ABSTRACT

Nature remains a primary focus of scientific and technological research, particularly in nanotechnology, due to its remarkable properties. Nanotechnology has garnered significant interest in recent years. This review provides an up-to-date overview of the classification, characterization, methods of preparation, and applications of nanoparticles.[1, 2]

The initial section of the review offers insights into various techniques for synthesizing nanoparticles, encompassing both bottom-up and top-down approaches. Different methods for the synthesis of nanoparticles are discussed in detail, highlighting the importance of controlling shape, size, and composition to develop nanoparticles and enhance their properties. These properties include enhanced surface area, unique optical, electronic, and magnetic characteristics, and improved mechanical properties. Understanding these attributes is essential for effectively harnessing nanoparticles in different applications.[3]

A broad spectrum of applications for nanoparticles is also discussed. Additionally, nanoparticles have found applications in catalysis, environmental remediation, and antimicrobial coatings, contributing to sustainable development and environmental protection. Overall, nanoparticles represent a progressive area of research with tremendous potential for innovation and societal impact.

Our evaluation serves as a solid reference, assisting the scientific community in better comprehending the discussed topic by showing the role of each technique in a comparable manner. As the field of nanoparticles is constantly evolving, this review incorporates the latest research, developments, and advancements up to its publication. A comprehensive understanding of their properties, synthesis methods, and applications is crucial for future advancements in nanotechnology.[3-5]

keywords :- Nanoparticles; green synthesis; metal; microorganism; plant

INTRODUCTION

Background

Material researchers have spent the last 50 years investigating in great detail how to use nanoparticles and nanostructured materials in various fields. Exploiting the special characteristics of materials at the nanoscale is known as nanotechnology. Nanotechnology has taken center stage and has received massive attention over time, especially when technological advancements are discussed. Nanotechnologies have had a substantial impact on practically all areas of society and industries because they provide better-built, longer-lasting, safer, cleaner, and smarter products for medicine, daily life, agriculture, communications, and other industries. The term "Nanotechnology" has been incorporated into many disciplines, and it is rapidly evolving by producing nanoproducts with novel size-related physicochemical properties that distinguish them from larger matter. The primary goal of nanotechnology is to process, separate, consolidate, and deform materials with a single atom or molecule.

Nanotechnology has numerous applications. At the nanoscale, nanotechnology is related to the physical, chemical, biological, and engineering sciences[2]. Tools based on nanotechnology may be capable of identifying disease in very low amounts of tissue or cells[3]. Nanotechnology can potentially aid tissue reproduction and repair[4]. Medieval stained glass is one of history's most well-known examples of nanotechnology[5]. Nanotechnology's rapid advancement gives effective methods to apply this interesting technology in broad applications, such as biofuel synthesis. The use of various types of nanoparticles, particularly metallic ones, in biofuel production, like biohydrogen, biodiesel, bioethanol, and biogas, can enhance production efficiency and performance[6].[6, 7]

Nanoparticles are thought to be the foundation of nanotechnology. Methods for producing nanoparticles are constantly being researched and developed. Nature contains several types of nanoparticles, each with remarkable applications in their field. Nanoparticles include both nanocapsules and nanospheres. Nanospheres are a matrix system with uniform drug distribution, whereas nanocapsules are a system with the drug surrounded by a special polymeric membrane. Nanoparticles are the smallest microscopic or ultrafine particles; sizes range from 1 to 100 nm.

The unique properties of nanoparticles have already been utilized in a broad spectrum of potential uses, including biomedical devices, renewable energies, medicine, environmental remediation, antimicrobials, and biological sensor production.[8, 9]

Objectives

1. To investigate the methods and efficacy of liposomal encapsulation in drug delivery.
2. To explore the potential of nanoformulation techniques in improving the bioavailability of therapeutic agents.
3. To evaluate the combination of glutathione and repaglinide in a minitablet form within a capsule for enhanced therapeutic effects.

Significance

The research aims to contribute to the field of nanomedicine by providing insights into the optimization of drug delivery systems. Enhancing the bioavailability and efficacy of therapeutic agents through advanced encapsulation techniques can lead to better clinical outcomes, reduced side effects, and improved patient compliance. This study has the potential to impact various fields, including medicine, pharmacology, and biotechnology, by offering innovative solutions for drug delivery challenges.

Literature review

1. Ali, M. (2023). "What function of nanoparticles is the primary factor for their hyper-toxicity?" Adv Colloid Interface Sci **314**: 102881.

    a. Nanomaterials have applications in environmental protection, hygiene, medicine, agriculture, and the food industry due to their enhanced bio-efficacy/toxicity as science and technology have progressed, notably nanotechnology. The extension in the use of nanoparticles in day-to-day products and their excellent efficacy raises worries about safety concerns associated with their use. Therefore, to understand their safety concerns and find the remedy, it is imperative to understand the rationales for their enhanced toxicity at low concentrations to minimize their potential side effects. The worldwide literature quotes different nanoparticle functions responsible for their enhanced bio-efficacy/ toxicity. Since the literature on the comparative toxicity study of nanoparticles of different shapes and sizes having different other physic-chemical properties like surface areas, surface charge, solubility, etc., evident that the nanoparticle's toxicity is not followed the fashion according to their shape, size, surface area, surface charge, solubility, and other Physico-chemical properties. It raises the question then what function of nanoparticle is the primary factor for their hyper toxicity. Why do non-spherical and large-sized nanoparticles show the same or higher toxicity to the same or different cell line or test organism instead of having lower surface area, surface charge, larger size, etc., than their corresponding spherical and smaller-sized nanoparticles? Are these factors a secondary, not primary, factor for nanoparticles hyper-toxicity? If so, what function of nanoparticles is the primary function for their hyper-toxicity? Therefore, in this article, literature related to the comparative toxicity of nanoparticles was thoroughly studied, and a hypothesis is put forth to address the aforesaid question, that the number of atoms/ions/ molecules per nanoparticles is the primary function of nanoparticles toxicity.

2. Ashrafizadeh, H., et al. (2020). "Trace element nanoparticles improved diabetes mellitus; a brief report." Diabetes Metab Syndr **14**(4): 443-445.

    a. BACKGROUND: Diabetes mellitus is a chronic metabolic disease that induces several complications in various organs such as the liver, kidney, and reproductive system. Trace elements such as copper, zinc, selenium, and magnesium play an essential role in the management or treatment of diabetes mellitus. AIM: the aim of the present study was conducted to investigate the effect of these trace elements nanoparticles and their probable mechanism of action on diabetes and its complications. METHODS: The present brief report was conducted with a search of articles published in several databases including PubMed, ScienceDirect, Google Scholar, and Scopus. The articles were selected from 2011 to 2018 using the keywords "zinc," "copper," "selenium," "magnesium," and "diabetes." Following the eligibility criteria were selected 16 articles and 1 book. RESULTS: The scientific results of the presented brief report show that zinc, copper, selenium, and magnesium have antidiabetic effects. Also, they improved the diabetes-induced complications through increase antioxidant enzyme level, glucose utilization, and insulin sensitivity. CONCLUSION: While zinc, copper, selenium, and

magnesium revealed antidiabetic effects, but their nanoparticles were more potent for the treatment of this disease.

3. Baetke, S. C., et al. (2015). "Applications of nanoparticles for diagnosis and therapy of cancer." Br J Radiol **88**(1054): 20150207.

   a. During the last decades, a plethora of nanoparticles have been developed and evaluated and a real hype has been created around their potential application as diagnostic and therapeutic agents. Despite their suggestion as potential diagnostic agents, only a single diagnostic nanoparticle formulation, namely iron oxide nanoparticles, has found its way into clinical routine so far. This fact is primarily due to difficulties in achieving appropriate pharmacokinetic properties and a reproducible synthesis of monodispersed nanoparticles. Furthermore, concerns exist about their biodegradation, elimination and toxicity. The majority of nanoparticle formulations that are currently routinely used in the clinic are used for therapeutic purposes. These therapeutic nanoparticles aim to more efficiently deliver a (chemo-) therapeutic drug to the pathological site, while avoiding its accumulation in healthy organs and tissues, and are predominantly based on the "enhanced permeability and retention" (EPR) effect. Furthermore, based on their ability to integrate diagnostic and therapeutic entities within a single nanoparticle formulation, nanoparticles hold great promise for theranostic purposes and are considered to be highly useful for personalizing nanomedicine-based treatments. In this review article, we present applications of diagnostic and therapeutic nanoparticles, summarize frequently used non-invasive imaging techniques and describe the role of EPR in the accumulation of nanotheranostic formulations. In this context, the clinical potential of nanotheranostics and image-guided drug delivery for individualized and improved (chemo-) therapeutic interventions is addressed.

4. Chen, Y. and X. Feng (2022). "Gold nanoparticles for skin drug delivery." Int J Pharm **625**: 122122.

   a. Nanoparticle-based drug carriers are being pursued intensely to overcome the skin barrier and improve even hydrophilic or macromolecular drug delivery into or across the skin efficiently. Over the past few years, the application of gold nanoparticles as a novel kind of drug carrier for skin drug delivery has attracted increasing attention because of their unique properties and versatility. In this review, we summarized the possible factors contributing to the penetration behaviors of gold nanoparticles, including size, surface chemistry, and shape. Drug loading, release, and penetration patterns were captured towards implicating the design of gold nanoparticles for dermal or transdermal drug delivery. Physical methods applicable for future enhancing the delivery efficacy of GNPs were also presented, which mainly included microneedles and iontophoresis. As a promising "drug", the inherent activities of GNPs were finally discussed, especially regarding their application in the treatment of skin disease. Thus, this paper provided a comprehensive review of the use of gold nanoparticles for skin drug delivery, which would help the design of multifunctional systems for skin drug delivery based on gold nanoparticles.

