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A Review of Revolutionizing Green Synthesis of Nanoparticles in Pharmacy and Healthcare

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Review Article

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ABSTRACT

Science's newest and fastest-growing field is nanotechnology. The foundation of nanotechnology is made up of nanoparticles. The sizes of nanoparticles range from 1 to 100 nm. A variety of classes, including inorganic, organic, ceramic, and carbon-based nanoparticles, are used to categorise the nanoparticles. Nanoparticles are becoming a more widely used material like electronic devices to medicine in industries. Green synthesis is a feasible and environmentally acceptable alternative that produces nanoparticles using natural resources and biological processes. In addition to using environmentally friendly reducing and stabilising agents, the green synthesis approach makes use of a variety of biological resources, including bacteria, fungus, plants, and algae. The synthesis of nanoparticles has grown in importance as a means of promoting targeted drug delivery, imaging, diagnostics, and therapeutic interventions in the pharmaceutical and healthcare industries. These natural resources guarantee the biocompatibility and stability of the final nanoparticles by acting as capping agents in addition to reducing agents The creation of safer and more effective medical solutions through green synthesis has great potential to transform the nanoparticle manufacturing process. Green nanotechnology for pharmacy and healthcare is experiencing innovation which is

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usefulness as a resource for researchers, practitioners, and policymakers. Additionally, nanoparticles can be categorised into one, two, or three methods. The synthesis of nanoparticles using chemical, physical, and environmentally friendly methods is covered in this review. To make the nanoparticles, a variety of qualitative and quantitative techniques are applied. FTIR, SEM, and TEM are examples of qualitative techniques.

Keywords: Nanoparticles; green synthesis; plants; metallic and diagnostics.

1. INTRODUCTION

Science's nanotechnology field studies materials in the nanoscale, or typically between 1 and 100 nm. This science operates on a nanoscale, providing different perspectives to a wide range of scientific disciplines, including bioengineering, dentistry, and pharmaceuticals [1]. In light of nanomaterials' potential, the green chemistry approach is important. The development of secure, environmentally friendly NPs should be the ultimate goal of this field of nanoscience, and nanotechnology should broadly embrace it [2]. Size, physicochemical characteristics, and shape of incorporated particles are all greatly influenced by the solvents and reducing operators used in NP reduction, and this morphology has an impact on NP utilisation. The two distinct approaches for combining NPs are "bottom up" and "top down." Using a variety of methods such as grinding, milling, sputtering, thermal/laser ablation, etc., appropriate bulk material is size-reduced into smaller fine particles in a top-to-bottom manner. As opposed to the "bottom-up" approach, which uses chemical and biological methods to synthesise NPs through the self-assembly of atoms into new nuclei that grow into nanosize particles, the "bottom-up" approach uses sono-decomposition, chemical reduction, and electrochemical methods [3]. Though studies have shown that green methods, which have the advantages of low cost, easy characterization, and fewer failure chances, are more effective for generating nanoparticles (NPs), traditional methods have been used for many years [4]. Because of their hazardous metabolites, the environmental effects of creating NPs through chemical and physical methods have been numerous. Plant-based NP synthesis is undoubtedly a simple process; using plant extract, a metal salt is created, and at room temperature, the reaction takes only a few hours to several minutes. Green methods for producing NPs are not only economically sound but also easily scaleable. Nowadays, environmentally planned NPs are preferred over conventionally supplied NPs due to their remarkable qualities. Increased use of chemicals, which are hazardous and toxic to the environment and human health, may increase the reactivity and toxicity of particles and have unintended negative health effects due to compositional uncertainty and lack of assurance [5]. Because they have the potential to lessen NP toxicity, green synthesis methods are very appealing. This has led to a significant increase in the use of vitamins, amino acids, and plant extracts in modern times [6].

1.1 Nanotechnology in Medicine and Health Care

The word "nanomedicine" describes the use of nanotechnologies in healthcare and medicine. In particular, nanomedicine prevents, detects, tracks, and treats illnesses through the use of nanoscale technologies and nano enabled methods [7]. Nanotechnologies have shown great promise in the medical field, particularly in the areas of drug delivery, tissue engineering, implants, psychiatric and neurological disorders, diabetes, and musculoskeletal disorders. They have also improved the treatment of a number of diseases, including cancer, cardiovascular disease, musculoskeletal disorders, bacterial and viral infections, and musculoskeletal disorders [8] The field of nanotechnology and nanodrugs is so vast and diverse. Significant advancements in nanomedicine have raised the drug to a new level with important implications for healthcare. Research on the enormous potential of nanotechnology in healthcare is necessary. In the medical field, a great deal of research is being conducted on optimal techniques and approaches, such as nephrology, cardiovascular disease therapeutic genes, and cancer therapy. Traditional medicine has undergone tremendous advancement, and both nanotechnology and nanoparticle quality have improved and produced positive outcomes [9,10]. Nanoparticle drugs have also been utilised in gene therapy. Numerous studies concentrated on the use of viral vectors thought to be drug delivery systems.

1.2 Nanoparticles and Their Properties

We can categorise nanomaterials based on their origins, dimensions, and structural configurations. Nanomaterials are the cornerstone of nanotechnology and have been a longstanding part of our lives because of the contributions of numerous sciences. Natural nanomaterials, which are found in nature and include viruses, proteins, enzymes, and minerals, and artificial nanomaterials, which are not found in nature and must be produced through specific processes, are the two main categories into which nanomaterials are divided based on their origin. Because they can display different properties and functions than typical bulk materials, nanoparticles are currently attracting the attention of scientists. The most significant factor that makes it possible to produce nanostructures with the appropriate size, shape, and properties and makes them useful in a variety of fields is the reduction of classical physics' effects and the activation of quantum physics. Additional explanations for the varying behaviours of nanoparticles in terms of physical, chemical, optical, electrical, and magnetic aspects include the constraints placed on load carriers, electronic structures that are dependent on size, an increased surface to volume ratio, and other factors resulting from the distinct characteristics of atoms. Nanomaterials are categorised into four groups based on their dimensions. A subset of metallic and semiconductor nanoparticles are known as nano-sized nanocrystals, or zero dimensions. Some examples of one-dimensional nanomaterials are nanowires, nanobots, and nanotubes. Bulkers are examples of three-dimensional nanomaterials. Two-dimensional nanomaterials include nanocomposites and nanoplates. Nanomaterials are categorised into four main groups based on their structural configurations: metallic nanomaterials, carbon-based nanomaterials, dendrimers, and composites [11-16].

