Review Article

Synthesis, Characterization, and Applications of Nanoparticles

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Received: 09-08-2022; **Revised:** 21-10-2022; **Accepted:** 28-10-2022; **Published on:** 15-11-2022.

ABSTRACT

There is a growing interest among researchers in the field of nanotechnology. This is because of its diverse applications especially in medicine. Materials at the nanoscale exhibit different and improved physical, chemical, and biological properties from the bulk material. This is because of the increased surface area of the material at the nanoscale which is made available for interaction. Nanoparticles are particles in the nanometer range usually between 1 nm and 1,000 nm. In this review, we explained the different methods of synthesizing nanoparticles. Emphasis was placed on green synthesis because of its advantages over other methods such as affordability, accessibility and environment friendly. The applications of nanoparticles were discussed. Nanoparticles could serve as potential drug delivery systems that could be used to improve efficacy and minimize adverse effects of drugs.

Keywords: Nanoparticles, green synthesis, metallic precursor, reducing agent.

QUICK RESPONSE CODE →

DOI:
10.47583/ijpsrr.2022.v77i01.003

DOI link: http://dx.doi.org/10.47583/ijpsrr.2022.v77i01.003

INTRODUCTION

There is now an industrial revolution in the manner in which products are synthesized and manufactured.[1] This came up as a result of the combination of knowledge from different fields such as biology, chemistry, physics, and engineering to give rise to a new field called nanotechnology. The word 'nanotechnology' is made up of two words, "nano" which is the prefix and "technology" which is the suffix. The prefix, "nano" is a Greek word that means "dwarf".[2] It can be said that the word "nano" means extremely small size. The word "nano" refers to a billionth. When looking at the two words, "nano" and "technology", it can confidently be said that nanotechnology is the technology which is applied to materials to make their sizes be at the nano level. Nanotechnology is defined as the study, synthesis, design, manipulation, manufacture and application of materials and devices at the nanometer level. One nanometer is equal to a billionth of a metre (1 nm = 10^{-9} M). The appropriate unit of measurement used in nanotechnology is the nanometer (nm). Generally, nanotechnology considers sizes of materials that are in the nanometer scale usually between 1 nm and 1000 nm.

The characteristics of a material at the nanolevel are usually different from the bulk (Larger scale) material. When there is a reduction in the size of a material, the characteristics might remain the same in the first instance, when the size is further reduced, little changes take place, and when the size of the material is continuously reduced below 1000 nm, there is a significant change in the properties of the material. Materials at the nanoscale level exhibit different and improved physical, chemical and biological properties from the bulk material. This is because of the increased surface area of the material at the nanoscale which is made available for interaction.

Medical applications of nanotechnology

The application of nanotechnology in medicine is known as nanomedicine. Nanotechnology has found application in medicine in areas such as the diagnosis of disease, treatment of disease, and novel drug delivery systems for potentially ineffective and toxic drugs. The common areas where nanotechnology has potential application in medicine include the following:

a. site-specific drug delivery

b. treatment of neurodegenerative disorders

c. avoidance of antibiotic resistance

Site specific drug delivery

The conventional drug delivery systems exhibit numerous challenges especially lack of site specific targeting and untoward side effects. This is due to the fact that when the drug is administered, it does not only get to the morbid cell, which is meant to be its site of action, but also to other parts of the body. Since the body is flooded with drugs that attaches to other receptors, it leads to serious adverse effects. The idea of 'drug targeting' comes up when a drug is administered, it gets only to the diseased site in order to elicit its action.[3] Site-specific targeting helps in the reduction of drug waste since only the required dose of the drug is taken. It also reduces cost for the patients. Since the drug attaches to the required receptor without getting to the unwanted cells, this prevents other parts of the

body from experiencing the adverse effects of such drug. Another importance of site specific targeting is that the drug can be made accessible to some tissues that cannot be accessible by the drug that is not site-specific in its action. For instance, it might be possible that a drug might not get to certain tissues of the body because of its poor solubility. This drug with poor solubility can be formulated with a drug delivery system such as a nano-drug delivery system having both the hydrophilic and hydrophobic chains so as to enhance its solubility. Nanoparticles can be successfully use in site-specific drug delivery.[4]

Treatment of neurodegenerative disorders

Neurodegenerative disorders are group of disorders that result from the progressive loss of the function or structure of neurons and even death of neurons at the nervous system. [5] The nervous system is made up of the central nervous system and the peripheral nervous system. Some examples of neurodegenerative disorders include: Parkinson's disease, amyotrophic lateral sclerosis, and Alzheimer's disease. Neurodegenerative diseases cannot be treated.[6] As a result of the incurable nature of such diseases, this leads to progressive degeneration of neurons or death of the neuron. Sometimes, it might also lead to both degeneration and death of the neuron cells.