5. Chibh, S., et al. (2022). "Cysteine-phenylalanine-derived self-assembled nanoparticles as glutathione-responsive drug-delivery systems in yeast." J Mater Chem B **10**(42): 8733-8743.

a. Despite the availability of different antifungal drugs in the market, their overall usefulness remains questionable due to the relatively high toxic profiles exerted by them in many cases. In addition, the emergence of drug resistance against these antifungal agents is a matter of concern. Thus, it becomes imperative to explore innovative drug-delivery vehicles to deliver these antifungal drugs for enhanced efficacy, mitigating unwanted side effects and tackling the surge in antifungal resistance. Considering this fact, in this piece of work, we have synthesized stimulus (glutathione)-responsive dipeptide-based self-assembled nanoparticles (NPs) to explore and establish the redox-responsive antifungal drug delivery of a relatively hydrophobic drug, terbinafine (Terb), in Saccharomyces cerevisiae (S. cerevisiae). The NPs were prepared using a relatively aqueous environment as opposed to other Terb formulations that are administered in mostly non-polar solvents and with limited biocompatibility. The NPs demonstrated an encapsulation efficiency of around 99% for Terb and resulted in complete inhibition of yeast-cell growth at a dose of 200 μg mL(-1) of the drug-loaded formulation. Thus, these biocompatible and aqueous dipeptide-based redox-responsive NPs can offer a promising drug-delivery platform to provide enhanced antifungal drug delivery with heightened efficacy and biocompatibility.

6. Dang, B. N., et al. (2024). "Nanoparticle-based immunoengineering strategies for enhancing cancer immunotherapy." J Control Release **365**: 773-800.

a. Cancer immunotherapy is a groundbreaking strategy that has revolutionized the field of oncology compared to other therapeutic strategies, such as surgery, chemotherapy, or radiotherapy. However, cancer complexity, tumor heterogeneity, and immune escape have become the main hurdles to the clinical application of immunotherapy. Moreover, conventional immunotherapies cause many harmful side effects owing to hyperreactivity in patients, long treatment durations and expensive cost. Nanotechnology is considered a transformative approach that enhances the potency of immunotherapy by capitalizing on the superior physicochemical properties of nanocarriers, creating highly targeted tissue delivery systems. These advantageous features include a substantial specific surface area, which enhances the interaction with the immune system. In addition, the capability to finely modify surface chemistry enables the achievement of controlled and sustained release properties. These advances have significantly increased the potential of immunotherapy, making it more powerful than ever before. In this review, we introduce recent nanocarriers for application in cancer immunotherapy based on strategies that target different main immune cells, including T cells, dendritic cells, natural killer cells, and tumor-associated macrophages. We also provide an overview of the role and significance of nanotechnology in cancer immunotherapy.

7. Ďúranová, H., et al. (2024). "Nanoparticle-plant interactions: Physico-chemical characteristics, application strategies, and transmission electron microscopy-based ultrastructural insights, with a focus on stereological research." Chemosphere **363**: 142772.

a. Ensuring global food security is pressing among challenges like population growth, climate change, soil degradation, and diminishing resources. Meeting the rising food demand while reducing agriculture's environmental impact requires innovative solutions. Nanotechnology, with its potential to revolutionize agriculture, offers novel approaches to these challenges. However, potential risks and regulatory aspects of nanoparticle (NP) utilization in agriculture must be considered to maximize their benefits for human health and the environment. Understanding NP-plant cell interactions is crucial for assessing risks of NP exposure and developing strategies to control NP uptake by treated plants. Insights into NP uptake mechanisms, distribution patterns, subcellular accumulation, and induced alterations in cellular architecture can be effectively drawn using transmission electron microscopy (TEM). TEM allows direct visualization of NPs within plant tissues/cells and their influence on organelles and subcellular structures at high resolution. Moreover, integrating TEM with stereological principles, which has not been previously utilized in NP-plant cell interaction assessments, provides a novel and quantitative framework to assess these interactions. Design-based stereology enhances TEM capability by enabling precise and unbiased quantification of three-dimensional structures from two-dimensional images. This combined approach offers comprehensive data on NP distribution, accumulation, and effects on cellular morphology, providing deeper insights into NP impact on plant physiology and health. This report highlights the efficient use of TEM, enhanced by stereology, in investigating diverse NP-plant tissue/cell interactions. This methodology facilitates detailed visualization of NPs and offers robust quantitative analysis, advancing our understanding of NP behavior in plant systems and their potential implications for agricultural sustainability.

8. Martínez-Esquivias, F., et al. (2021). "A Review of the Effects of Gold, Silver, Selenium, and Zinc Nanoparticles on Diabetes Mellitus in Murine Models." Mini Rev Med Chem **21**(14): 1798-1812.

    a. Diabetes mellitus is a disease that presents great challenges for healthcare systems worldwide, and the identification of alternative therapies for the treatment of this disease is of vital importance. Metallic nanoparticles (gold, silver, and selenium) and metallic oxide (ZnO) have been studied in different areas such as medicine, biotechnology, the environment, and the food industry with promising results. In medicine, current research has revealed these nanoparticles' anti-diabetic properties thanks to the implementation of animal models. This review will address the existing antecedents and the effects of gold, silver, selenium, and zinc oxide nanoparticles in diabetes administered alone, functionalized with other molecules, or combined with drugs that have shown promising therapeutic effects. The anti-diabetic effects of these nanoparticles are related to the regulation of glucose, insulin, and lipid profiles. In addition, oxidative stress markers, liver and kidney markers, the reduction of inflammation, apoptosis of the pancreas, and the restoration of normal liver and kidney histology are also reported in the literature after using these nanoparticles. However, the therapeutic effects that these nanoparticles provide are limited due to the lack of specific protocols dictated by international organizations to evaluate the risks of using these nanoparticles.

9. Nasirmoghadas, P., et al. (2021). "Nanoparticles in cancer immunotherapies: An innovative strategy." Biotechnol Prog **37**(2): e3070.

   a. Cancer has been one of the most significant causes of mortality, worldwide. Cancer immunotherapy has recently emerged as a competent, cancer-fighting clinical strategy. Nevertheless, due to the difficulty of such treatments, costs, and off-target adverse effects, the implementation of cancer immunotherapy described by the antigen-presenting cell (APC) vaccine and chimeric antigen receptor T cell therapy ex vivo in large clinical trials have been limited. Nowadays, the nanoparticles theranostic system as a promising target-based modality provides new opportunities to improve cancer immunotherapy difficulties and reduce their adverse effects. Meanwhile, the appropriate engineering of nanoparticles taking into consideration nanoparticle characteristics, such as, size, shape, and surface features, as well as the use of these physicochemical properties for suitable biological interactions, provides new possibilities for the application of nanoparticles in cancer immunotherapy. In this review article, we focus on the latest state-of-the-art nanoparticle-based antigen/adjuvant delivery vehicle strategies to professional APCs and engineering specific T lymphocyte required for improving the efficiency of tumor-specific immunotherapy.

10. Tang, K. S. (2019). "The current and future perspectives of zinc oxide nanoparticles in the treatment of diabetes mellitus." Life Sci **239**: 117011.

   a. Diabetes mellitus (DM) is a multifaceted and costly disease, which requires serious attention. Finding a cheaper anti-diabetic alternative that can act on multiple disease-related targets and pathways is the ultimate treatment goal for DM. Nanotechnology has offered some exciting possibilities in biomedical and drug delivery applications. Zinc oxide nanoparticles (ZnO-NPs), a novel agent to deliver zinc, have great implications in many disease therapies including DM. This review summarizes the pharmacological mechanisms by which ZnO-NPs alleviate DM and diabetic complications. Research implications and future perspectives were also discussed.