2. METHODOLOGY

2.1 Synthesis Method of Nanoparticle

Two fundamental approaches that comprise a variety of preparation techniques and have been known since ancient times are used to create nanoparticles, which can originate from natural sources or be artificially created and have unique properties at the nanoscale. It includes two types, they are:

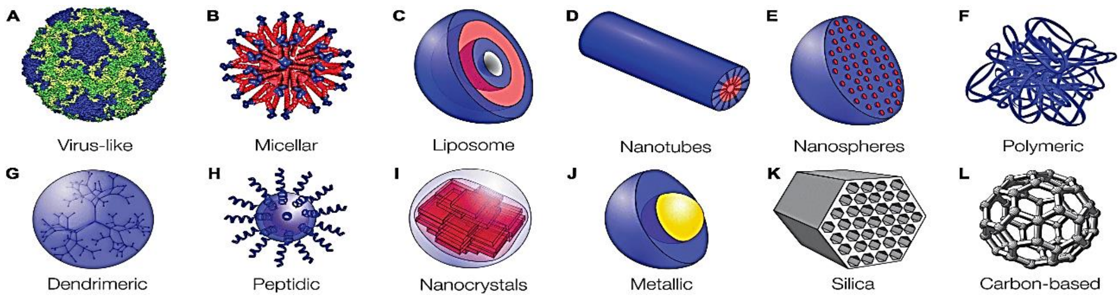

Fig. 1. Types of nanoparticles

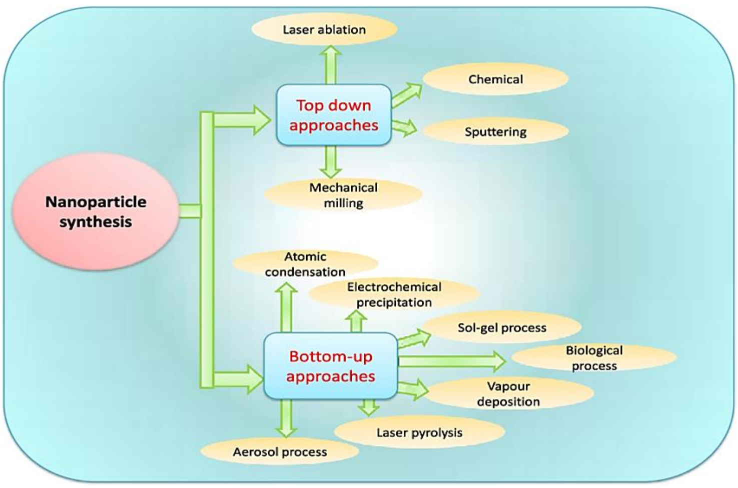

Fig. 2. Nanoparticle synthesis

3. METHODS

- Top-down method.
- Bottom-up method.

3.1 Top-down Method

The first strategy is known as the "top-down" method, and it involves using an external force to break solid materials into tiny bits. This method uses a variety of thermal, chemical, and physical processes to supply the energy required to produce nanoparticles [17].

3.1.1 Technique of thermal degradation

Heat is the source of chemical breakdown in this endothermic process. This heat breaks the compound's chemical bond. The precise temperature at which an element undergoes chemical breakdown is known as the decomposition temperature. The formation of nanoparticles results from the breakdown of meta at a particular temperature. Heat decomposition is used to functionalize synthesised gadolinium oxide nanoparticles with paramagnetic polyethylene glycol [18].

3.1.2 Lithographic technique

Lithographic techniques are top-down techniques that can produce most part micron size features, but they are expensive to use and energy intensive. For the past few decades, lithography has been utilised in the production of computers and printed circuit boards. One type of lithography that differs from conventional lithography is nanoimprint lithography. It is comparable to the synthesis of templates. Nanosphere lithography forms templated matrices using latex spheres. There are various kinds of lithography techniques, such as dip pin lithography, photo lithography electron beam lithography, soft lithography, and focused ion lithography [19].

3.2 Bottom- up Method

The "bottom-up" strategy, which is the second method, involves assembling and merging atoms or molecules of gas or liquid. The bottom-up strategy yields good results in nanoparticle synthesis, but the top-down approach, which is more expensive to apply, cannot produce the possibility of cavities and roughness in nanoparticles, making them the perfect surfaces and edges. In addition, the bottom-up approach produces no waste materials that need to be removed and permits the creation of smaller nanoparticles due to its improved control over nanoparticle sizes [20].

3.2.1 Chemical vapour deposition (CVD)

The process that deposits a gaseous reactant thin layer on the substrate. The thin-film depositing procedure takes place in reaction chamber. When a substrate gets heated, a chemical reaction takes place and a combining gas come into contact. Thin layer of product that this reaction produces on the substrate's surface. The CVD method produces hard, strong, uniform, and incredibly pure nanoparticles. The disadvantages of the CVD technique involves the requirement for specialised tools and the production of extremely toxic gaseous byproducts. It is coated and synthesised Titanium oxide (TiO_2) through the use of chemical method of vapour deposition Titanium tetra iso-peroxide (TTIP) was the precursor they employed. The outcomes of dip-coated, chemical method of vapour deposition-coated, and non-coated beads are shown in a SEM micrograph. Whereas the surface of the chemical method of vapour deposition-coated bead was uniform and regular, the dip-coated bead had areas that were partially coated and uncoated [21].

3.2.2 Sol - gel method

The terms "sol" and "gel" combine to form the term "sol-gel method." Sol is a colloid that is made up of suspended solid particles in a liquid that is continuous. Gel is a macromolecule that is solid and dissolves in a solvent. The sol–gel method is the most widely used bottom-up technique for producing nanoparticles because of its ease of use. This process uses an appropriate chemical solution as a precursor. In metal oxide and chloride are frequently used as precursors in the sol-gel process. The precursor is distributed throughout the host liquid by employing a variety of techniques, including stirring, sonicating, shaking. Various techniques such as centrifugation, sedimentation, and filtration are employed to separate the resultant solution into a liquid and a solid phase with the aim of retrieving the nanoparticles [22,23].

4. GREEN SYNTHESIS METHOD

An environmentally friendly way to synthesise the biological approach, which is provided as an alternative to chemical and physical methods, is how nanoparticles are made. Furthermore, expensive, hazardous, or toxic chemicals are not needed for this process. Recently, a lot of work has been done using the biological approach to create metallic nanoparticles with a variety of contents, sizes, forms, and physicochemical properties. Synthesis can be finished in a single step using biological entities such as bacteria, actinobacteria, yeasts, moulds, algae, and plants, or their byproducts. Alkaloids, pigments, proteins, enzymes, amines, phenolic compounds, and microorganisms are among the molecules that carry out the reduction process that produces nanoparticles [24-27].

