2021.01.009

Alderwick LJ, Harrison J, Lloyd GS, Birch HL (2015) The mycobacterial cell wall--peptidoglycan and arabinogalactan. Cold Spring Harb Perspect Med 5(8):a021113. https://doi.org/10.1101/cshperspect.a021113

Alves NJ, Turner KB, DiVito KA, Daniele MA, Walper SA (2017) Affinity purification of bacterial outer membrane vesicles (OMVs) utilizing a His-tag mutant 168(2):139–146. https://doi.org/10.1016/j.resmic.2016.10.001

Anderson HC (1969) Vesicles associated with calcification in the matrix of epiphyseal cartilage. J Cell Biol 41(1):59–72

Aqil F, Kausar H, Agrawal AK, Jeyabalan J, Kyakulaga A-H, Munagala R, Gupta R (2016) Exosomal formulation enhances therapeutic response of celastrol against lung cancer. Exp Mol Pathol 101(1):12–21. https://doi.org/10.1016/j.yexmp.2016.05.013

Arntzen M, Várnai A, Mackie RI, Eijsink VGH, Pope PB (2017) Outer membrane vesicles from Fibrobacter succinogenes S85 contain an array of carbohydrate-active enzymes with versatile polysaccharide-degrading capacity. Environ Microbiol 19(7):2701–2714. https://doi.org/10.1111/1462-2920.13770

Bai Y, Han Y-D, Yan X-L, Ren J, Zeng Q, Li X-D et al (2018) Adipose mesenchymal stem cell-derived exosomes stimulated by hydrogen peroxide enhanced skin flap recovery in ischemia-reperfusion injury. Biochem Biophys Res Commun 500(2):310–317. https://doi.org/10.1016/j.bbrc.2018.04.065

Balhuizen MD, Veldhuizen EJA, Haagsman HP (2021) Outer membrane vesicle induction and isolation for vaccine development. Front Microbiol 12:629090. https://doi.org/10.3389/fmicb.2021.629090

Banizs AB, Huang T, Dryden K, Berr SS, Stone JR, Nakamoto RK et al (2014) In vitro evaluation of endothelial exosomes as carriers for small interfering ribonucleic acid delivery. Int J Nanomedicine 9:4223–4230. https://doi.org/10.2147/IJN.S64267

Bansal S, Tokman S, Fleming T, Maine GN, Sanborn K, Hachem R et al (2021) SARS-CoV-2 infection in lung transplant recipients induces circulating exosomes with SARS-CoV-2 spike protein S2. Clin Transl Med 11(11):e576. https://doi.org/10.1002/ctm2.576

Baumgarten T, Sperling S, Seifert J, von Bergen M, Steiniger F, Wick LY, Heipieper HJ (2012) Membrane vesicle formation as a multiple-stress response mechanism enhances Pseudomonas putida DOT-T1E cell surface hydrophobicity and biofilm formation. Appl Environ Microbiol 78(17):6217–6224. https://doi.org/10.1128/AEM.01525-12

Bayer ME, Anderson TF (1965) The surface structure of Escherichia coli. Proc Natl Acad Sci U S A 54:1592–1599

Berleman J, Auer M (2013) The role of bacterial outer membrane vesicles for intra- and interspecies delivery. Environ Microbiol 15(2):347–354. https://doi.org/10.1111/1462-2920.12048

Besse B, Charrier M, Lapierre V, Dansin E, Lantz O, Planchard D et al (2016) Dendritic cell-derived exosomes as maintenance immunotherapy after first line chemotherapy in NSCLC. OncoImmunology 5(4):e1071008. https://doi.org/10.1080/2162402X.2015.1071008

Biller SJ, Schubotz F, Roggensack SE, Thompson AW, Summons RE, Chisholm SW (2014) Bacterial vesicles in marine ecosystems. Science 343(6167):183–186. https://doi.org/10.1126/science.1243457

Biller SJ, McDaniel LD, Breitbart M, Rogers E, Paul JH, Chisholm SW (2017) Membrane vesicles in sea water: heterogeneous DNA content and implications for viral abundance estimates. ISME J 11(2):394–404. https://doi.org/10.1038/ismej.2016.134

Bose S, Aggarwal S, Singh DV, Acharya N (2020) Extracellular vesicles: an emerging platform in Gram-positive bacteria. Microb Cell 7(12):312–322. https://doi.org/10.15698/mic2020.12.737

Braun RK, Chetty C, Balasubramaniam V, Centanni R, Haraldsdottir K, Hematti P, Eldridge MW (2018) Intraperitoneal injection of MSC-derived exosomes prevent experimental bronchopulmonary dysplasia. Biochem Biophys Res Commun 503(4):2653–2658. https://doi.org/10.1016/j.bbrc.2018.08.019

Cai Q, Qiao L, Wang M, He B, Lin FM, Palmquist J et al (2018) Plants send small RNAs in extracellular vesicles to fungal pathogen to silence virulence genes. Science 360(6393):1126–1129. https://doi.org/10.1126/science.aar4142

Casadevall A, Nosanchuk JD, Williamson P, Rodrigues ML (2009) Vesicular transport across the fungal cell wall. Trends Microbiol 17(4):158–162. https://doi.org/10.1016/j.tim.2008.12.005

Castagna M, Yagello M, Rabourdin-Combe C, Fridman WH (1980) Tumor-promoting phorbol diesters inhibit in vitro antibody synthesis. Cancer Lett 8:365