11. Vodyashkin, A., et al. (2024). "Promising biomedical systems based on copper nanoparticles: Synthesis, characterization, and applications." Colloids Surf B Biointerfaces **237**: 113861.

   a. Copper and copper oxide nanoparticles (CuNPs) have unique physicochemical properties that make them highly promising for biomedical applications. This review discusses the application of CuNPs in biomedicine, including diagnosis, therapy, and theranostics. Recent synthesis methods, with an emphasis on green approaches, are described, and the latest techniques for nanoparticle characterization are critically analyzed. CuNPs, including Cu(2)O, CuO, and Cu, have significant potential as anti-cancer agents, drug delivery systems, and photodynamic therapy enhancers, among other applications. While challenges such as ensuring biocompatibility and stability must be addressed, the state-of-the-art research reviewed here provides strong evidence for the

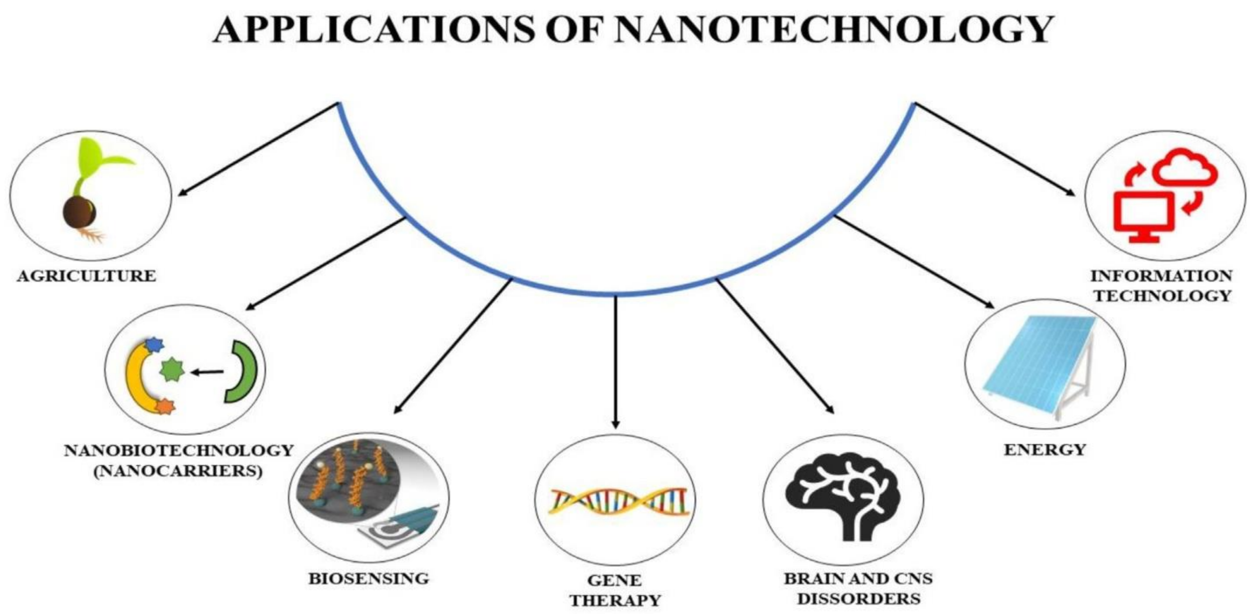


Fig. 1 Different applications of nanotechnology.[4, 10, 11]

Table 1 Classification of nanomaterials in different dimensions.[8, 9]

NANOMATERIAL	CLASSIFICATION	SIZE (DIAMETERS)
Zero Dimension	Fullerenes	0.5–1 nm
	Quantum dots	2–10 nm
	Atomic clusters	1–10 nm
One Dimension	Nanotubes	1–100 nm
	Fibers and filaments	<50 nm
Two Dimension	Nano discs	10–100 nm

NANOMATERIAL	CLASSIFICATION	SIZE (DIAMETERS)
	Nano lasers	<10 nm
Three Dimension	Clusters	1–10 nm
	Crystallites	1–100 nm

Classification of Nanomaterials

In Table 1, the classification of nanomaterials is based on the number of dimensions. Nanostructured materials are classified as:

- **Zero Dimensional (0D)**: These materials have all three dimensions at the nanoscale. Examples include fullerenes, quantum dots, and atomic clusters.
- **One-Dimensional (1D)**: These materials have one dimension outside the nanoscale. Examples include nanotubes and fibers/filaments.
- **Two-Dimensional (2D)**: These materials have two dimensions outside the nanoscale. Examples include nanodiscs and nano lasers.
- **Three-Dimensional (3D)**: These materials have all three dimensions outside the nanoscale. Examples include clusters and crystallites.

Nanomaterial Synthesis in Nanotechnology

Nanotechnology is fundamentally transforming the synthesis of materials and the manufacturing of devices. The synthesis of nanomaterials is a critical component of nanotechnology and nanoscience. During the synthesis process, several factors such as temperature, reactant concentrations, reaction time, and pH play significant roles in the nucleation and stabilization of nanoparticles.[7, 12]

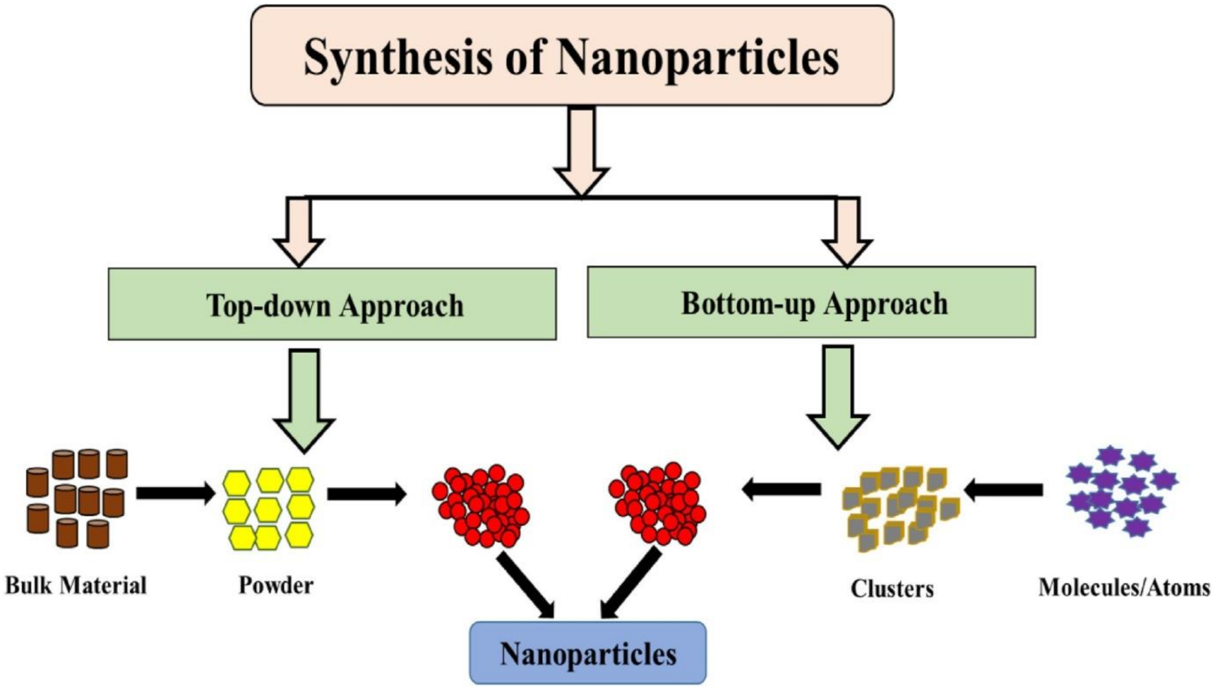


Fig. 2 Schematic representation of 'top-down approach' and 'bottom-up approach' for synthesis of nanoparticles.

Top-down Approach

A collection of fabrication technologies is referred to as a top-down approach that begins with a bulk block material that is the same as the base substrate. This route takes the bulk material and reduces it in size by using physical processes such as crushing, milling, or grinding to break up large particles. Top-down approaches are typically simpler, relying on bulk material elimination or bulk fabrication technique miniaturization to create the desired structure with the desired properties. This synthesis method is an improvement on those used to develop micron-sized particles.[13-16]

The flaws in the surface structure are the most significant issue with the top-down approach. For the fabrication of many man-made materials, the top-down approach is currently dominant in industry. Top-down approaches have primarily focused on attrition methods as well as more complex methods involving microfluidics and lithography. The semiconductor industry is a good example, where photolithography, a lithography-based process, is used to imprint features of MOSFETs (metal oxide semiconductor field effect transistors) onto a silicon wafer. Top-down approaches use larger initial structures that can be controlled externally during nanostructure processing; ball milling and plastic deformation are two examples. The major problem with the top-down approach is flaws in the surface structure. For instance, lithographic nanowires have a rough surface and may include several contaminants and structural flaws.[13-16]

- **Simplicity**: The top-down approach is relatively straightforward. It relies on the elimination or miniaturization of bulk material to achieve the desired structure and properties. This simplicity makes it a popular choice in various industrial applications.
- **Industrial Dominance**: This approach is widely used in industries, particularly for the fabrication of man-made materials. For example, the semiconductor industry employs photolithography, a lithography-based process, to imprint features of MOSFETs (metal oxide semiconductor field effect transistors) onto silicon wafers.
- **Techniques**: Common techniques in the top-down approach include attrition methods, microfluidics, and lithography. Attrition methods involve mechanical processes to break down materials, while microfluidics and lithography offer more precise control over the fabrication process.
- **Surface Flaws**: One of the main issues with the top-down approach is the presence of surface flaws. For instance, lithographic nanowires often have rough surfaces and may contain contaminants and structural defects. These flaws can affect the performance and reliability of the nanomaterials.

Bottom-up Approach

Bottom-up approaches include material component miniaturization, followed by a self-assembly process that results in the formation of nanostructures. The synthesis of nanosized materials is of great interest due to their distinct properties that differ from bulk materials. The bottom-up approach means building material from the ground up: molecule by molecule, atom by atom, or cluster by cluster. This method is more economical and has the potential to produce less waste.The bottom-up approach involves constructing a material from the smallest units, such as atoms, molecules, or clusters and is frequently employed in the production of nanoscale materials. The process allows for the creation of uniform shapes, sizes, and distributions in many nanoscale materials.[17-20]

This approach is employed in the continuous synthesis of inorganic nanoparticles, which involves using a wet chemical technique. By rapidly mixing two precursor solutions, it is possible to achieve a narrow particle size distribution for various inorganic nanoparticles, including zinc oxide, magnetite, and brushite. Titanium dioxide (TiO_2) nanoparticles were synthesized using a bottom-up hydrolytic sol-gel synthesis and evaluated using green metrics with two different approaches, namely Life Cycle Assessment (LCA) methodology and Environmental Assessment Tool for Organic Syntheses (EATOS) software. The bottom-up approach's main concern is surface layer adhesion to the base substrate.[21]

Bottom-up techniques are well-known for the preparation of luminescent nanoparticles. Bottom-up nanofabrication pushes the limits of miniaturization, provides virtually limitless opportunities for the fabrication and design of functional nanostructured materials, and has the potential to be considerably more cost-effective than top-down nanofabrication.