When used in conventional chemical and physical methods, the reducing agents used in the reduction of metal ions and the stabilising agents used to prevent the unwanted agglomeration of the generated nanoparticles carry a risk of toxicity to the environment and the cell. Furthermore, the generated nanoparticles' size, shape, and surface chemistry are thought to be toxic. The biological organisms employed in the green synthesis method, which produces biocompatible nanoparticles, contain the agents. Because of their rapid growth, low cost of culture, and ease of control and manipulation of the growth environment, bacteria are a prime candidate for the synthesis of nanoparticles. At the same time, it is known that some species of bacteria have special defences against the metals [28-32].

4.1 Green Synthesis Produced Metals

4.1.1 Copper (Cu) and copper oxide (CuO)

Many plant extracts have been used to create copper oxide nanoparticles. Copper salts are reduced by the electrons produced by the plant extract. Reduction occurs when phytochemicals react with copper ions to form copper oxide nanoparticles. To obtain copper oxide nanomaterials, the colloidal heat combination process is employed. Utilising carboxy methyl cellulose a highly stable and sensitive Cu nanocomposite as a substrate was created by decontaminating and drying the incorporated cuo to produce distinct sizes of the Cuo nanoparticles. Copper oxide (CuO) nanoparticles are the focus of attention among all other nanoparticles due to their numerous applications. The term "green synthesis" describes the use of environmentally friendly techniques to create copper oxide nanoparticles without the need of harsh conditions or toxic chemicals.

Advantages:

- Green synthesis techniques typically involve lower operating temperatures and pressures, which results in a lower energy consumption when compared to conventional synthesis routes.
- Green synthesis techniques frequently produce biocompatible nanoparticles, which can be used in biology and medicine without endangering living things.
- Certain green synthesis methods reduce process costs by using readily available and reasonably priced raw materials.

Disadvantages:

- The performance of nanoparticles produced by green synthesis methods may be impacted by their variable stability and size distribution.
- The overall production efficiency may be impacted by certain green synthesis techniques that call for longer reaction times than traditional techniques.
- It may be difficult to optimise and troubleshoot green synthesis methods due to incomplete understanding of the underlying mechanisms [33,34].

4.1.2 Zinc oxide (ZnO)

Zinc oxide (ZnO) nanoparticles are made using environmentally friendly processes that frequently use natural resources rather than dangerous chemicals. This process is known as "green synthesis." One class of inorganic metal oxides that is readily available is zinc oxide (ZnO), which comes in a variety of nanostructures. ZnO nanoparticles have a potent antibacterial effect on spores that can withstand high temperatures and pressure. ZnS NPs were synthesised in an aqueous rough concentrate of Stevia rebaudiana using a characteristic sweetener glycoside (250–300 times sweeter than sucrose), which worked well being an excellent bio- ZnO nanoparticles have a broad range of uses across all industries. The antimicrobial activity of ZnO nanoparticles is particularly noteworthy.

Advantages:

- Green synthesised ZnO nanoparticles are frequently more biocompatible, which qualifies them for use in biotechnology and medicine.
- By avoiding using potentially harmful substances, green synthesis techniques generally support ecologically friendly practices
- When compared to traditional synthesis routes, green synthesis methods save energy by operating at lower temperatures and pressures.
- ZnO nanoparticle size and morphology can be more precisely controlled using green synthesis techniques, which can enhance their performance in a range of applications.

Disadvantages:

- These traits can vary, which may have an impact on their uses and qualities. The synthesis process may become more complex and variable when biological or natural components are used.
- The final zinc oxide nanoparticles' size and shape might not always be precisely controlled by green synthesis techniques
- Utilising biological entities, such as microorganisms or plant extracts, could contaminate or introduce impurities that compromise the stability and purity of the ZnO nanoparticles [35-37].

4.1.3 Cerium oxide (CeO_2)

Cerium Oxide NPs' antioxidant properties as a possible medication strategy for treating obesity. In addition, CNP has quick electron transfer kinetics and works well as a co-immobilization material for many different enzymes, including horseradish peroxidase, glucose oxidase, and cholesterol oxidase. Excellent antibacterial qualities were demonstrated by the Gloriosa superba leaf extract; CeO_2 NPs had a spherical shape and an average size of 5 nm. The green synthesis of cerium oxide (CeO_2) nanoparticles uses energy-efficient techniques to reduce the usage of dangerous chemicals and other environmental pollutants. The following are some benefits and drawbacks related to the environmentally friendly synthesis of cerium oxide.

Advantages:

- Greater control over the shape and size of CeO2 nanoparticles can be achieved through green synthesis techniques, which will enhance their performance in a range of applications.
- Green-synthesized CeO2 nanoparticles may have a range of useful characteristics, such as antioxidant, antibacterial, and catalytic effects, which would make them appropriate for a number of uses.
- The overall cost-effectiveness of the process is increased by using inexpensive and readily available raw materials in some green synthesis techniques.

Disadvantages:

- Green synthesis techniques could produce nanoparticles with a range of properties, such as stability and size distribution.
- It can be difficult to comprehend and regulate the reaction mechanisms involved in green synthesis. When natural or biological components are used, the synthesis process may become more variable.
- In comparison to traditional methods, some green synthesis techniques might call for longer reaction times. This might have an effect on the synthesis process's overall effectiveness [38,39].

4.1.4 Cadmium sulphide (CdS)

Due to its numerous applications in nonlinear optical materials, photodetectors, solar cells, photo-catalysts, and antimicrobial activities, cadmium sulphide (CdS) is one of the most promising direct bandgap semiconductors. CdS nanoparticles were created using a variety of techniques, including chemical synthesis, laser ablation, hydrothermal processing, and sol–gel templates. Obtaining CdS nanoparticles can be done easily, affordably, and cleanly using the chemical method. The process of thermally breaking down thioacetamide (TA) in an acidic solution of cadmium nitrate yields nanoparticles and produces the supersaturating conditions required for the homogenous precipitation of CdS. In this study, we examine the optoelectronic characteristics of CdS nanoparticles made by thermally breaking down thioacetamide (TA).