Chahar HS, Bao X, Casola A (2015) Exosomes and their role in the life cycle and pathogenesis of RNA viruses. Viruses 7(6):3204–3225. https://doi.org/10.3390/v7062770

Chatterjee SN, Das J (1967) Electron microscopic observations on the excretion of cell-wall material by Vibriu chulerae. J Gen Microbiol 49:1–11

Chelakkot C, Choi Y, Kim DK, Park HT, Ghim J, Kwon Y et al (2018) Akkermansia muciniphila-derived extracellular vesicles influence gut permeability through the regulation of tight junctions. Exp Mol Med 50(2):e450. https://doi.org/10.1038/emm.2017.282

Chen L, Lu F-B, Chen D-Z, Wu J-L, Hu E-D, Xu L-M et al (2018) BMSCs-derived miR-223-containing exosomes contribute to liver protection in experimental autoimmune hepatitis. Mol Immunol 93:38–46. https://doi.org/10.1016/j.molimm.2017.11.008

Chen Y, Zhai L-Y, Zhang L-M, Ma X-S, Liu Z, Li M-M et al (2021) Breast cancer plasma biopsy by in situ determination of exosomal microRNA-1246 with a molecular beacon. Analyst 146(7):2264–2276. https://doi.org/10.1039/D0AN02224A

Cheng K, Zhao R, Li Y, Qi Y, Wang Y, Zhang Y et al (2021) Bioengineered bacteria-derived outer membrane vesicles as a versatile antigen display platform for tumor vaccination via Plug-and-Display technology. Nat Commun 12(1):2041. https://doi.org/10.1038/s41467-021-22308-8

Chronopoulos A, Kalluri R (2020) Emerging role of bacterial extracellular vesicles in cancer. Oncogene 39(46):6951–6960. https://doi.org/10.1038/s41388-020-01509-3

Collins SM, Nice JB, Chang EH, Brown AC (2021) Size exclusion chromatography to analyze bacterial outer membrane vesicle heterogeneity. J Vis Exp (169). https://doi.org/10.3791/62429

Colombo M, Raposo G, Thery C (2014) Biogenesis, secretion, and intercellular interactions of exosomes and other extracellular vesicles. Annu Rev Cell Dev Biol 30:255–289. https://doi.org/10.1146/annurev-cellbio-101512-122326

Cooper LF, Ravindran S, Huang C-C, Kang M (2020) A role for exosomes in craniofacial tissue engineering and regeneration. Front Physiol 10:1569. https://doi.org/10.3389/fphys.2019.01569

Crawfo N (1971) The presence of contractile proteins in platelet microparticles isolated from human and animal platelet-free plasma. Br J Haematol 21:53

Cufaro MC, Pieragostino D, Lanuti P, Rossi C, Cicalini I, Federici L et al (2019) Extracellular vesicles and their potential use in monitoring cancer progression and therapy: the contribution of proteomics. J Oncol 2019:1639854. https://doi.org/10.1155/2019/1639854

Dalton AJ (1975) Microvesicles and vesicles of multivesicular bodies versus "virus-like" particles. J Natl Cancer Inst 54(5):1137

Dinh NTH, Lee J, Lee J, Kim SS, Go G, Bae S et al (2020) Indoor dust extracellular vesicles promote cancer lung metastasis by inducing tumour necrosis factor-alpha. J Extracell Vesicles 9(1):1766821. https://doi.org/10.1080/20013078.2020.1766821

Dorward DW, Garon CF (1990) DNA is packaged within membrane-derived vesicles of gram-negative but not gram-positive bacteria. Appl Environ Microbiol 56:1960–1962

Doyle LM, Wang MZ (2019) Overview of extracellular vesicles, their origin, composition, purpose, and methods for exosome isolation and analysis. Cells 8(7):727. https://doi.org/10.3390/cells8070727

Du Y-M, Zhuansun Y-X, Chen R, Lin L, Lin Y, Li J-G (2018) Mesenchymal stem cell exosomes promote immunosuppression of regulatory T cells in asthma. Exp Cell Res 363(1):114–120. https://doi.org/10.1016/j.yexcr.2017.12.021

Dziomba S, Wysocka M, Jonca J, Sola L, Stec A, Waleron K, Wielgomas B (2021) Investigation of selected parameters of capillary zone electrophoresis method for analysis of isolates of outer membrane vesicles. Electrophoresis 42(20):2010–2017. https://doi.org/10.1002/elps.202000360

Eirin A, Riester SM, Zhu X-Y, Tang H, Evans JM, O'Brien D et al (2014) MicroRNA and mRNA cargo of extracellular vesicles from porcine adipose tissue-derived mesenchymal stem cells. Gene 551(1):55–64. https://doi.org/10.1016/j.gene.2014.08.041

Ellen AF, Albers SV, Huibers W, Pitcher A, Hobel CF, Schwarz H et al (2009) Proteomic analysis of secreted membrane vesicles of archaeal Sulfolobus species reveals the presence of endosome sorting complex components. Extremophiles 13(1):67–79. https://doi.org/10.1007/s00792-008-0199-x

Ellen AF, Zolghadr B, Driessen AM, Albers SV (2010) Shaping the archaeal cell envelope. Archaea 2010:608243. https://doi.org/10.1155/2010/608243

Emelyanov A, Shtam T, Kamyshinsky R, Garaeva L, Verlov N, Miliukhina I et al (2020) Cryo-electron microscopy of extracellular vesicles from cerebrospinal fluid. PLoS One 15(1):e0227949. https://doi.org/10.1371/journal.pone.0227949