- **Material Miniaturization**: The bottom-up approach starts at the molecular or atomic level and builds up to form nanostructures. This method allows for precise control over the composition and structure of the nanomaterials.
- **Uniformity**: One of the significant advantages of the bottom-up approach is the ability to create uniform shapes, sizes, and distributions in nanoscale materials. This uniformity is crucial for applications that require consistent performance and properties.
- **Cost-Effectiveness**: The bottom-up approach is generally more economical and produces less waste compared to the top-down method. By building materials from the ground up, this approach minimizes material loss and reduces the environmental impact.
- **Techniques**: Common techniques in the bottom-up approach include wet chemical methods, such as rapidly mixing precursor solutions to achieve a narrow particle size

distribution. For example, titanium dioxide (TiO_2) nanoparticles can be synthesized using a hydrolytic sol-gel method. This method involves the hydrolysis and condensation of precursors to form a gel, which is then dried and calcined to produce nanoparticles.

- **Surface Adhesion**: A primary concern with the bottom-up approach is the adhesion of the surface layer to the base substrate. Ensuring strong adhesion is essential for the stability and functionality of the nanomaterials.
- **Applications**: Bottom-up techniques are well-known for preparing luminescent nanoparticles and pushing the limits of miniaturization. These techniques offer virtually limitless opportunities for the fabrication and design of functional nanostructured materials.[22-24]

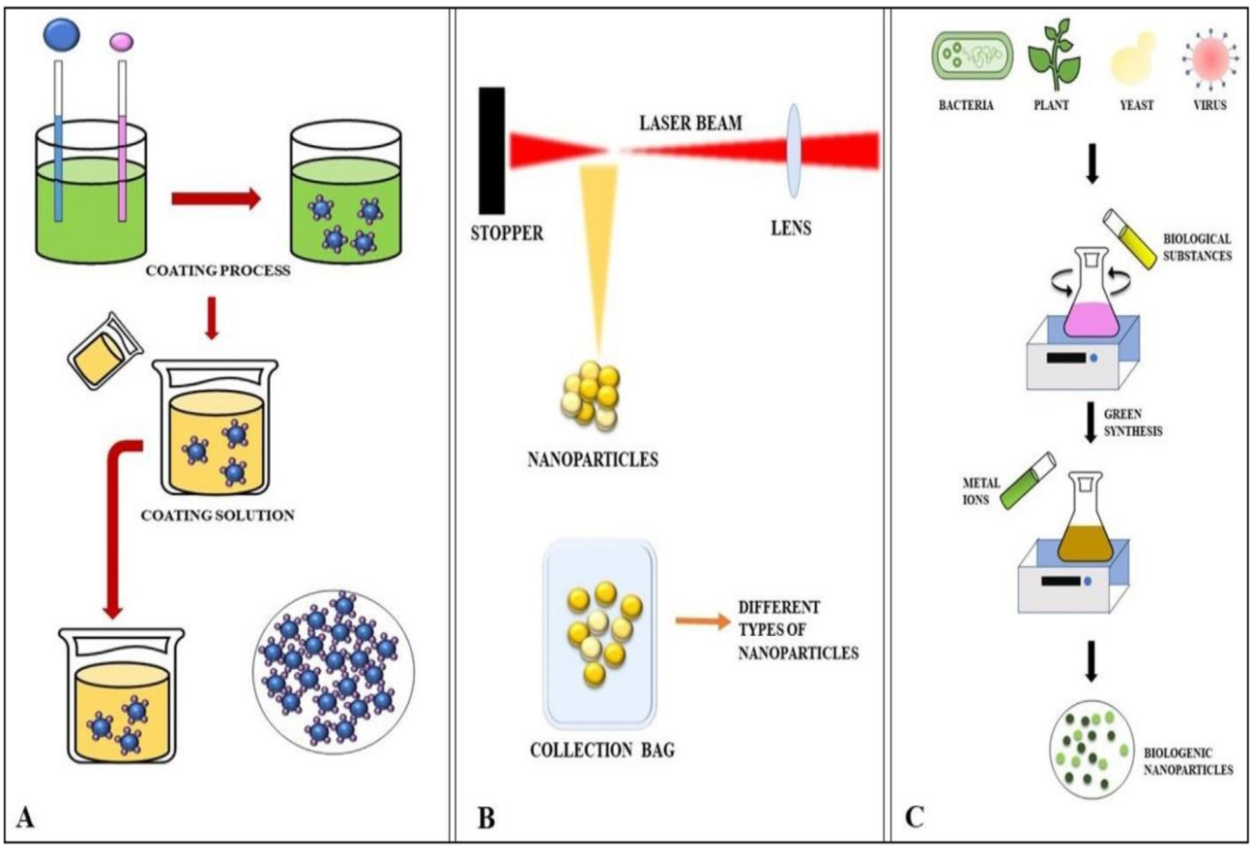


Fig. 3 Methods of synthesis of Nanoparticles (A) Chemical synthesis by the means of reduction/precipitation reactions (B) Physical synthesis of nanoparticles, and (C) Biological synthesis utilizing microorganisms or plant extracts as reducing agents.

Different Methods for Synthesis of Nanoparticles

Various chemical, physical, and biological techniques are presently accessible to create different varieties of nanoparticles. Though chemical and physical methods are more commonly used for nanoparticle synthesis, their applications are limited due to the use of toxic compounds and yields. Because of the simplicity and versatility of the procedures, the development of environmentally safe biogenetic production methods is becoming more popular. Nanoparticles' distinctive physical, chemical, and biological properties make them ideal for a variety of applications in various industries and biomedical sectors. Various techniques are involved in the synthesis of nanoparticles.

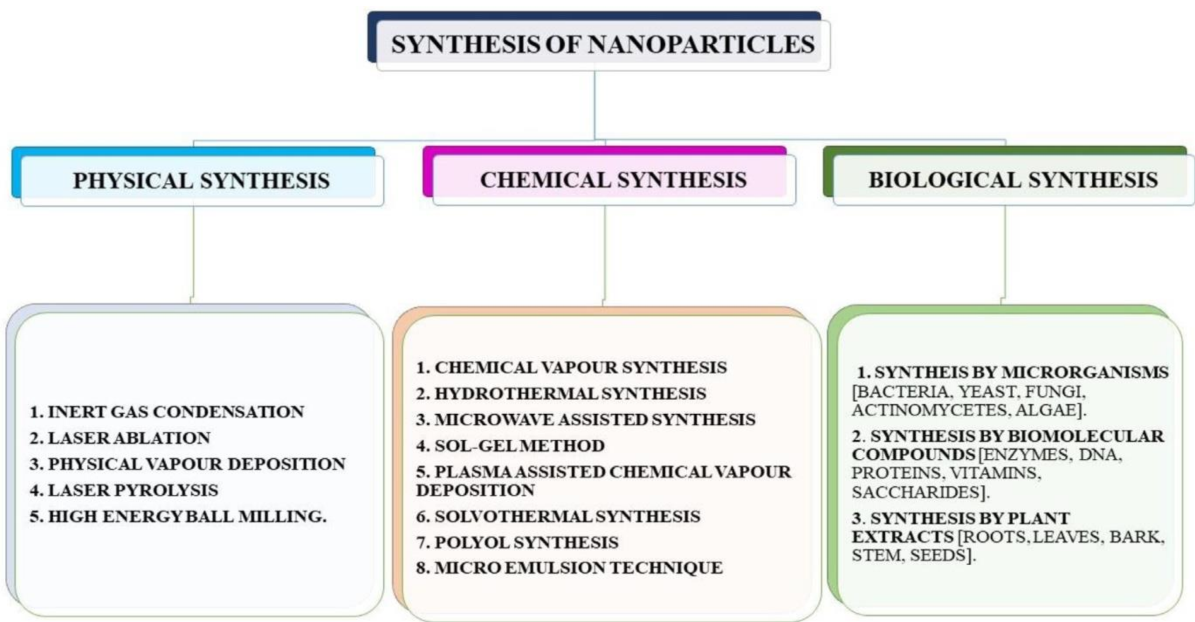


Fig. 4 Various techniques for synthesis of Nanoparticles.