Advantages:

- When compared to conventional methods, green synthesis techniques are more environmentally friendly because they generally avoid or use fewer hazardous chemicals.
- In comparison to traditional synthesis methods, green synthesis frequently uses lower temperatures and pressures, which results in less energy being used.
- To cut costs, some green synthesis techniques make use of cheap raw materials, waste products, or readily available natural sources.
- Green synthesis techniques give CdS nanoparticles more control over their shape and size, enabling customisation for particular uses.
- Potential uses for green-synthesized CdS nanoparticles may be increased by their adaptable qualities, which include photocatalytic, antimicrobial, and sensing capabilities.

Disadvantages:

- Because natural sources and plant extracts vary so much, standardising green synthesis methods can be difficult.
- There may be difficulties when moving production from the laboratory to the industrial scale. At larger scales, it can be challenging to maintain reproducibility and consistency.
- Because of the complexity of the biological or natural components involved, characterising nanoparticles synthesised using green methods may require advanced techniques. This may raise the price and lengthen the characterization process.
- Plant extracts and microorganisms are examples of biological entities that may introduce contaminants or impurities that could compromise the stability and purity of the CdS nanoparticles [40-42].

4.1.5 Silver (ag) and gold (au) nanoparticles

According to several studies, a wide range of plants are utilised to create gold and silver nanoparticles. For readers to gain a comprehensive understanding of methodology, reaction conditioning, and optimisation in a condensed manner, a literature review on the green synthesis of nanoparticles will be beneficial. By giving the metal ions an electron, these phytochemicals can reduce the metal ions and cause metallic particles to form. Temperature, pH, and the presence of other compounds are examples of reaction conditions that are favourable to this reduction process. As the concentration of nanoparticles in the solution increases, honey can speed up the reduction process. Nanoparticles formed through honey mediation have unique properties like biosensing, anticorrosive, catalytic, and antimicrobial activity. Produced au and ag nanoparticles by extracting leaf from the corresponding metal salt precursors [43, 44].

Advantages:

- It contributes to environmental sustainability by avoiding the use of hazardous chemicals that are frequently used in conventional methods.
- Uses less energy than conventional synthesis methods because it works at lower pressures and temperatures.
- Cost savings can be achieved by using cheap raw materials or plant extracts in certain green synthesis techniques [45].

Disadvantages:

- Standardising the synthesis process may be difficult due to variations in plant extracts or natural sources.
- The shift from laboratory-to-industrial-scale production can pose difficulties and compromise reproducibility.
- When dealing with biological or natural components, characterization may call for sophisticated techniques.

- It can be difficult to precisely control the characteristics of silver nanoparticles made using green synthesis [46].

5. EVALUATION TESTS

5.1 Fourier Transmission Infrared Ray (FTIR)

FTIR is a method for obtaining an infrared spectrum of a solid, liquid, or gas's absorption or emission. High-resolution spectral data over a broad spectral range are simultaneously collected by an FTIR spectrometer. Additionally, different nanomaterials and proteins in hydrophobic membrane environments are studied using FTIR. Research indicates that FTIR can be used to directly ascertain the polarity of a transmembrane protein at a specific location along its backbone. FTIR can be used to quantitatively analyse the bond characteristics of different organic and inorganic nanomaterials. FTIR is used to identify biomolecules that are in charge of stabilization, reduction, and capping [47].

Fig. 3. Fourier transform infrared rays (FTIR)

Fig. 4. Ultra -violet visible spectrophotometric

5.2 UV – Visible Spectrophometric

Using Uv-visible, the nanoparticles of different metals with sizes ranging from 2 to 100 nm are characterized. typically, a wavelength between 300 and 800 nm is employed. this method determines the stability and formation of nanoparticles in aqueous solution. Using the Beer-Lambert law, this qualitative, quantitative, and analytical method determines how much discrete ultraviolet and visible light is absorbed or transmitted through a given sample by comparing it to a blank or reference sample. It conducts research in a vacuum [48].

5.3 Scanning Electron Microscopy (SEM)

A focused electron beam is used to scan a sample's surface in a scanning electron microscope (SEM), creating images of the sample. the sample's atoms and electrons interact to produce a variety of signals that reveal details about the sample's composition and surface topography. an image is created by combining the intensity of the detected signal with the position of the electron beam as it scans in a raster scan pattern. in the most popular SEM mode, a secondary electron detector (everhart–thornley detector) is used to detect secondary electrons released by atoms excited by the electron beam. Using SEM, an output image is created by using electrons rather than light. SEM is used to characterize the morphology, size, shape, and distribution of synthesised nanoparticles [49].

Fig. 5. Scanning electron microscope

5.4 X Ray Diffraction (XRD)

X ray diffraction is used to determine a material's atomic structure. Both qualitative and quantitative analysis employ it. it is employed in the computation of crystalline nanoparticle size, the determination of crystal structure, and the verification of nanoparticles. The basis of X-ray diffraction is the constructive interference of a crystalline sample with monochromatic X-rays. A cathode ray tube produces these X-rays, which are then collimated to concentrate them, filtered to produce monochromatic radiation, and directed towards the sample. When an incident of monochromatic x-rays happens on a crystal. The Crystal causes the atomic electrons to vibrate. They accelerate at the same frequency as the incident ray's frequency. The radiation that these accelerated electrons then release is directed in all directions at the same frequency as the incident x-rays [50].

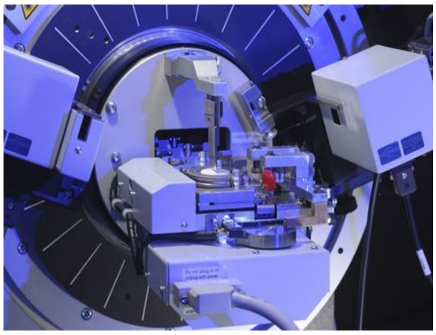

Fig. 6. X-ray diffraction

5.5 Transmission Electron Microscopy (TEM)

A beam of electrons is passed through a specimen to create an image in a process known as transmission electron microscopy (TEM). most frequently, the specimen is a suspension on a grid or an ultrathin section that is less than 100 nm thick. as the beam passes through the specimen, the interaction of the electrons with the sample creates an image. after that, the image is enlarged and focused onto an imaging medium, like a charge-coupled device connected to a scintillator sensor, a photographic film layer, or a fluorescent screen. It is employed in the study of crystal structure and material particle size at the nanoscale [51].