A drawback in the failure of current therapy to effectively cure these disorders is the inability of the conventional drugs to effectively cross the blood brain barrier (BBB) and reach the morbid cell .[7] The BBB is a membrane whose function is to protect the brain. The BBB acts as a barrier by preventing the passage of large molecules into the brain while allowing the passage of small molecules like oxygen to pass through. From the knowledge of the above physiology of the BBB, nanodrug delivery systems such as nanoparticles can be effectively designed in such a way that they can successively permeate the BBB and reach the diseased cell.

Avoidance of antibiotic resistance

Currently, the treatment of bacterial infections is posing a serious challenge to healthcare providers. This is because of resistance exhibited by most antibacterial agents. This has led to severe life-threatening infections. The development of resistance by most antibacterial drugs has led to the search for new agents with antimicrobial properties. Metal nanoparticles have the potential to be used as agents that can eliminate microorganisms.[8] Tuberculosis is a life-threatening infection which has a long duration of treatment. The long duration involved in the treatment of tuberculosis affects the patient's quality of life and is usually worrisome to patients. The treatment of tuberculosis involves the use of many drugs which gives rise to polypharmacy. Polypharmacy is known to hinder patient's adherence to drugs. In most cases, the poor adherence of the anti-tuberculosis drugs by patients can lead to the emergence of the multi-drug resistant strains of the bacteria.[9] The development of a nanodrug delivery system in the form of nanoparticles to encapsulate the anti-tuberculosis drugs can lead to a more efficacious tuberculosis therapy and can also be used to avoid drug interactions when anti-tuberculosis drugs are used concomitantly with anti-retroviral drugs. Generally, antibiotic resistance could be circumvented when nano-based drugs especially nanoparticles are used either in combination therapy or to encapsulate drugs. This might lead to improved pharmacokinetic properties of the drug.

Methods of Synthesizing Nanoparticles

Nanoparticles can be synthesized using two approaches which are top-down approach and bottom-up approach. The bottom-up approach involves the building-up of substances from atom to clusters and then to nanoparticles. In the bottom-up approach, there is the assembling or coalescence of atoms and molecules to form different size of nanoparticles. The examples of the bottom-up approach are sol-gel processing, biosynthesis, laser pyrolysis, chemical vapour deposition (CVD), and the self-assembly of monomer molecules. The top-down approach deals with the reduction of the bulk material to particles having the nanometric scale range. Mechanical milling, thermal decomposition, laser ablation and nanolithography are some of the commonly used top-down approach for the synthesis of nanoparticles. A diagrammatic representation of the two approaches is depicted in Figure 1.1.

Generally, the synthesis of nanoparticles involves three methods namely:

i. Chemical methods

ii. Physical methods

iii. Biosynthesis or bio-assisted methods

Chemical methods: Some of the commonly used chemical methods for the synthesis of nanoparticles include sol-gel method, microemulsion technique, polyol synthesis, hydrothermal synthesis, plasma enhanced chemical vapour deposition and chemical vapour synthesis.

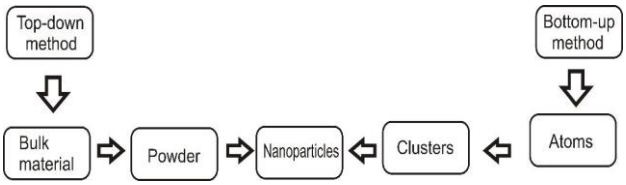

Figure 1: Top-down and Bottom-up Approaches used in the synthesis of nanoparticles[10]

a. Sol-gel method

The sol-gel method involves two components which are 'sol' and 'gel'. The sol refers to a colloidal suspension of solids suspended in a liquid medium. On the other hand, the gel refers to solid polymers which are submerged in a liquid. In the sol-gel method, a chemical solution serves as a precursor for the whole system of individual particles. In the sol-gel process, there are basically two steps, viz: hydrolysis and condensation. During the process of hydrolysis, water is used to break down the bonds of the precursor and this is