4.1 Physical Methods of Nanoparticle Synthesis

Nanoparticles have traditionally been produced using physical methods, which utilize thermal energy, high-energy radiation, and mechanical pressure to cause material condensation, evaporation, abrasion, or melting. Physical methods are superior to chemical approaches in terms of solvent contamination absence in thin films and nanoparticle distribution homogeneity. Physical methods employ a top-down approach, are solvent-free, and yield consistent monodisperse nanoparticles. Laser ablation, laser pyrolysis, physical vapor deposition, high-energy ball milling, and inert gas condensation are among the physical methods commonly used to generate nanoparticles[7, 10, 17, 18, 20, 23, 25, 26]

4.2 Chemical Methods of Nanoparticle Synthesis

The chemical method uses inorganic and organic reducing agents for the synthesis of nanoparticles. Reducing agents reduce ions, resulting in metal formation and agglomeration into oligomeric clusters. Metallic colloidal particles are formed as a result of these clusters. It is critical to utilize protective agents during the preparation of metal nanoparticles to stabilize dispersive nanoparticles. Nanoparticle surfaces can absorb or bind protective agents, preventing agglomeration. Polyethylene glycol (PEG), polymethylmethacrylate (PMMA), Polyvinyl pyrrolidone (PVP), and Poly (methacrylic acid) (PMAA) have all been widely used as protective agents. The protective agent prevents the nanoparticles from clumping together. Chemical methods used to create nanoparticles include microwave-assisted synthesis, hydrothermal synthesis, polyol synthesis, microemulsion technique, solvothermal synthesis, sol-gel method, plasma, and chemical vapors synthesis. These methods are classified as bottom-up nanoparticle synthesis. .[23-31]

Physical Methods of Nanoparticle Synthesis[7, 10, 17, 18, 20, 23, 25, 26]	**Chemical Methods of Nanoparticle Synthesis[1, 3, 5, 8, 9, 12, 13, 17, 18, 23-38]**
Inert Gas Condensation (IGC)	**Chemical Vapors Synthesis**
Laser Ablation	**Hydrothermal Synthesis**
Physical Vapors Deposition (PVD)	**Microwave Assisted Synthesis**
Laser Pyrolysis	**Sol-Gel Method**
High Energy Ball Milling (HEBM)	**Polyol Synthesis**

4.3. Biological Methods of Nanoparticle Synthesis

Even though physical and chemical methods are efficient in creating well-defined nanoparticles, they have some drawbacks, including a long synthesis time, higher production costs, difficulty in purification, as well as the discharge of dangerous by-products. Chemical synthesis techniques can also contribute to the appearance of hazardous chemical species that have been adsorbed, which can have negative consequences in medical applications. Green synthesis methods have advantages over traditional methods that use chemical agents which are toxic to the environment. Nanoparticles are synthesized by biological entities both intracellularly and extracellularly. A living system's ability to remodel inorganic metal ions into nanoparticles using its inherent organic chemistry processes has revealed a previously unknown area of biochemical analysis. The combination of nanotechnology and biology results in nanobiotechnology, which is an advanced field comprising living entities of both eukaryotic and prokaryotic origin. The nanoparticle biosynthesis technique follows the bottom-up method which involves the primary reaction (oxidation/reduction). To create metal and metal-oxide nanoparticles, these methods use biological systems such as fungi, actinomycetes, bacteria, viruses, yeast, biomolecules, different plant-based extracts, and so on. [13, 22, 23, 25, 27, 28, 32, 36, 37, 39-44]

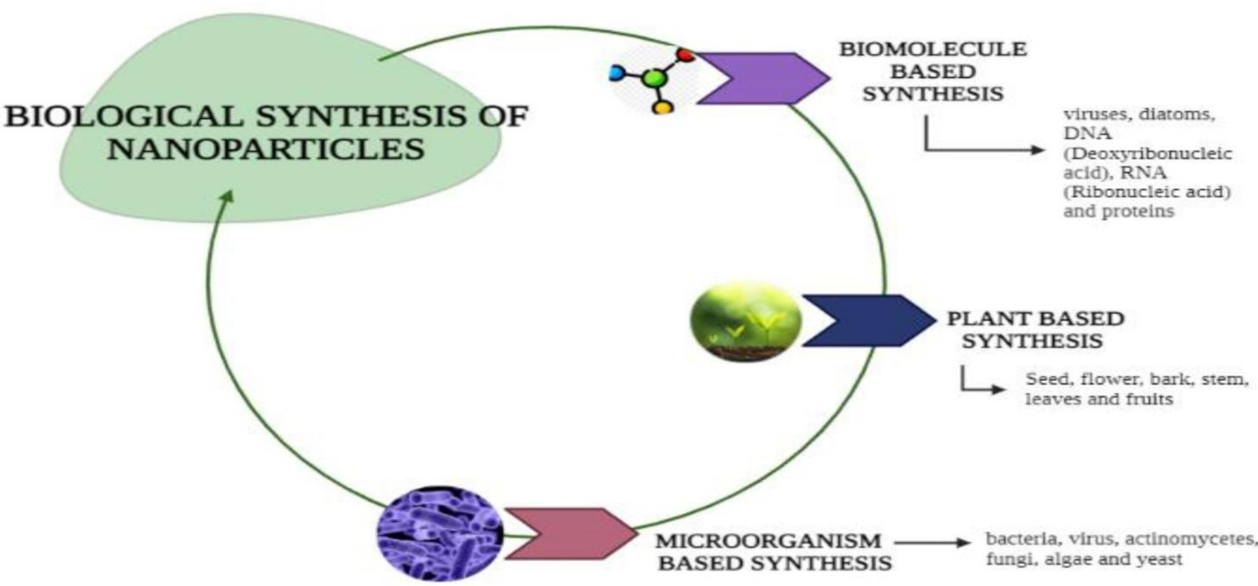


Fig. 5 Different biological synthesis of nanoparticles.

Biological methods of nanoparticle synthesis can be generally categorized into different categories:

1. **Biomolecules based synthesis**
2. **Microorganisms based synthesis**
3. **Plants based synthesis**

4.3.1. Biological Synthesis of Nanoparticles Using Biomolecules

Biomolecules are sophisticated nanostructures, programmed by sequence information and adapted by evolution. Viruses, diatoms, DNA, RNA, and proteins are all powerful tools that are used as blueprints (templates) for the synthesis of nanoparticles. Actin filaments serve as a template for nanowire formation. DNA is regarded as an admirable biomolecular template and a promising candidate with a strong affinity for transition metal ions. The amino acid functional groups found in molecular enzymes can function as reducing agents for metal nanoparticle synthesis, while the remaining polypeptide chain may help to stabilize the nanoparticles.

Many biological complexes function as actual systems and equipment for nanotechnology. Additionally, DNA can be used for peptide fibers and protein for the nanoparticle's synthesis. Different researchers have reported that DNA is used as templates or organic scaffolds to synthesize a wide range of nanoparticles and nanoparticle assemblies. Because of their

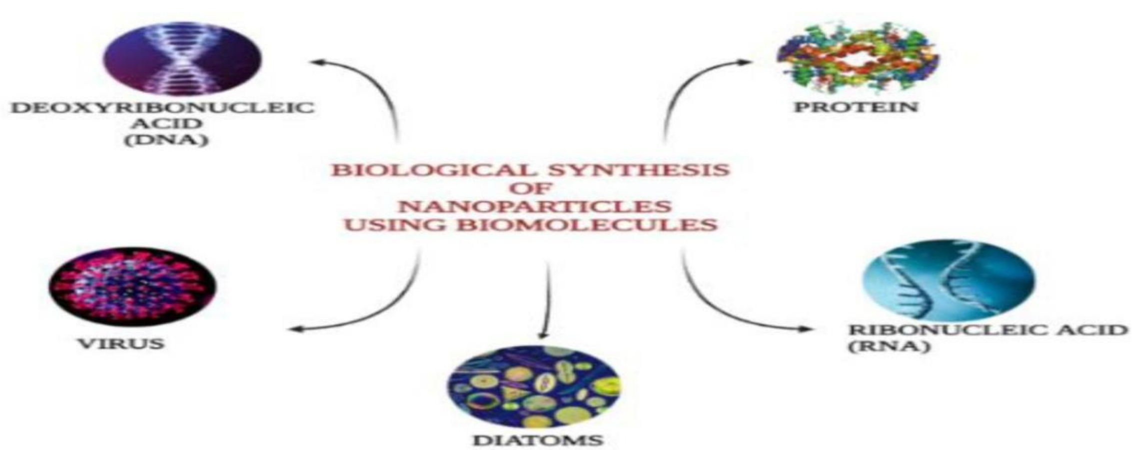


Fig. 6 Biomolecules mediated synthesis of nanoparticles.

biocompatibility, water solubility, and potential applications, lipid bilayer nanomaterials are being modified such as carbon nanotubes, semiconductor quantum dots, and silica nanoparticles.

Researchers focus on noble metal synthesized nanoparticles. Using double-stranded DNA (dsDNA) as a template, researchers present an easy and universal process for producing metal-graphene oxide (GO) heterostructures with controlled nanoparticle size and shape. DNA-directed silver (Ag) nanoparticles (NPs) were successfully synthesized and these composites decrease Xanthomonas perforans cell viability in culture and on plants. A multifunctional and biocompatible nano platform called DNA aptamer-conjugated magnetic graphene oxide (Apt@MGO) was created by researchers to selectively and quickly eradicate MRSA (Methicillin-resistant Staphylococcus aureus). According to an in vitro study, Apt@MGO is a targeted, biocompatible, and light-activated photothermal agent that effectively and quickly kills MRSA in the aggregated condition when exposed to NIR light. [5, 9, 17, 22, 25, 26, 31, 32, 34, 45, 46]

4.3.2. Biological Synthesis of Nanoparticles Using Microorganisms

Microbes are small organisms that include bacteria, fungi, and viruses. Some microorganisms can survive on metal ions and grow in a variety of environments due to their resistance. A green chemistry method that combines nanotechnology and microbial biotechnology is called microbial nanoparticle synthesis. Biosynthesis of tellurium, platinum, alloy of gold-silver, silver, zirconia, titanium, palladium, silica, quantum dots, uraninite, magnetite, and gold nanoparticles has been discovered by bacteria, actinomycetes, fungi, yeasts, and viruses. Microbial NP synthesis has combined several disciplines, including biotechnology, microbiology, and nanotechnology, to form a new field known as nanobiotechnology. Metal nanoparticle synthesis in bacteria is dependent on the localization of the cell’s reductive components. Extracellular nanoparticle production has broader applications in optoelectronics, bioimaging, sensor technology, and electronics than intracellular accumulation. Bacteria, viruses, fungi, algae, yeast, and actinomycetes are all commonly used as bioreactors in the synthesis of nanoparticles.