Fig. 7. Transmission electron microscope

6. ADVANTAGES OF NANOPARTICLES

- **Environmentally friendly**: The fact that green synthesis methods are environmentally sustainable is one of their main benefits. These methods reduce the use of hazardous chemicals and their overall impact on the environment by making use of natural sources and bio-friendly materials.
- **Reduced toxicity:** Typically, biocompatible substances like microbial agents or plant extracts are used in green synthesis. Because of this, the nanoparticles that are created are frequently less hazardous than those that are created through traditional means, making them safer for use in a variety of applications.
- **Energy efficiency:** Green synthesis techniques frequently use less energy and operate at lower temperatures than conventional chemical techniques. This improved energy efficiency makes the production process more economical and sustainable.
- **Biomedical application:** Because they are frequently biocompatible, green-synthesized nanoparticles can be used in a variety of biomedical applications. These include the administration of drugs, imaging, and other therapeutic applications where it is essential to reduce toxicity and guarantee compatibility with biological systems.
- **Versatility of source materials:** Numerous source materials, such as plant extracts, bacteria, fungi, and other bio-friendly substances, can be used with green synthesis techniques. Because of their adaptability, manufacturers and researchers have a wide range of options when creating nanoparticles that are suited for particular uses.

Disadvantages of nanoparticles:

- **Variable Product Quality:** The inherent variability in natural sources may lead to variable product quality when using green synthesis methods. Variations in the composition of microbial cultures or plant extracts can result in variations in the properties of the synthesised nanoparticles.
- **Limited control over particle size and shape:** It can be difficult to precisely control the size and shape of nanoparticles using green synthesis techniques. For some applications, more precise control over these characteristics can be obtained through conventional chemical methods**.**
- **Biological contaminants:** It is possible to introduce contaminants like proteins, nucleic acids, or other cellular components when using biological materials in green synthesis. These impurities may need further purification procedures and have an impact on the stability and functionality of the nanoparticles.
- **Storage and stability issues:** When it comes to storage stability, nanoparticles made with green methods might not be as stable as those made with traditional methods. Over time, stability problems may have an impact on the nanoparticles' effectiveness and shelf life.
- **Cost of purification:** Depending on the source material used, additional purification steps may be required to remove impurities. The cost and complexity of purification processes can impact the overall economic feasibility of green synthesis methods.

7. APPLICATIONS OF NANOPARTICLES

- In the past ten years, the number of scientific publications in the field of nanotechnology has dramatically increased.
- Nanomaterials produced using green synthesis are important for applying nanotechnology to a variety of fields.
- In order to achieve sustainable development, green nanotechnology refers to the creation of green nanoproducts and their application.
- Green synthetic nanoparticles (NPs) are important in medicine, clinical settings, and in vitro diagnostic applications.
- Nanoparticles made using environmentally friendly processes have strong antibacterial properties, antifungal effects anti-parasitic activity.

- To extend shelf life and guard against microbial contamination, food packaging materials can employ green-synthesized nanoparticles.
- Certain nanoparticles' antimicrobial qualities can improve food safety.
- Textiles can be given special qualities like improved mechanical strength, UV resistance, and antimicrobial activity by incorporating nanoparticles. The textile industry's increasing interest in environmentally friendly and sustainable practises is in line with green synthesis methods [52-56].
- In recent times, noble nanoparticles have garnered significant interest due to their remarkable applications in the fields of electronics, medicine, and biology.
- The biological method has gained widespread acceptance among synthesis techniques, including physical and chemical methods, due to its simplicity, dependability, lack of toxicity, and environmentally friendly nature.
- The various possibilities for metallic nanoparticles that are compatible with biology and cytology were made possible by the fusion of green chemistry and nanotechnology.
- The medicinal properties of different metals are detailed in detail in the ancient Indian Ayurvedic medicine book "Charak Samhita," which mentions the use of silver as early as 300 BC.
- Silver nanoparticles (Ag) or AgNPs, are one of the many types of nanoparticles that are commonly used in biomedical, drug delivery, water treatment, agricultural, electronic devices, adhesives, and other applications.
- AgNPs have many uses as anti-microbial, anti-parasitic, and anti-fouling agents due to their unique properties. They can also be employed as an agent for water purification systems and medication tailored to a specific location.
- The complex and little-studied mechanism by which AgNPs affect bacteria is best described theoretically. AgNPs have two different ways of acting on microorganisms: bactericidal action and inhibitory action.
- AgNPs have antibacterial activity against both gram-positive and gram-negative bacteria, however conflicting reports from various researchers have not yet been verified.
- Nanotechnology is also thought to be important in the early detection of cancer by enabling the molecular level visualisation of cancer cells.
- The exact location of the tumor can also be determined, and the expression and activity of particular molecules that affect tumor behaviour and its response to therapy can be ruled out.
- In biomedical applications, pure platinum nanoparticles or those alloyed with other nanoparticles have found widespread use. Palladium nanoparticles find application in chemical sensors, optoelectronics, biological sensors, and antibacterial applications.
- Antibacterial applications, cosmetic formulations, and medical treatments have also made use of other non-noble metallic nanoparticles, including iron, copper, zinc oxide, and selenium [57].

7.1 Applications of Green Nano-technology

In recent years we have seen a sharp increase in interest in nanotechnology because of its numerous applications in fields including medicine, pharmaceuticals, catalysis, energy, and materials. These nanoparticles, which range in size from 1 to 100 nm, may find use in industry, medicine, and agriculture. Researchers have worked hard to create nanoparticles using a variety of techniques, such as chemical, biological, and physical approaches [58] Due to the challenges of scaling up the process, separating and purifying the nanoparticles from the micro-emulsion (oil, surfactant, co-surfactant, and aqueous phase), and using a significant amount of surfactants, these methods have numerous drawbacks [59]. The utilisation of plant extracts in green methods to synthesise nanoparticles is advantageous due to its simplicity, convenience, eco-friendliness, and reduced reaction time. They play a crucial role in increasing the usefulness of NPs, especially in the pharmaceutical industry.

7.1.1 Agricultural engineering

Nanosized ligno-cellulosic materials are derived from trees and harvests, which has created a new market for valuable and innovative nano-sized goods and materials. In this field, NPs can be applied as nano-fertilizer, nano-pesticides that intertwine with nano-herbicides, nano-coating, etc. The potential for improving fertilisation, plant growth regulators, and pesticides in agriculture may be increased by using nanomaterials produced using environmentally friendly and sustainable processes [59] They also reduce the quantity of dangerous chemicals that contaminate the environment. As a result, this technology aids in the reduction of environmental pollutants. Nanotechnology has also recently attracted attention because of its numerous applications in a variety of industries, including agriculture, medicine, and the environment [60]. The tiny nanoparticles' large surface area, in particular, makes them appealing for addressing problems that chemical and physical pesticides as well as biological control methods cannot meet.