EV-TRACK Consortium, Van Deun J, Mestdagh P, Agostinis P, Akay O, Anand S et al (2017) EV-TRACK: transparent reporting and centralizing knowledge in extracellular vesicle research. Nat Methods 14(3):228–232. https://doi.org/10.1038/nmeth.4185

Farooqi AA, Desai NN, Qureshi MZ, Librelotto DRN, Gasparri ML, Bishayee A et al (2018) Exosome biogenesis, bioactivities and functions as new delivery systems of natural compounds. Biotechnol Adv 36(1):328–334. https://doi.org/10.1016/j.biotechadv.2017.12.010

Foster BP, Balassa T, Benen TD, Dominovic M, Elmadjian GK, Florova V et al (2016) Extracellular vesicles in blood, milk and body fluids of the female and male urogenital tract and with special regard to reproduction. Crit Rev Clin Lab Sci 53(6):379–395. https://doi.org/10.1080/10408363.2016.1190682

Fu S, Wang Y, Xia X, Zheng JC (2020) Exosome engineering: current progress in cargo loading and targeted delivery. NanoImpact 20:100261. https://doi.org/10.1016/j.impact.2020.100261

Gardiner C, Di Vizio D, Sahoo S, Thery C, Witwer KW, Wauben M, Hill AF (2016) Techniques used for the isolation and characterization of extracellular vesicles: results of a worldwide survey. J Extracell Vesicles 5:32945. https://doi.org/10.3402/jev.v5.32945

Ge Q, Zhou Y, Lu J, Bai Y, Xie X, Lu Z (2014) miRNA in plasma exosome is stable under different storage conditions. Molecules 19(2):1568–1575. https://www.mdpi.com/1420-3049/19/2/1568

Gerritzen MJH, Martens DE, Wijffels RH, Stork M (2017) High throughput nanoparticle tracking analysis for monitoring outer membrane vesicle production. J Extracell Vesicles 6(1):1333883. https://doi.org/10.1080/20013078.2017.1333883

Ghafouri-Fard S, Niazi V, Hussen BM, Omrani MD, Taheri M, Basiri A (2021) The emerging role of exosomes in the treatment of human disorders with a special focus on mesenchymal stem cells-derived exosomes. Front Cell Dev Biol 9:653296–653296. https://doi.org/10.3389/fcell.2021.653296

Gill S, Catchpole R, Forterre P (2019) Extracellular membrane vesicles in the three domains of life and beyond. FEMS Microbiol Rev 43(3):273–303. https://doi.org/10.1093/femsre/fuy042

Gilligan KE, Dwyer RM (2017) Engineering exosomes for cancer therapy. Int J Mol Sci 18(6): 1122. https://doi.org/10.3390/ijms18061122; Accession No. 28538671

Grange C, Brossa A, Bussolati B (2019) Extracellular vesicles and carried miRNAs in the progression of renal cell carcinoma. Int J Mol Sci 20(8):1832. https://www.mdpi.com/1422-0067/20/8/1832

Groussin M, Poyet M, Sistiaga A, Kearney SM, Moniz K, Noel M et al (2021) Elevated rates of horizontal gene transfer in the industrialized human microbiome. Cell 184(8):2053–2067 e2018. https://doi.org/10.1016/j.cell.2021.02.052

Hassan PA, Rana S, Verma G (2015) Making sense of Brownian motion: colloid characterization by dynamic light scattering. Langmuir 31(1):3–12. https://doi.org/10.1021/la501789z

Hirai K, Ousaka D, Fukushima Y, Kondo M, Eitoku T, Shigemitsu Y et al (2020) Cardiosphere-derived exosomal microRNAs for myocardial repair in pediatric dilated cardiomyopathy. Sci Transl Med 12(573). https://doi.org/10.1126/scitranslmed.abb3336

Hock A, Miyake H, Li B, Lee C, Ermini L, Koike Y et al (2017) Breast milk-derived exosomes promote intestinal epithelial cell growth. J Pediatr Surg 52(5):755–759. https://doi.org/10.1016/j.jpedsurg.2017.01.032

Hong J, Dauros-Singorenko P, Whitcombe A, Payne L, Blenkiron C, Phillips A, Swift S (2019) Analysis of the Escherichia coli extracellular vesicle proteome identifies markers of purity and culture conditions. J Extracell Vesicles 8(1):1632099. https://doi.org/10.1080/20013078.2019.1632099

Hood JL (2016) Post isolation modification of exosomes for nanomedicine applications. Nanomedicine 11(13):1745–1756. https://doi.org/10.2217/nnm-2016-0102

Hovhannisyan L, Czechowska E, Gutowska-Owsiak D (2021) The role of non-immune cell-derived extracellular vesicles in allergy. Front Immunol 12(3310). https://doi.org/10.3389/fimmu.2021.702381

Hu L, Wickline SA, Hood JL (2015) Magnetic resonance imaging of melanoma exosomes in lymph nodes. Magn Reson Med 74(1):266–271. https://doi.org/10.1002/mrm.25376

Jang SC, Gho YS (2014) Could bioengineered exosome-mimetic nanovesicles be an efficient strategy for the delivery of chemotherapeutics? Nanomedicine 9(2):177–180. https://doi.org/10.2217/nnm.13.206

Jarrige M, Frank E, Herardot E, Martineau S, Darle A, Benabides M et al (2021) The future of regenerative medicine: cell therapy using pluripotent stem cells and acellular therapies based on extracellular vesicles. Cells 10(2):240. https://doi.org/10.3390/cells10020240