Bacteria: Bacteria are unicellular organisms growing very quickly in warm, moist environments. Many bacteria are capable of producing nanoparticles such as silver NPs, zinc oxide NPs, gold NPs, magnesium NPs, arsenic NPs, iron oxide NPs, and so on. To reduce interacting metal ions, bacteria use a variety of anionic functional groups, reducing sugars, proteins, enzymes, and other bacterial biomass components. Nanoparticles are manufactured using gram-positive bacteria as well as gram-negative bacteria. Gram-positive bacteria enclose in a cell wall rich in anionic functional groups, and the cell wall consists of peptidoglycan, and various acids including lipoteichoic and teichoic, different polysaccharides, and various proteins serving as a site for subsequent reduction and cation biosorption. The use of cultural supernatants in the synthesis of metallic nanoparticles of Ag of Enterobacter cloacae, Escherichia coli, and Klebsiella pneumonia. The metal ions majority show toxic behavior towards bacteria, to overcome the hazardous nature of the ions bacteria developed a defense system to counteract such toxicity, and ion reduction is one such mechanism. Vaidyanathan et al. synthesized nanoparticles using Bacillus licheniformis, which secretes NADPH and NADPH-dependent enzymes, and one such example is nitrate reductase, which successfully transforms Ag+ to Ag0. Ag-NPs produced non-enzymatically using bacterial bio-matrix as a reducing and capping agent were described. Silver nanoparticles synthesized from Saccharomyces cerevisiae, Bacillus subtilis, and E. coli and studied their antimicrobial effects against different pathogens and anticancer activity on the MCF-7 cell line. Bacteria are an extremely important tool for nanoparticle synthesis due to their diversity and excellent ability for adaptability toward extreme environmental conditions. In the literature, various research regarding NPs synthesized biologically using bacteria have been reported, including elementary compounds and substances. Therefore, using bacteria as nano-factories might offer a novel approach to metal or metalloid ion removal and fabrication of materials with unique characteristics.[22]

Fungus: Several fungi have been used as novel tools for the extracellular and intracellular development of nanoparticles. The fungal-mediated green chemistry method for NPs synthesis has several benefits, which include economic viability, higher bioaccumulation, and a method for synthesis that is easily scalable due to easy downstream processing and biomass handling. Fungi, as opposed to bacteria, can produce more nanoparticles due to increased protein secretion, which directly translates to increased nanoparticle productivity. Most fungi have a wide range of growth for sodium chloride, pH, and temperature, making changes in culture conditions to produce homogeneous nanoparticles possible.

Fig. 7 Variety of microorganisms used for synthesis of nanoparticles.

Additionally, numerous investigations have shown that extracellular myco-synthesis nanoparticles of silver via Ag+ ion reduction using the genus Aspergillus which includes a variety of species, such as Aspergillus niger, Aspergillus flavus, Aspergillus terreus, and A. fumigatus. The synthesis of Ag nanoparticles biologically via Aspergillus terreus has also been reported, and the proposed mechanism is an NADH (nicotinamide adenine dinucleotide (NAD) + hydrogen (H)) dependent enzyme catalyzed extracellular reaction process. Several other reports on the biosynthesis of Ag NPs using diverse species of fungus are available which also include Bryophilous Rhizoctonia, A. flavus, Pleurotus ostreatus, etc. It has been reported that metallic nanoparticles are produced by various Fusarium species for intra and extracellular silver nanoparticles. To create metallic nanoparticles, some filamentous fungi such as Penicillium were also studied. For this reason, various studies have been performed using species of Penicillium such as Penicillium brevicompactum, Penicillium fellutanum, Penicillium sp., Penicillium citrinum, and Penicillium Sangiovese. Fungi can generate a substantial number of extracellular enzymes including glucanases, chitinases, glycosyl hydrolases, xylanases, mannanases, cellulases, and proteases under the right conditions. Fusarium solani, an endophytic fungus used for the synthesis of gold nanoparticles was isolated from the Chonemorpha fragrans plant. The synthesized gold nanoparticles showed cytotoxic activity against different cancer cells.

Yeast: Single-celled eukaryotes belonging to the fungus kingdom. For biomineralization, yeast cells serve as a template, the primary mechanism for the NPs formation such as Au NPs using Thermomonospora fusca, Thermomonospora curvata, and Thermomonospora chromogena species. Yarrowia lipolytica was also used for the production of gold NPs. Researchers showed the relevance of Hanensula anomala species in reducing gold salt-generating AuNPs. It has also been reported that yeast can be used to make PbS and Cd nanoparticles using Candida glabrata and Rhodosporidium diobovatum species. BDU-XR1 yeast strain isolated from yogurt (spontaneous) synthesizes Ag-NPs in Azerbaijan. Depending on the preparation methods, Ag-NPs were produced inside the cells and in the cell wall. Transcriptome analysis using RNAseq in yeast cells treated with spherical citrate-coated silver NPs revealed[22]

Actinomycetes: Actinomycetes are microorganisms that resemble fungi and bacteria. The thermomonospora sp. is used for the biosynthesis of Au-nanoparticles. Au-nanoparticles were synthesized intracellularly by using alkali-tolerant rhodoscoccus sp. The cytoplasmic membrane contained more nanoparticles than the cell wall, according to the research. Actinomycetes have gotten a lot of attention because they are underutilized and could be a good candidate for metal nanoparticle synthesis. Due to their saprophytic behavior, actinomycetes are recognized as superior groups among commercially significant microbial species. Actinobacteria have successfully reported the biological synthesis of metallic nanoparticles, and as a result, actinomycetes have been considered for NP synthesis.[23, 32]

Algae: A diverse group of plants that is being researched for its potential applications in nanotechnology. In 2019, Sharma et al. reported Platinum nanoparticles (PtNPs) derived from S. myriocystum and employed as biosensors to measure the level of adrenaline in the human body. Hormone-based drug Adrenaline is used to treat asthma, allergies, and heart attacks. Gracilaria edulis was used for the synthesis of silver and zinc oxide nanoparticles. Brown algae were used for the biological synthesis of TiO2NPs and ZnO-NPs. Another study used S. muticum to synthesize ZnONPs. Ag-NPs derived from the Ulva latica (green algae) and Hypnea musciformis (the red algae) have shown inhibition of growth in fungal strains such as A. niger, Candida parasitosis, and Candida albicans. Likewise, Au-NPs and Ag-NPs were synthesized from Neodesmuspupukensis and tested for antifungal activity. When compared to cyanobacterial extract, the Ag-NPs synthesized from Microchaeta demonstrated superior de-colorization capability counter-to dyes like ‘methyl red azo’. In a recent study, it was discovered that Chlorella ellipsoidea-mediated biomatrix-loaded Ag-NPs had high photocatalytic activity for the destruction of the harmful pollutant colors methylene orange and blue.[44]

Biological Synthesis of Nanoparticles Using Plants: A diverse array of phytochemical constituents is present in plants and are thus used in the pharmaceutical industry, indirectly or directly. Plants have various applications other than acting as medicines, such as food supplements and nutraceuticals. The medicinal properties of plants have been known since human civilization started. The findings of the medical efficacy of plants have already been tried by ethnopharmacologists, botanists, microbiologists, and natural-product chemists. Plants, in particular, secrete functionally active biomolecules, reducing metal ions, and making biological nanoparticle synthesis biocompatible. Plants contain phytochemicals and various metabolites. Plants are used to make nanoparticles because they are spontaneous, inexpensive, and have a single-step biosynthesis process. Several plants and their different parts are used for the bio-synthesis of nanoparticles. Many different plant extracts have been employed as precursors in the creation of nanoparticles (NPs) with potential applications. Certain plants have been identified as hyperaccumulators because they accumulate higher concentrations of metals than other sources. Quinines, organic acids, and flavones are the primary water-soluble phytochemicals responsible for immediate reduction. Tannic acid, a polyphenolic compound present in different plants, can be used as a functional stabilization of nanoparticles, especially for gold nanoparticles. Researchers synthesized silver nanoparticles using ellagic acid-rich berry extracts and investigated their antimicrobial properties towards model dental pathogens C. albicans and Enterococcus faecalis with potential mechanisms. Recently, research on the synthesis of ZnONPs has utilized plants like Zanthoxylum armatum. In 2020, Chauhan et al. studied cannabis sativa for its uses as a reducing and stabilizing agent in the synthesis of nanoparticles. The use of anthocyanin-rich red cabbage extract (RCE) with its antimicrobial and antioxidant capabilities for the synthesis of stable iron oxide (Fe3O4) NPs. The Fe3O4 NPs displayed antimicrobial and antioxidant properties along with greater stability.[1, 5, 11, 12, 22, 25, 26, 28, 30, 31, 36, 39, 42, 43, 46-49]