7.1.2 Nanotechnology in pesticides and fertilizers

One significant route for their bioaccumulation into the food chain can be provided by plants. Recent advancements in agriculture deal with the use of NPs to apply chemicals to plants in a safer and more efficient manner. Many researchers have documented the effects of various NPs on plant growth and phytotoxicity. These include zinc oxide in mungbean, magnetite (Fe3O4) nanoparticles and plant growth, alumina, zinc, and zinc oxide on seed germination and root growth of five higher plant species: radish, rape, lettuce, corn and cucumber, silver nanoparticles and seedling growth in wheat , sulphur nanoparticles on tomato , zinc oxide in mungbean, and nanoparticles of AlO, CuO, FeO, MnO, NiO, and ZnO [61,62].

7.1.3 X – Ray imaging

Quantum dots (QDs) are semiconductor crystals that range in size from 1 to 10 nanometers and have a standard core-shell structure. The band gap is the name given to the energy gap that exists between the valence and conduction layers. Band gaps are determined by the sizes of the quantum dots, and different band gaps require different energies to excite the quantum dots [63]. Because of its high X-ray retention coefficient, ease of engineered control, nontoxicity, surface functionalization for colloidal dependability, and conveyance-focused design, AuNPs have gained significant attention as X-ray differentiate specialists.

- Personalised medicine development.
- Accurate and precise drug delivery methods.
- Surgical methods that are automated and robotic.
- Retinal implants and cochlear implants both use this technology to repair damaged nerves.

7.1.4 Drug delivery system

AuNPs have many unique characteristics that make them an attractive nano-carrier for drug delivery systems (DDSs), such as their remarkable optical and physicochemical properties, biocompatibility, viable flexibility, controlled dispersity, and nontoxicity. The treatment of endocellular diseases is significantly aided by Au NP conjugates with drug molecules . Drug efficacy might be enhanced by them. Via physical absorption or ionic or covalent bonding, antibiotics or other drug molecules can directly conjugate with Au NPs. For example, methotrexate and 13 nm colloidal Au have been mixed together [64]. Methotrexate is an analogue of folic acid that has been traditionally used as an anticancer medication because it can inhibit the growth and multiplication of cancer cells. After an overnight incubation period, the carboxylic groups on the methotrexate molecule can bind to the surface of Au NPs. It has been suggested that the concentration of methotrexate bound to Au NPs is greater than the concentration of Au NPs absent at the same volume. In an additional investigation, doxorubicin (DOX) was coupled to Au NPs measuring 30 nm via a pH-sensitive linker. Once inside acidic organelles, this kind of DOX-Au NP attachment enables the intracellularly triggered release of DOX from the Au NPs. Due to this, intracellular DOX concentration was able to rise quickly, improving therapeutic effects in tumour cells that were resistant to drugs [65].

8. CONCLUSION

Green nanoparticles (nanoparticles) find wide-ranging applications in various fields, including biosensing, dentistry, and pharmaceuticals. in developing nations where such material may be found only in their native resources, the majority of plant-based products can be produced locally. Metal nanoparticles for green synthesis have recently been produced with efficiency using a range of microorganisms and plant extracts. green synthesis is the most practical, straightforward, environmentally friendly method for creating nanoparticles. it reduces the negative effects of chemical and physical methods by avoiding the use of toxic chemicals and the creation of hazardous byproducts. due to their superior properties, nanoparticles are widely used and have been the subject of extensive research in recent years. green synthesis produces antimicrobial, antioxidant, and non-toxic nanoparticles, and these properties are becoming more and more significant in terms of their physical and therapeutic effects. For green synthesised nanomaterials to be produced and used in practical applications, a number of obstacles and drawbacks must be addressed, including low yield, non-uniform particle sizes, intricate extraction processes, seasonal and regional raw material availability, and other issue.

CONSENT AND ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Muhammed Rafique, Iqra Sadaf, M Shahid Rafique, M. Bilal Tahir et al. A review on green synthesis of silver nanoparticles and their applications. Artificial Cells Nanomedicine Biotechnology. 2017;45(7): 1272–1291.
2. Varma RS. Greener approach to nanomaterials and their sustainable applications. Current Opinion in Chemical Engineering. 2012;1(2):123–128.
3. Mathur, Prateek, Jha, Swati, Ramteke, Suman, Jain, N. K, et al. pharmaceutical aspects of silver nanoparticles. Artificial Cells Nanomedicine Biotechnology. 2018; 46(1):115-126.
4. Nadagouda MN, Varma RS. Green synthesis of silver and palladium nanoparticles at room temperature using coffee and tea extract. Green Chem. 2008; 10(8):859–862.
5. 5)Zhang, Xi-Feng, Liu, Zhi-Guo, Shen, Wei, Gurunathan, Sangili Yandi et al. silver nanoparticles: synthesis, characterization, properties, applications, and therapeutic approaches. International Journal of Molecular Sciences. 2016;17(9):1534.
6. Abdelghany TM, Al-Rajhi Aisha MH, Al Abboud, Mohamed A, Alawlaqi, MM, et al. Recent advances in green synthesis of silver nanoparticles and their applications: About future directions. A review. Bionanoscience. 2018;8(1):5–16.
7. Farokhzad OC, Langer R. Nanomedicine: Developing smarter therapeutic and diagnostic modalities. Advanced Drug Delivery Review. 2006;58:1456–1459.
8. Lombardo D, Kiselev MA, Caccamo MT. Smart Nanoparticles for Drug Delivery Application: Development of Versatile Nanocarrier Platforms in Biotechnology and Nanomedicine. Journal of Nanomaterials. 2019;12:1–26.
9. V Kumar, M Bhatele (Eds.), Proceedings of All India Seminar on Biomedical Engineering 2012 (AISOBE 2012): Lecture Notes in Bioengineering, Springer, Bengaluru; 2013.
10. Keskinbora KH, Jameel MA. Nanotechnology applications and approaches in medicine: A review Journal of Nanoscience Nanotechnology Research. 2018;2(2).
11. Schrofel A, Kratosova G, Safarik I, Safarikova M, Raska I, Short LM. Applications of biosynthesized metallic nanoparticles - A review. Acta Biomaterialia. 2014;10:4023-42.
12. Singh P, Kim YJ, Zhang D, Yang DC. Biological Synthesis of Nanoparticles from Plants and Microorganisms. Trends Biotechnology. 2016;34(7):588-599.
13. Byrappa K, Ohara S, Adschiri T. Nanoparticles synthesis using supercritical fluid technology - towards biomedical applications. Advanced Drug Delivery Reviews. 2008;60(3):299–327.
14. Xiangqian Li, Huizhong Xu, Zhe-Sheng Chen and Guofang Chen. Biosynthesis of nanoparticles by microorganisms and their applications. Journal of Nano materials; 2011.