Jeyaram A, Lamichhane TN, Wang S, Zou L, Dahal E, Kronstadt SM et al (2020) Enhanced loading of functional miRNA cargo via pH gradient modification of extracellular vesicles. Mol Ther 28(3):975–985. https://doi.org/10.1016/j.ymthe.2019.12.007

Jiang L, Driedonks T, Lowman M, Jong WSP, van den Berg van Saparoea HB, Dhakal S et al (2021). A bacterial extracellular vesicle-based intranasal vaccine against SARS-CoV-2. *bioRxiv*, 2021.2006.2028.450181. https://doi.org/10.1101/2021.06.28.450181

Johnstone RM, Adam M, Hammond JR, Orr L, Turbide C (1987) Vesicle formation during reticulocyte maturation. Association of plasma membrane activities with released vesicles (exosomes). J Biol Chem 262(19):9412–9420

Ju S, Mu J, Dokland T, Zhuang X, Wang Q, Jiang H et al (2013) Grape exosome-like nanoparticles induce intestinal stem cells and protect mice from DSS-induced colitis. Mol Ther 21(7): 1345–1357. https://doi.org/10.1038/mt.2013.64

Kalani A, Chaturvedi P, Kamat PK, Maldonado C, Bauer P, Joshua IG et al (2016) Curcumin-loaded embryonic stem cell exosomes restored neurovascular unit following ischemia-reperfusion injury. Int J Biochem Cell Biol 79:360–369. https://doi.org/10.1016/j.biocel.2016.09.002

Kalluri R, LeBleu VS (2020) The biology, function, and biomedical applications of exosomes. Science 367(6478):eaau6977. https://doi.org/10.1126/science.aau6977

Kim JH, Lee J, Park J, Gho YS (2015) Gram-negative and Gram-positive bacterial extracellular vesicles. Semin Cell Dev Biol 40:97–104. https://doi.org/10.1016/j.semcdb.2015.02.006

Klimentova J, Stulik J (2015) Methods of isolation and purification of outer membrane vesicles from gram-negative bacteria. Microbiol Res 170:1–9. https://doi.org/10.1016/j.micres.2014.09.006

Konoshenko MY, Lekchnov EA, Vlassov AV, Laktionov PP (2018) Isolation of extracellular vesicles: general methodologies and latest trends. Biomed Res Int 2018:8545347. https://doi.org/10.1155/2018/8545347

Lam SM, Zhang C, Wang Z, Ni Z, Zhang S, Yang S et al (2021) A multi-omics investigation of the composition and function of extracellular vesicles along the temporal trajectory of COVID-19. Nat Metab 3(7):909–922. https://doi.org/10.1038/s42255-021-00425-4

Lee E-Y, Choi D-S, Kim K-P, Gho YS (2008) Proteomics in gram-negative bacterial outer membrane vesicles. Mass Spectrom Rev 27(6):535–555. https://doi.org/10.1002/mas.20175

Lee EY, Choi DY, Kim DK, Kim JW, Park JO, Kim S et al (2009) Gram-positive bacteria produce membrane vesicles: proteomics-based characterization of Staphylococcus aureus-derived membrane vesicles. Proteomics 9(24):5425–5436. https://doi.org/10.1002/pmic.200900338

Lee J, Yoon YJ, Kim JH, Dinh NTH, Go G, Tae S et al (2018) Outer membrane vesicles derived from Escherichia coli regulate neutrophil migration by induction of endothelial IL-8. Front Microbiol 9:2268. https://doi.org/10.3389/fmicb.2018.02268

Liang G, Zhu Y, Ali DJ, Tian T, Xu H, Si K et al (2020) Engineered exosomes for targeted co-delivery of miR-21 inhibitor and chemotherapeutics to reverse drug resistance in colon cancer. J Nanobiotechnol 18(1):10–10. https://doi.org/10.1186/s12951-019-0563-2

Liu L, Zhou Q, Xie Y, Zuo L, Zhu F, Lu J (2017) Extracellular vesicles: novel vehicles in herpesvirus infection. Virol Sin 32(5):349–356. https://doi.org/10.1007/s12250-017-4073-9

Liu J, Cvirkaite-Krupovic V, Commere PH, Yang Y, Zhou F, Forterre P et al (2021) Archaeal extracellular vesicles are produced in an ESCRT-dependent manner and promote gene transfer and nutrient cycling in extreme environments. ISME J 15(10):2892–2905. https://doi.org/10.1038/s41396-021-00984-0

Lu M, Huang Y (2020) Bioinspired exosome-like therapeutics and delivery nanoplatforms. Biomaterials 242:119925. https://doi.org/10.1016/j.biomaterials.2020.119925

Lu Y, Zhou Y, Zhang R, Wen L, Wu K, Li Y et al (2019) Bone mesenchymal stem cell-derived extracellular vesicles promote recovery following spinal cord injury via improvement of the integrity of the blood-spinal cord barrier. Front Neurosci 13:209. https://doi.org/10.3389/fnins.2019.00209

Luan X, Sansanaphongpricha K, Myers I, Chen H, Yuan H, Sun D (2017) Engineering exosomes as refined biological nanoplatforms for drug delivery. Acta Pharmacol Sin 38(6):754–763. https://doi.org/10.1038/aps.2017.12

Luo Z, Ji Y, Gao H, Gomes Dos Reis FC, Bandyopadhyay G, Jin Z et al (2021) CRIg(+) macrophages prevent gut microbial DNA-containing extracellular vesicle-induced tissue inflammation and insulin resistance. Gastroenterology 160(3):863–874. https://doi.org/10.1053/j.gastro.2020.10.042