Copper oxide nanoparticles (CuO-NPs) were created using two methods: green synthesis (CuO(G)-NPs) and microwave irradiation (CuO(M)-NPs) using Z. armatum plant extract. The silver-doped zinc oxide nanoparticles (AgZnO) were fabricated using the seed extract of Moringa oleifera. Cannabis sativa was also used in a green route for the synthesis of Cu, Mg, and Ag doping nanoparticles. Aqueous extracts of three different Sideritis species; S. brevidens (SB), Sideritis argyrea (SA), and S. lycia (SL) were used to create silver nanoparticles (AgNPs). The cholinesterase (BChE: butyrylcholinesterase and AChE: acetylcholinesterase) and tyrosinase activities were also checked. Utilizing plants for the synthesis of nanoparticles has the benefit of being convenient, handled easily, and containing a variety of metabolites that may abet in reduction. Many natural biomolecules in plants play a crucial role in the bio-reduction, formation, capping, and stabilization of NPs.[2, 26, 34, 50]

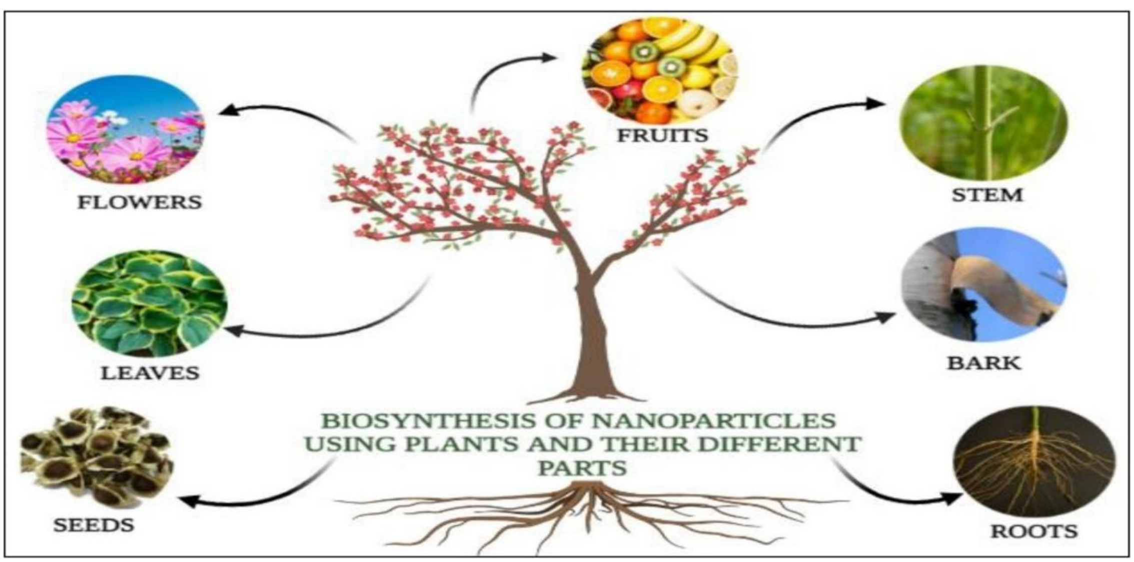


Fig. 8 Plant-mediated synthesis of nanoparticles.[18, 26, 31, 32]

Characterization Techniques for Synthesized Nanoparticles

The expansion of nanotechnology in numerous research fields has necessitated the use of analytical techniques for nanoparticle analysis and characterization. Nanoparticle characterization is a critical step in understanding the reaction mechanism and its applications. UV-Vis spectroscopy, X-ray diffraction (XRD), scanning electron microscopy (SEM), Brunauer-Emmett-Teller (BET), and transmission electron microscopy (TEM) are all generally used techniques for the characterization of nanoparticles. These techniques are useful for determining nanoparticles' shape, size, crystallinity, and surface area. The following analytical tools are used to characterize synthesized nanomaterials in detail:

Ultraviolet-Visible Spectroscopy Analysis: UV-Vis spectroscopy is a relatively simple and inexpensive characterization technique frequently used for the study of nanomaterials. It measures the intensity of light reflection from a sample and contrasts it with the light reflection intensity from a reference material. The optical absorbance spectra are measured to indicate nanoparticle production. UV-Vis spectroscopy provides information about the transmission and absorption properties of the sample. Nanoparticles have optical properties that are sensitive to concentration, shape, size, agglomeration state, and refractive index close to the nanoparticle surface. UV-Vis spectroscopy is an important tool to characterize, investigate, and identify these materials as well as assess the stability of nanoparticle colloidal solutions.[18, 26, 31, 32]

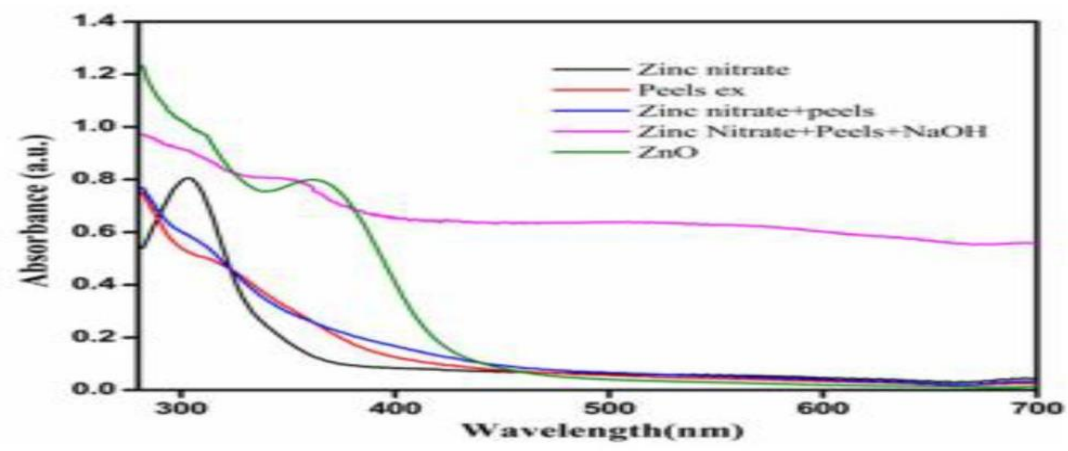
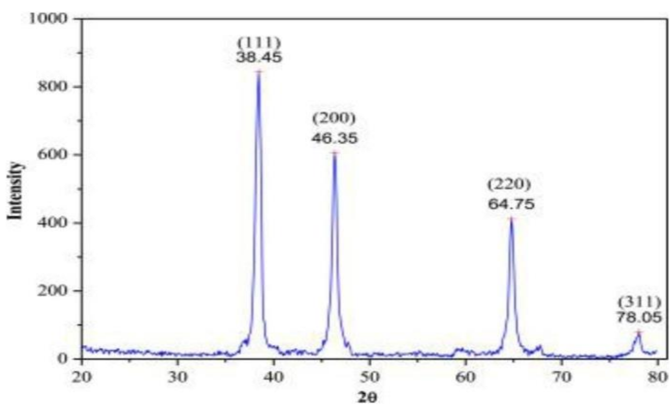


Fig. 9 UV vis absorption spectra of Zinc oxide Nanoparticles

X-ray Diffraction (XRD) Analysis: X-ray diffraction is one of the most often applied techniques for characterizing nanoparticles. It also provides chemical information for elemental analysis as well as for phase analysis. X-ray diffraction is an imperative technique for analyzing a wide range of materials, including fluids, powders, and crystals. The crystalline nature of nanoparticles is confirmed by X-ray crystallography. XRD is highly useful for stress measurements and texture analysis, in addition to chemical characterization. The phase, structural analysis, and grain size of the synthesized nanoparticles are analyzed using this technique.[18, 26]



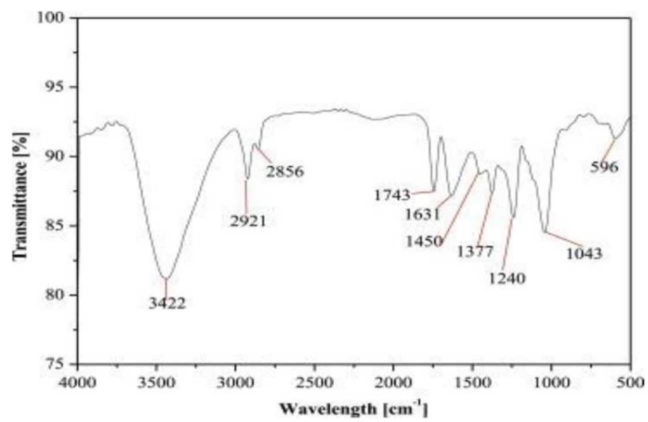


Fig. 10 XRD pattern of the Ag nanoparticles Fig. 11 FT-IR spectrum of biosynthesized ZnO

5.5. Fourier Transform Infrared Spectroscopy (FTIR)

FTIR is a technique based on the measurement of electromagnetic radiation absorption at wavelengths between the mid-infrared regions (4000-400 cm^{-1}). It is a method for obtaining an infrared spectrum of a solid, liquid, or gas's absorption or emission. A molecule's dipole moment is altered as it absorbs IR light, making it IR active. A recorded spectrum reveals the location of bands related to the type and strength of a bond as well as specific functional groups, offering details on the interactions and molecular structures. The FTIR spectrum shows absorption bands at 3422, 2921, 2856, 1743, 1631, 1450, 1377, 1240, 1043, and 596 cm^{-1}, indicating the presence of a capping agent with the nanoparticles. The observed intense bands were compared with standard values to identify the functional groups.[18, 26]