15. Ince S. Determination of retention, characterization and anti-microbial properties of Ag, Au and Pt nanoparticles by green synthesis method using yolks of quail eggs. Master Thesis. Erzurum; 2017.
16. Monaliben Shah, Derek Fawcett, Shashi Sharma, Suraj Kumar Tripathy, Gered Eddy Jai Poinern Green Synthesis of Metallic Nanoparticles via Biological Entities. Materials. 2015; 29;8(11): 7278-7308
17. Iravani S. Green synthesis of metal nanoparticles using plants. Green Chemistry. 2011;13:2638–50.
18. Bello SA, Agunsoye JO, Hassan SB. Synthesis of coconut shell nanoparticles via a top-down approach: Assessment of milling duration on the particle sizes and morphologies of coconut shell nanoparticles. Mater. Lett. 2015;159: 514–519.
19. Amendola V, Meneghetti M. Laser ablation synthesis in solution and size manipulation of noble metal nanoparticles physical chemistry chemical physics. 2009;11(20): 3805–3821.
20. Sreekar Bhaviripudi, Ervin Mile, Stephen A Steiner 3, Aurea T Zare, Jing Kong, Angela M Belcher et al. CVD Synthesis of Single walled Carbon Nanotubes from Gold Nanoparticle Catalysts. Journal of American Chemical Society. 2007;129(6): 1516–1517.
21. Adachi M, Tsukui S, Okuyama K. Nanoparticle synthesis by ionizing source gas in chemical vapor deposition Japanese. Journal of Applied Physics. 2003;42(1A):L77.
22. Smith N, Raston CL, Saunders M, Woodward Ret al. Synthesis of magnetic nanoparticles using spinning disc processing. Technical Proceedings of the 2006 NSTI Nanotechnology Conference and Trade Show. Nano Science and Technology Institute, 2006;1:343-346
23. Kammler HK, Mädler L, Pratsinis SE. Flame synthesis of nanoparticles. Chemical. Engineering Technology Indian Chemical Plant Equipment Process Engineering Biotechnology. 2001;24(6): 583–596.
24. Rosaria D’Amato, Mauro Falconieri, Serena Gagliardi, Ernest Popvici, Emanuele Serra, Gaetano Terranova, Elisabetta Borasella et al. Synthesis of ceramic nanoparticles by laser pyrolysis: From research to applications. Journal of Analytical and Applied Pyrolysis. 2013;104: 461–469.
25. Moghaddam AB, Namvar F, Moniri M, Tahir PM, Azizi S, Mohamad R. Nanoparticles biosynthesized by fungi and yeast: A review of their preparation, properties, and medical applications. Molecules. 2015;20:16540–65.
26. Hayrunnia Nadaroglu, Azize Aliayli, Gungor, Selvi Ince, Anyur Babagil. Green synthesis and characterisation of platinum nanoparticles using quail egg yolk. Spectrochemical Acta Part a-Molecular and Biomolecular Spectroscopy. 2017;11: 411–9.
27. Cicek S, Gungor AA, Adiguzel A, Nadaroglu H. Biochemical evaluation and green synthesis of nano silver using peroxidase from Euphorbia (*Euphorbia amygdaloides*) and Its Antibacterial Activity. Journal of Chemistry; 2015. DOI: 10.1155/2015/486948
28. Narayanan KB, Sakthivel N. Biological synthesis of metal nanoparticles by microbes. Advances in Colloid and Interface Science; 2010.
29. Mukhopadhyay NK, Yadav TP. Some Aspects of Stability and Nanophase Formation in Quasicrystals during Mechanical Milling. Israel Journal of Chemistry. 2011;51:1185–96. DOI: 10.1002/ijch.201100145
30. Manoj D, Saravanan R, Santhanalakshmi J Shilpi Agarwal, Vinod Kumar Gupta, Rabah Boukherroub et al. Towards green synthesis of monodisperse Cu nanoparticles: An efficient and highly sensitive electrochemical nitrite sensor. Sensors Actuators B Chemical. 2018;266: 873-882
31. Ramesh P, Rajendran A, Sundaram M. Green synthesis of zinc oxide nanoparticles using flower extract Cassia auriculata. J Nanoscience Nanotechnology. 2014;2(1):41-45.
32. Alijani HQ, Pourseyedi S, Torkzadeh Mahani M, Khatami M et al. Green synthesis of zinc sulfide (zns) nanoparticles using stevia rebaudiana bertoni and evaluation of its cytotoxic properties. Journal of Molecular Structure. 2019;1175:214-218.
33. Khatami M, Varma RS, Zafarnia N, Yaghoobi H, Sarani M, Vinod G Kumar, et al. Applications of green synthesized Ag, ZnO and Ag/ZnO nanoparticles for making

clinical antimicrobial wound-healing bandages. Sustainable Chemical and Pharmacy. 2018;10:9-15.