Machhi J, Shahjin F, Das S, Patel M, Abdelmoaty MM, Cohen JD et al (2021) A role for extracellular vesicles in SARS-CoV-2 therapeutics and prevention. J Neuroimmune Pharmacol 16(2):270–288. https://doi.org/10.1007/s11481-020-09981-0

Maestre-Carballa L, Lluesma Gomez M, Angla Navarro A, Garcia-Heredia I, Martinez-Hernandez-F, Martinez-Garcia M (2019) Insights into the antibiotic resistance dissemination in a wastewater effluent microbiome: bacteria, viruses and vesicles matter. Environ Microbiol 21(12):4582–4596. https://doi.org/10.1111/1462-2920.14758

Mashburn LM, Whiteley M (2005) Membrane vesicles traffic signals and facilitate group activities in a prokaryote. Nature 437(7057):422–425. https://doi.org/10.1038/nature03925

Mashburn-Warren LM, Whiteley M (2006) Special delivery: vesicle trafficking in prokaryotes. Mol Microbiol 61(4):839–846. https://doi.org/10.1111/j.1365-2958.2006.05272.x

Mathivanan S, Ji H, Simpson RJ (2010) Exosomes: extracellular organelles important in intercellular communication. J Proteomics 73(10):1907–1920. https://doi.org/10.1016/j.jprot.2010.06.006

Mause SF, Ritzel E, Liehn EA, Hristov M, Bidzhekov K, Müller-Newen G et al (2010) Platelet microparticles enhance the vasoregenerative potential of angiogenic early outgrowth cells after vascular injury. Circulation 122(5):495–506. https://doi.org/10.1161/circulationaha.109.909473

McBroom AJ, Kuehn MJ (2007) Release of outer membrane vesicles by Gram-negative bacteria is a novel envelope stress response. Mol Microbiol 63(2):545–558. https://doi.org/10.1111/j.1365-2958.2006.05522.x

Mencher A, Morales P, Valero E, Tronchoni J, Patil KR, Gonzalez R (2020) Proteomic characterization of extracellular vesicles produced by several wine yeast species. Microbial Biotechnol 13(5):1581–1596. https://doi.org/10.1111/1751-7915.13614

Monguio-Tortajada M, Galvez-Monton C, Bayes-Genis A, Roura S, Borras FE (2019) Extracellular vesicle isolation methods: rising impact of size-exclusion chromatography. Cell Mol Life Sci 76(12):2369–2382. https://doi.org/10.1007/s00018-019-03071-y

Morse MA, Garst J, Osada T, Khan S, Hobeika A, Clay TM et al (2005) A phase I study of dexosome immunotherapy in patients with advanced non-small cell lung cancer. J Transl Med 3(1):9. https://doi.org/10.1186/1479-5876-3-9

Ñahui Palomino RA, Vanpouille C, Laghi L, Parolin C, Melikov K, Backlund P et al (2019) Extracellular vesicles from symbiotic vaginal lactobacilli inhibit HIV-1 infection of human tissues. Nat Commun 10(1):5656. https://doi.org/10.1038/s41467-019-13468-9

Nasiri Kenari A, Kastaniegaard K, Greening DW, Shambrook M, Stensballe A, Cheng L, Hill AF (2019) Proteomic and post-translational modification profiling of exosome-mimetic nanovesicles compared to exosomes. Proteomics 19(8):1800161. https://doi.org/10.1002/pmic.201800161

Nolivos S, Cayron J, Dedieu A, Page A, Delolme F, Lesterlin C (2019) Role of AcrAB-TolC multidrug efflux pump in drug-resistance acquisition by plasmid transfer. Science 364(6442):778–782. https://doi.org/10.1126/science.aav6390

Oliveira DL, Nakayasu ES, Joffe LS, Guimaraes AJ, Sobreira TJ, Nosanchuk JD et al (2010) Characterization of yeast extracellular vesicles: evidence for the participation of different pathways of cellular traffic in vesicle biogenesis. PLos One 5(6):e11113. https://doi.org/10.1371/journal.pone.0011113

Orench-Rivera N, Kuehn MJ (2016) Environmentally controlled bacterial vesicle-mediated export. Cell Microbiol 18(11):1525–1536. https://doi.org/10.1111/cmi.12676

Osborn J, Pullan JE, Froberg J, Shreffler J, Gange KN, Molden T et al (2020) Echogenic exosomes as ultrasound contrast agents. Nanoscale Adv 2(8):3411–3422. https://doi.org/10.1039/D0NA00339E

Osteikoetxea X, Balogh A, Szabo-Taylor K, Nemeth A, Szabo TG, Paloczi K et al (2015) Improved characterization of EV preparations based on protein to lipid ratio and lipid properties. PLos One 10(3):e0121184. https://doi.org/10.1371/journal.pone.0121184

Pan BT, Johnstone RM (1983) Fate of the transferrin receptor during maturation of sheep reticulocytes in vitro: selective externalization of the receptor. Cell 33:967

Pan B-T, Teng K, Wu C, Adam M, Johnstone RM (1985) Electron microscopic evidence for externalization of the transferrin receptor in vesicular form in sheep reticulocytes. J Cell Biol 101:942–948

Panepinto J, Komperda K, Frases S, Park YD, Djordjevic JT, Casadevall A, Williamson PR (2009) Sec6-dependent sorting of fungal extracellular exosomes and laccase of Cryptococcus neoformans. Mol Microbiol 71(5):1165–1176. https://doi.org/10.1111/j.1365-2958.2008.06588.x