5.6. Transmission Electron Microscopy (TEM) Analysis

TEM is commonly used for the analysis of nanoparticles. Based on the electron transmittance principle, it provides information on the bulk material at magnifications ranging from extremely low to high. This technique is used to study the various morphologies of nanoparticles. Size, particle shape, and grain size are precisely measured by TEM. In TEM, the filament is the electron source of the instrument; electrons are emitted either by a thermionic filament or a field emission filament. The electron produced from the filament is accelerated by an electrode or cathode to attain high energy. The electromagnetic lens gives the images of the samples. Crystal plane, Miller indices, and interatomic distance were studied through High-Resolution Transmission Electron Microscopy (HRTEM). In TEM, the Selected Area Electron Diffraction (SAED) pattern provides details about the nature of the sample, whether amorphous or crystalline. The concentric ring indicates the amorphous nature of the sample, while systematically arranged dots indicate the crystallinity of the sample. TEM micrographs with SAED patterns show morphologies of nanoparticles, confirming that the flower-like structure is developed by small thin films. The SAED pattern clearly shows that the nanostructures formed are crystalline.[11, 12, 18, 21, 26, 35, 38, 44, 50]

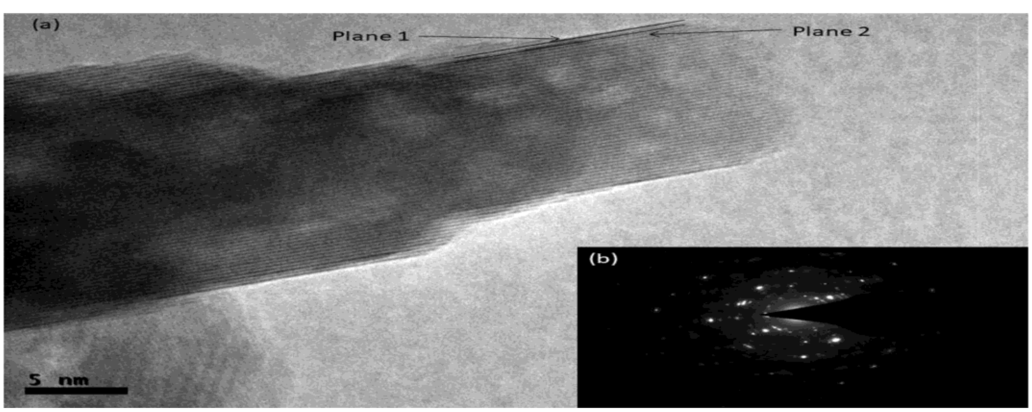


Fig. 12 TEM micrograph with SAED pattern for Ag-doped ZnO nanoparticles

Applications of Different Types of Nanoparticles

Nanoparticles have a wide range of applications across various fields due to their unique properties. Here are some elaborated applications:[1, 3, 5, 6, 27, 47, 50]

1. Medicine:

Drug Delivery: Nanoparticles can deliver drugs directly to cancer cells, minimizing damage to healthy cells1.

Regenerative Medicine: Used in tissue engineering to create scaffolds that support cell growth and tissue regeneration2.

Bioimaging: Enhance the contrast in imaging techniques, aiding in the diagnosis of diseases2.

2. Cosmetics and Sunscreens:

UV Protection: Nanoparticles like zinc oxide and titanium dioxide provide effective UV protection in sunscreens1.

Anti-Aging Products: Improve the delivery of active ingredients in anti-aging creams1.

3. Electronics:

Conductive Inks: Used in printed electronics for flexible displays and circuits1.

Transistors: Carbon nanotubes are used to build smaller and more efficient transistors3.

4. Environmental Applications:

Water Treatment: Nanoparticles can remove contaminants from water, making it safe for drinking

. Air Purification: Used in filters to remove pollutants from the air

5.Energy:

Batteries: Nanoparticles improve the efficiency and capacity of batteries.

Solar Cells: Enhance the efficiency of solar cells by improving light absorption1.

6. Agriculture:

Pesticides: Nanoparticles can be used to deliver pesticides more effectively, reducing the amount needed

Nutrient Delivery: Improve the delivery of nutrients to plants, enhancing growth and yield

7.Catalysis:

Chemical Reactions: Nanoparticles increase the efficiency of catalysts used in chemical reactions, making processes faster and more efficient1.

8.Textiles:

Antimicrobial Fabrics: Nanoparticles are used to create fabrics that resist bacteria and odors.

Smart Fabrics: Incorporate nanosensors to monitor health or environmental conditions.

Table 2 Nanoparticle Applications [1, 3-10, 12-17, 19, 20, 22, 23, 25-29, 31-35, 38, 40, 42-44, 46-48, 50-53]

Nanoparticles	**Size**	**Structural Properties**	**Applications**
Carbon nanotubes	2 - 100 nm	Single-wall carbon nanotubes (SWCNTs) and multi-wall CNTs (MWCNTs)	Drug delivery and anti-cancer, energy-related devices, high thermal conductivity, corrosion resistance
			Controlled drug delivery, biocompatibility, high loading capacity
			Cardiovascular therapy, anti-inflammatory therapy, anti-bacterial therapy, imaging diagnostics
Nanocapsules	100 - 500 nm	Shell and core combinations	Hydrophobic and hydrophilic drug delivery, biocompatibility, biodegradability, non-

Nanoparticles	**Size**	**Structural Properties**	**Applications**
			toxicity
			Tissue regeneration, anti-microbial properties
Dendrimers	1 - 15 nm	Highly branched ends and central core	Tissue regeneration and drug delivery, anti-Alzheimer activity, neurodegenerative disease
Liposomes	100 - 200 nm	Lipid bi-layer globules	
Polymeric nanoparticles	1 - 1000 nm	Polymers such as chitosan, PLGA	
Nanosphere	100 - 150 n	Spherical shaped	

Table 3: Patented technology

Sr No	Patent for	Country	No	author
1	Preparation of Nanoparticle Materials	United States	US20110070443A1	Paul O'Brien, Nigel Picket
2	Ferritin nanoparticle compositions and methods to modulate cell activity	United States	US10786570B2	Jeffrey Friedman, Sarah Stanley
3	Method for producing nanoparticles	United States	US8697479B2	Rajesh Mukherjee, Hironaka Fujii, Toshitaka Nakamura, Amane Mochizuki
4	Polymer nanotechnology	United States	US7341757B2	Tapesh Yadav
5	Policosanol nanoparticle	Denmark	DK2398476T3	Palayakotai R Raghavan
6	Nanoparticles for protein drug delivery	United States	US20070116772A1	Hsing-Wen Sung,Yu-Hsin Lin,Hosheng Tu
7	Polymeric nanoparticles and the process of preparation thereof	WIPO (PCT)	WO2013160773A2	Harpal Singh

Table 4 Marketed preparations

Sr.No	Nanotechnology	Therapeutic agent	Therapeutic role	Product	Company name	Route of administration
1.	Nanocrystal	Morphine sulphate	Psychostimulant	Avinza	King pharma Elan	Oral
2.	Depofoam	Aprepitant	Antiemetic	Emend	Merck Elan	Oral
3.	SLN Nebulisation	Rifampicin +isoniazide	Tuberculosis	Clinical trials	-	Inhalation
4.	Nanoparticles	Panacea	Lung cancer	Pacliall	Panacea	Intravenous (I.V)
5.	Liposomes	Doxorubicin	Breast cancer	Myocet	Zeneus pharma sopherion	Intravenous (I.V)
6.	PAMAM dendrimers	SN38	Hepatic colorectal cancer	Clinical trials	-	Oral
7.	Liposomes	Cytarabine	Lymphomatousmeninggitis	Deposit	Sky pharma union	Intravenous (I.V)
8.	Nanocapsules	Streptomycin	Tuberculosis	Clinical trials	Alpha RX	Intramuscular
9.	Liposomes	Amikacin	Tuberculosis	Mikasome	Nex star pharmaceuticals	Intravenous (I.V)s

9. Conclusion

Conclusion Recent studies have given a great deal of attention to nanotechnologies and nanomaterials. Nanomaterials are quite interesting since they have a lot of potential to develop novel and innovative products across many areas. Nanoparticles have better features because of their small size, such as a larger surface area, high reactivity, stability, strength, sensitivity, etc. Due to their unique and intriguing characteristics above their bulk counterparts, nanoparticles having one or more dimensions of the order of 100 nm or less have attracted significant interest and are used in a variety of applications. Nanoparticles are particularly prone to severe oxidation when being stored until use because of their small sizes. Both top-down and bottom-up strategies are used in the synthesis of nanoparticles. For academic research and commercial business purposes, the nanoparticles are produced using several techniques that can be divided into three primary categories; biological, physical, and chemical processes. In this review, we covered the preparation of nanoparticles using different techniques. The ability to produce particles with various chemical compositions, Monodispersed, sizes, and shapes is necessary for the use of nanoparticles. Compared to physical and chemical processes, which not only cost more money but also produce toxic byproducts that harm the environment. The role of several approaches for the characterization of nanoscale materials was also discussed in this review. Researchers will benefit from a better understanding of the health and safety implications of nanoparticles as well as the ability to develop safer nanomaterials.[36-38, 46, 49, 52, 53]

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