34. Rocca A, Moscato S, Ronca F, Simone Nitti, Virgilo Mattoli, Mario Giorgi, Gianni Cifoni et al. Pilot in vivo investigation of cerium oxide nanoparticles as a novel anti-obesity pharmaceutical formulation. Nanomedicine. 2015;11(7):1725-34.
35. Charbgoo F, Ramezani M, Darroudi M. Bio-sensing applications of cerium oxide nanoparticles: Advantages and disadvantages. Biosens Bioelectron; 2017.
36. Arumugam A, Karthikeyan C, Haja Hameed AS, Kasi Gopinath, Shanmugam Gowri, Viswanathan Karthika et al. Synthesis of cerium oxide nanoparticles using *Gloriosa superba* L. leaf extract and their structural, optical and antibacterial properties. Materials Science and Engineering: C. 2015;49:408-415.
37. Miri A, Sarani M. Biosynthesis, characterization and cytotoxic activity of CeO2 nanoparticles. Ceramics International. 2018;44(11):12642-12647.
38. Cardenas S, Issell D, Gomez-Ramirez M, Norma Gabrelia Rojas- Avelizapa, Monica Araceli Vidales- Hurtado et al. Synthesis of cadmium sulfide nanoparticles by biomass of Fusarium oxysporum f. sp. lycopersici. Journal Nano Research. 201;46:179-191.
39. Bhadwal AS, Tripathi RM, Gupta RK, Biogenic synthesis and photocatalytic activity of CdS nanoparticles. RSC Advances. 2014;19:9484-9490.
40. Elsalam SSA, Taha RH, Tawfeik AM, Mohamed O Abd El- Monem, Hanady A. Mohmoud et al. antimicrobial activity of bio and chemical synthesized cadmium sulfide nanoparticles. Egypt Journal of Hospital Medicine. 2018;70:1494–1507.
41. Balasooriya ER, Jayasinghe CD, Jayawardena UA. Honey mediated green synthesis of nanoparticles: New era of safe nanotechnology. Journal of Manometer; 2017.
42. Francis S, Joseph S, Koshy EP, et al. Green synthesis and characterization of gold and silver nanoparticles using Mussaenda glabrata leaf extract and their environmental applications to dye degradation. Environmental Science Pollution of Research International. 2017; 24:17347–17357.
43. Hussain I, Singh NB, Singh A, Singh H, Singh SC. Green synthesis of nanoparticles and its potential application. Biotechnology Letter. 2016;38(4):545-60.
44. Korbekandi H, Iravani S, Abbasi S. Production of nanoparticles using organisms. Critical Reviews in Biotechnology. 2009;29:279–306.
45. Gao Y, Wei Z, Li F, Yang ZM, Chen YM, Zrinyi M, et al. Synthesis of a morphology controllable Fe3O4 nanoparticle/hydrogel magnetic nanocomposite inspired by magnetotactic bacteria and its application in H2O2 detection. Green Chemistry. 2014;16:1255–61.
DOI: 10.1039/c3gc41535j
46. Manivasagan P, Venkatesan J, Sivakumar K, Kim SK. Actinobacteria mediated synthesis of nanoparticles and their biological properties: A review. Critical Reviews in Microbiology. 2016;42: 209–21.
DOI: 10.3109/1040841x.2014.917069
47. Chanda S. Silver nanoparticles (Medicinal Plants Mediated): A New generation of antimicrobials to combat microbial pathogens – A review. Microbial Pathogens and Strategies for Combating Them: Science Technology and Education. Formatex Research Centre, Badajoz, Spain; 2014.
48. Mohammadlou M, Maghsoudi H, Jafarizadeh-Malmiri HJIFRJ. A review on green silver nanoparticles based on plants: Synthesis, potential applications and eco-friendly approach. International Food Research Journal. 2016:23(2):446-463.
49. Manor Joshua, Feldblum Esther S, Arkin, Isaiah T. Environment polarity in proteins mapped noninvasively by FTIR spectroscopy. The Journal of Physical Chemistry Letters. 2012;3(7).
50. Brielle Esther S, Arkin Isaiah T. Site-specific hydrogen exchange in a membrane environment analyzed by infrared spectroscopy. The Journal of Physical Chemistry Letters. 2018;9(14).
51. Deepty M, Ch Srinivas, E. Ranjith Kumar, N. Krisha Mohan, CL. Prajapat, TV Chandrasekhar Rao, Sher Singh Meena, Amit Kumar Verma, and D. L. Sastry. XRD, EDX, FTIR and ESR spectroscopic studies of co-precipitated Mn–substituted Zn–ferrite nanoparticles. Ceramics International. 2019;45(6):8037-8044.
52. Shah M. Green synthesis of metallic nanoparticles via biological entities. Materials. 2015;8:7278–7308.

53. Fahimeh Charbgoo et al. Cerium oxide nanoparticles green synthesis and biological applications. International Journal of Nanomedicine. 2017;12: 1401–1413.
54. Sista Kameswara Srikar. Green synthesis of silver nanoparticles: A review. Green and Sustainable Chemistry. 2016;6:34-56.
55. Ghidan AY, Al-Antary TM, Salem NM, Awwad AM. Facile green synthetic route to the zinc oxide (ZnONPs) nanoparticles: Effect on green peach aphid and antibacterial activity. Journal of Agricultural Science. 2017a;9(2):131-138.
56. Pilarska A, Wysokowski M, Markiewicz E, Jesionowski T. Synthesis of magnesium hydroxide and its calcinates by a precipitation method with the use of magnesium sulfate and poly (ethylene glycols). Powder Technology. 2013;235: 148-157.
57. Ghidan AY, Al Antary TM, Awwad AM. Aphidicidal potential of green synthesized magnesium hydroxide nanoparticles using Olea europaea leaves extract. ARPN Journal of Agricultural and Biological Science. 2017b;12(10):293-301.
58. Huang S, Wang L, Liu L, Hou Y, Li L. Nanotechnology in agriculture, livestock, and aquaculture in China. A review. Agronomy for Sustainable Development. 2015;35:369-400.
59. Kah M, Hofmann T. Nano pesticide research: Current trends and future priorities. Environment International. 2014; 63:224-235.
60. Shankramma K, Yallappa S, Shivanna MB, Manjanna J. Fe_2O_3 magnetic nanoparticles to enhance S. lycopersicum (tomato) plant growth and their biomineralization. Applied Nanoscience. 2016;6:983-990.
DOI: 10.1007/s13204-015-0510-y
61. Lin D, Xing B. Phytotoxicity of nanoparticles: Inhibition of seed germination and root growth. Environmental Pollution. 2007;150(2): 243-250.
DOI: 10.1016/j.envpol.2007.01.016
62. Salem NM, Albanna LS, Abdeen A, Ibrahim OQ, Awwad AI. Sulfur nanoparticles improves root and shoot growth of tomato. Journal of Agricultural Science. 2016;8(4):179-185.
DOI: 10.5539/jas.v8n4p179
63. Naseri N, Ajorlou E, Asghari F and Pilehvar-Soltanahmadi Y, Artif Cells Nanomedicine Biotechnology. 2017; 1–11.
DOI: 10.1080/21691401.2017.1379014
64. Segets D, Lucas JM, Klupp Taylor RN, Scheele M, Zheng H, Alivisatos AP and Peukert W, ACS Nano. 2012;6:9021–9032. Gu H, Ho PL, Tong E, Wang L, Xu B. Presenting vancomycin on nanoparticles to enhance antimicrobial activities. Nano Lett. 2003;3:1261–1263.
65. Chen YH, Tsai CY, Huang PY, Chang MY, Cheng PC, Chou CH, Wu CL. Methotrexate conjugated to gold nanoparticles inhibits tumor growth in a syngeneic lung tumor model. Molecule of Pharmaceuticals. 2007;4:713–722.

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