Park K-S, Svennerholm K, Crescitelli R, Lässer C, Gribonika I, Lötvall J (2021) Synthetic bacterial vesicles combined with tumour extracellular vesicles as cancer immunotherapy. J Extracell Vesicles 10(9):e12120. https://doi.org/10.1002/jev2.12120

Perez-Cruz C, Carrion O, Delgado L, Martinez G, Lopez-Iglesias C, Mercade E (2013) New type of outer membrane vesicle produced by the Gram-negative bacterium Shewanella vesiculosa M7 (T): implications for DNA content. Appl Environ Microbiol 79(6):1874–1881. https://doi.org/10.1128/aem.03657-12

Piacenza F, Biesemeier A, Farina M, Piva F, Jin X, Pavoni E et al (2018) Measuring zinc in biological nanovesicles by multiple analytical approaches. J Trace Elem Med Biol 48:58–66. https://doi.org/10.1016/j.jtemb.2018.03.010

Potschka M (1987) Universal calibration of gel permeation chromatography and determination of molecular shape in solution. Anal Biochem 162(1):47–64. https://doi.org/10.1016/0003-2697(87)90009-1

Poutsiaka DD, Schroder EW, Taylor DD, Levy EM, Black PH (1985) Membrane vesicles shed by murine melanoma cells selectively inhibit the expression of Ia antigen by macrophages. J Immunol 134(1):138–144

Qin Y, Zhang J, Avellan-Llaguno RD, Zhang X, Huang Q (2021) DEHP-elicited small extracellular vesicles miR-26a-5p promoted metastasis in nearby normal A549 cells. Environ Pollut 272:116005. https://doi.org/10.1016/j.envpol.2020.116005

Raposo G, Nijman HW, Stoorvogel W, Liejendekker R, Harding CV, Melief CJ, Geuze HJ (1996) B lymphocytes secrete antigen-presenting vesicles. J Exp Med 183(3):1161–1172. https://doi.org/10.1084/jem.183.3.1161

Reshi QUA, Hasan MM, Dissanayake K, Fazeli A (2021) Isolation of extracellular vesicles (EVs) using benchtop size exclusion chromatography (SEC) columns. Methods Mol Biol 2273:201–206. https://doi.org/10.1007/978-1-0716-1246-0_14

Reysenbach AL, Liu Y, Banta AB, Beveridge TJ, Kirshtein JD, Schouten S et al (2006) A ubiquitous thermoacidophilic archaeon from deep-sea hydrothermal vents. Nature 442(7101):444–447. https://doi.org/10.1038/nature04921

Rutter BD, Innes RW (2017) Extracellular vesicles isolated from the leaf apoplast carry stress-response proteins. Plant Physiol 173(1):728–741. https://doi.org/10.1104/pp.16.01253

Santos P, Almeida F (2021) Exosome-based vaccines: history, current state, and clinical trials. Front Immunol 12(2837):711565. https://doi.org/10.3389/fimmu.2021.711565

Shin K-O, Ha DH, Kim JO, Crumrine DA, Meyer JM, Wakefield JS et al (2020) Exosomes from human adipose tissue-derived mesenchymal stem cells promote epidermal barrier repair by inducing de novo synthesis of ceramides in atopic dermatitis. Cells 9(3):680. https://doi.org/10.3390/cells9030680

Shin S, Park YH, Jung S-H, Jang S-H, Kim MY, Lee JY, Chung Y-J (2021) Urinary exosome microRNA signatures as a noninvasive prognostic biomarker for prostate cancer. NPJ Genom Med 6(1):45–45. https://doi.org/10.1038/s41525-021-00212-w

Shpacovitch V, Hergenroder R (2018) Optical and surface plasmonic approaches to characterize extracellular vesicles. A review. Anal Chim Acta 1005:1–15. https://doi.org/10.1016/j.aca.2017.11.066

Shrivastava S, Ray RM, Holguin L, Echavarria L, Grepo N, Scott TA et al (2021) Exosome-mediated stable epigenetic repression of HIV-1. Nat Commun 12(1):5541. https://doi.org/10.1038/s41467-021-25839-2

Simpson RJ, Jensen SS, Lim JW (2008) Proteomic profiling of exosomes: current perspectives. Proteomics 8(19):4083–4099. https://doi.org/10.1002/pmic.200800109

Soler N, Forterre P (2020) Vesiduction: the fourth way of HGT. Environ Microbiol 22(7):2457–2460. https://doi.org/10.1111/1462-2920.15056

Song Y, Dou H, Li X, Zhao X, Li Y, Liu D et al (2017) Exosomal miR-146a Contributes to the Enhanced Therapeutic Efficacy of Interleukin-1β-Primed Mesenchymal Stem Cells Against Sepsis. Stem Cells 35(5):1208–1221. https://doi.org/10.1002/stem.2564

Stetefeld J, McKenna SA, Patel TR (2016) Dynamic light scattering: a practical guide and applications in biomedical sciences. Biophys Rev 8(4):409–427. https://doi.org/10.1007/s12551-016-0218-6

Sun D, Zhuang X, Xiang X, Liu Y, Zhang S, Liu C et al (2010) A novel nanoparticle drug delivery system: the anti-inflammatory activity of curcumin is enhanced when encapsulated in exosomes. Mol Ther 18(9):1606–1614. https://doi.org/10.1038/mt.2010.105

Szatanek R, Baj-Krzyworzeka M, Zimoch J, Lekka M, Siedlar M, Baran J (2017) The methods of choice for extracellular vesicles (EVs) characterization. Int J Mol Sci 18(6):1153. https://doi.org/10.3390/ijms18061153

Takov K, Yellon DM, Davidson SM (2019) Comparison of small extracellular vesicles isolated from plasma by ultracentrifugation or size-exclusion chromatography: yield, purity and functional potential. J Extracell Vesicles 8(1):1560809. https://doi.org/10.1080/20013078.2018.1560809

Tao SC, Guo SC, Zhang CQ (2017) Platelet-derived extracellular vesicles: an emerging therapeutic approach. Int J Biol Sci 13(7):828–834. https://doi.org/10.7150/ijbs.19776

Tao S-C, Rui B-Y, Wang Q-Y, Zhou D, Zhang Y, Guo S-C (2018) Extracellular vesicle-mimetic nanovesicles transport LncRNA-H19 as competing endogenous RNA for the treatment of diabetic wounds. Drug Deliv 25(1):241–255. https://doi.org/10.1080/10717544.2018.1425774

Theodoraki MN, Laban S, Jackson EK, Lotfi R, Schuler PJ, Brunner C et al (2021) Changes in circulating exosome molecular profiles following surgery/(chemo)radiotherapy: early detection of response in head and neck cancer patients. Br J Cancer 125(12):1677–1686. https://doi.org/10.1038/s41416-021-01567-8

Thery C, Amigorena S, Raposo G, Clayton A (2006) Isolation and characterization of exosomes from cell culture supernatants and biological fluids. Curr Protoc Cell Biol Chapter 3:Unit 3.22. https://doi.org/10.1002/0471143030.cb0322s30

Théry C, Witwer KW, Aikawa E, Alcaraz MJ, Anderson JD, Andriantsitohaina R et al (2018) Minimal information for studies of extracellular vesicles 2018 (MISEV2018): a position statement of the International Society for Extracellular Vesicles and update of the MISEV2014 guidelines. J Extracell Vesicles 7(1):1535750. https://doi.org/10.1080/20013078.2018.1535750

Thery C, Witwer KW, Aikawa E, Alcaraz MJ, Anderson JD, Andriantsitohaina R et al (2018) Minimal information for studies of extracellular vesicles 2018 (MISEV2018): a position statement of the International Society for Extracellular Vesicles and update of the MISEV2014 guidelines. J Extracell Vesicles 7(1):1535750. https://doi.org/10.1080/20013078.2018.1535750

Tian Y, Ma L, Gong M, Su G, Zhu S, Zhang W et al (2018) Protein Profiling and Sizing of Extracellular Vesicles from Colorectal Cancer Patients via Flow Cytometry. ACS Nano 12(1):671–680. https://doi.org/10.1021/acsnano.7b07782

Tian Y, Gong M, Hu Y, Liu H, Zhang W, Zhang M et al (2020) Quality and efficiency assessment of six extracellular vesicle isolation methods by nano-flow cytometry. J Extracell Vesicles 9(1):1697028. https://doi.org/10.1080/20013078.2019.1697028

Toyofuku M, Tashiro Y, Hasegawa Y, Kurosawa M, Nomura N (2015) Bacterial membrane vesicles, an overlooked environmental colloid: Biology, environmental perspectives and applications. Adv Colloid Interface Sci 226(Pt A):65–77. https://doi.org/10.1016/j.cis.2015.08.013

Toyofuku M, Carcamo-Oyarce G, Yamamoto T, Eisenstein F, Hsiao CC, Kurosawa M et al (2017) Prophage-triggered membrane vesicle formation through peptidoglycan damage in Bacillus subtilis. Nat Commun 8(1):481. https://doi.org/10.1038/s41467-017-00492-w

Toyofuku M, Nomura N, Eberl L (2019) Types and origins of bacterial membrane vesicles. Nat Rev Microbiol 17(1):13–24. https://doi.org/10.1038/s41579-018-0112-2

Trams EG, Lauter CJ, Norman Salem J, Heine U (1981) Exfoliation of membrane ecto-enzymes in the form of micro-vesicles. Biochim Biophys Acta 645(1):63–70

Tulkens J, De Wever O, Hendrix A (2020) Analyzing bacterial extracellular vesicles in human body fluids by orthogonal biophysical separation and biochemical characterization. Nat Protoc 15(1):40–67. https://doi.org/10.1038/s41596-019-0236-5

van den Berg van Saparoea HB, Houben D, Kuijl C, Luirink J, Jong WSP (2020) Combining protein ligation systems to expand the functionality of semi-synthetic outer membrane vesicle nanoparticles. Front Microbiol 11(890). https://doi.org/10.3389/fmicb.2020.00890

van der Meijden PEJ, Heemskerk JWM (2019) Platelet biology and functions: new concepts and clinical perspectives. Nat Rev Cardiol 16(3):166–179. https://doi.org/10.1038/s41569-018-0110-0

van der Pol E, Coumans FA, Grootemaat AE, Gardiner C, Sargent IL, Harrison P et al (2014) Particle size distribution of exosomes and microvesicles determined by transmission electron microscopy, flow cytometry, nanoparticle tracking analysis, and resistive pulse sensing. J Thromb Haemost 12(7):1182–1192. https://doi.org/10.1111/jth.12602

van Niel G, D'Angelo G, Raposo G (2018) Shedding light on the cell biology of extracellular vesicles. Nat Rev Mol Cell Biol 19(4):213–228. https://doi.org/10.1038/nrm.2017.125

Wang X, Thompson CD, Weidenmaier C, Lee JC (2018) Release of Staphylococcus aureus extracellular vesicles and their application as a vaccine platform. Nat Commun 9(1):1379. https://doi.org/10.1038/s41467-018-03847-z

Wang J, Chen D, Ho EA (2021a) Challenges in the development and establishment of exosome-based drug delivery systems. J Control Release 329:894–906. https://doi.org/10.1016/j.jconrel.2020.10.020

Wang M, Nie Y, Wu XL (2021b) Extracellular heme recycling and sharing across species by novel mycomembrane vesicles of a Gram-positive bacterium. ISME J 15(2):605–617. https://doi.org/10.1038/s41396-020-00800-1

Watanabe K (2016) Bacterial membrane vesicles (MVs): novel tools as nature- and nano-carriers for immunogenic antigen, enzyme support, and drug delivery. Appl Microbiol Biotechnol 100(23):9837–9843. https://doi.org/10.1007/s00253-016-7916-7

Wickner W, Schekman R (2005) Protein translocation across biological membranes. Science 310: 1452–1456

Willms E, Cabanas C, Mager I, Wood MJA, Vader P (2018) Extracellular vesicle heterogeneity: subpopulations, isolation techniques, and diverse functions in cancer progression. Front Immunol 9:738. https://doi.org/10.3389/fimmu.2018.00738

Woith E, Melzig MF (2019) Extracellular vesicles from fresh and dried plants-simultaneous purification and visualization using gel electrophoresis. Int J Mol Sci 20(2):357. https://doi.org/10.3390/ijms20020357

Wolf P (1967) The nature and significance of platelet products in human plasma. Br J Haematol 13: 269

Wolfers J, Lozier A, Raposo G, Regnault A, Théry C, Masurier C et al (2001) Tumor-derived exosomes are a source of shared tumor rejection antigens for CTL cross-priming. Nat Med 7(3): 297–303. https://doi.org/10.1038/85438

Xia X, Yuan P, Liu Y, Wang Y, Cao W, Zheng JC (2021) Emerging roles of extracellular vesicles in COVID-19, a double-edged sword? Immunology 163(4):416–430. https://doi.org/10.1111/imm.13329

Xin W, Qiang S, Jianing D, Jiaming L, Fangqi L, Bin C et al (2021) Human bone marrow mesenchymal stem cell-derived exosomes attenuate blood-spinal cord barrier disruption via the TIMP2/MMP pathway after acute spinal cord injury. Mol Neurobiol 58(12):6490–6504. https://doi.org/10.1007/s12035-021-02565-w

Yang B, Chen Y, Shi J (2019) Exosome biochemistry and advanced nanotechnology for next-generation theranostic platforms. Adv Mater 31(2):1802896. https://doi.org/10.1002/adma.201802896

Ye Y, Zhang X, Xie F, Xu B, Xie P, Yang T et al (2020) An engineered exosome for delivering sgRNA:Cas9 ribonucleoprotein complex and genome editing in recipient cells. Biomater Sci 8(10):2966–2976. https://doi.org/10.1039/D0BM00427H

Yu YJ, Wang XH, Fan GC (2018) Versatile effects of bacterium-released membrane vesicles on mammalian cells and infectious/inflammatory diseases. Acta Pharmacol Sin 39(4):514–533. https://doi.org/10.1038/aps.2017.82

Yu S, Zhao Z, Xu X, Li M, Li P (2019) Characterization of three different types of extracellular vesicles and their impact on bacterial growth. Food Chem 272:372–378. https://doi.org/10.1016/j.foodchem.2018.08.059

Zabeo D, Cvjetkovic A, Lasser C, Schorb M, Lotvall J, Hoog JL (2017) Exosomes purified from a single cell type have diverse morphology. J Extracell Vesicles 6(1):1329476. https://doi.org/10.1080/20013078.2017.1329476

Zhan Q, Yi K, Qi H, Li S, Li X, Wang Q, Wang Y, Liu C, Qiu M, Yuan X, Zhao J, Hou X, Kang C (2020) Engineering blood exosomes for tumor-targeting efficient gene/chemo combination therapy. Theranostics 10(17):7889–7905. https://doi.org/10.7150/thno.45028

Zhang H, Freitas D, Kim HS, Fabijanic K, Li Z, Chen H et al (2018) Identification of distinct nanoparticles and subsets of extracellular vesicles by asymmetric flow field-flow fractionation. Nat Cell Biol 20(3):332–343. https://doi.org/10.1038/s41556-018-0040-4

Zhang M, Yu Q, Tang W, Wu Y, Lv J, Sun L et al (2021) Epithelial exosomal contactin-1 promotes monocyte-derived dendritic cell–dominant T-cell responses in asthma. J Allergy Clin Immunol 48:1545. https://doi.org/10.1016/j.jaci.2021.04.025

Zonneveld MI, van Herwijnen MJC, Fernandez-Gutierrez MM, Giovanazzi A, de Groot AM, Kleinjan M et al (2021) Human milk extracellular vesicles target nodes in interconnected signalling pathways that enhance oral epithelial barrier function and dampen immune responses. J Extracell Vesicles 10(5):e12071. https://doi.org/10.1002/jev2.12071

林华 (2019) 大肠杆菌属*Nissle 1917*胞外囊泡蛋白组分析及其对鼠巨噬细胞功能的免疫调控作用. 西北农林科技大学