the first step for the gel phase to be formed. The process of hydrolysis is followed by condensation which enables formation of nanomaterials. Excess water is then removed and this enables the establishment of the final structure of the material.[11] The chlorides and metal oxides are usually used as precursors in the sol-gel method. The precursor is dispersed in a liquid either by stirring or shaking and the formed system contains a solid and liquid phase. The nanoparticles are recovered by a phase separation using different methods such as filtration, sedimentation, and centrifugation. Finally, the moisture is removed by drying. The most preferable bottom-up approach is the sol-gel method because of its simplicity and most nanoparticles can also be synthesized.[10]

b. Microemulsion technique

Microemulsion is a thermally stable, optically transparent, macroscopically homogenous and isotropic dispersions consisting of at least three phases which are polar phase (usually water), non-polar phase (usually oil or hydrocarbon liquid) and surface acting agent (surfactant). The surfactant serves as a barrier which prevents the coalescence of the droplets. Microemulsion system is made up of monodispersed spherical droplets of either oil-in-water (O/W) or water-in-oil (W/O) with diameter which ranges from 600 nm to 8000 nm. [11] A good reaction site for the synthesis of nanoparticles is the water-in-oil reverse micellar system. Micelles are simply lipid molecules that are organized in a spherical form in solutions containing water.[12] The creation of a micelle is as a result of the amphipathic nature of fatty acids. This means that micelles contain both the polar head groups (hydrophilic regions) and the long hydrophobic chain (hydrophobic regions). The hydrophilic regions of the micelles form the outside and are attracted to water since they are polar. The hydrophobic tails of the micelles, which are inside, are away from water because they are nonpolar.

The reverse micelle is simply the W/O microemulsion, the polar head of the surfactant which creates the aqueous core resides inside while the organic tail of the surfactant is directed outside. The procedure used in the formulation of metallic nanoparticles in water- in- oil microemulsion involves the combination of two microemulsions containing a reducing agent and a metal salt. [13] Sodium borohydride usually serves as the reducing agent while the surfactant could be Triton X-100.

c. Polyol synthesis

The polyol process is simply the synthesis of metal-containing compounds which uses poly(ethylene glycols) as the reaction medium and this does the function of solvent, reducing agent and complexing agent concomitantly, with dissolved stabilizing agents. A wide range of metal based nanoparticles (Cu, Ag, Pd, Pt), metal oxide nanoparticles (Cu_2O, ZnO) and magnetic nanoparticles can be synthesized using the polyol synthesis. The synthesis of polycrystalline nanoparticles of Cu_2O can be carried out using copper nitrate (which serves as the precursor), ethylene glycol (which serves as the reducing agent) and poly(vinyl pyrrolidone) acting as the stabilizing agent.[11]

Physical methods

The physical methods make use of mechanical pressure, thermal energy, electrical energy or high energy radiations to enable material abrasion, evaporation, melting or condensation so as to generate nanoparticles. The physical methods usually operate on top-down method. The advantage of this method is that there is a production of uniform monodisperse nanoparticles and are devoid of solvent contamination. [14] On the other hand, the physical processes are less economical as a result of the numerous waste produced during the process of synthesis. The high energy ball milling, electrospraying, laser ablation, inert gas condensation, melt mixing, and laser pyrolysis are some of the common physical methods that could be used to generate nanoparticles.[15]

High energy ball milling

In this process, there is a transfer of kinetic energy from the moving balls to the milled material.[16] This brings about the splitting of their chemical bonds and breaking of the milled materials into smaller particles having newly created surfaces. The high energy ball milling process can also be said to be a machanochemical synthesis process because it involves very high temperature and pressure conditions.

Melt mixing

This method takes place when a polymer is mixed mechanically with nanofillers by kneading or extrusion.[17] Since this process is well-suited for present industrial practices and also environment friendly, it can be said to be the most commonly used mechanical process.

Pyrolysis

Pyrolysis deals with the burning of precursor with flame.[18] The precursor can either be a vapour or liquid that is fed through a small hole into the furnace at high pressure where it burn. For the nanoparticles to be recovered, the by-product or combustion gases is then air classified. A few of the furnaces make use of plasma and laser rather than flame to produce high temperature for evaporation. The benefits of pyrolysis are simple, cost-effective, continuous and efficient process having high yield.

Biosynthesis of nanoparticles

Biosynthesis, green synthesis or bio-assisted methods provides an environment friendly, cost-effective, low-toxic, efficient and biodegradable protocol to synthesize nanoparticles. These methods make use of biological systems such as fungi, bacteria, viruses, actinomycetes, plant extracts, yeast etc to enable the synthesis of metal oxide nanoparticles and metal nanoparticles. The chemical synthesis of nanoparticles causes several hazards such as cytotoxicity, carcinogenicity and genotoxicity.[19] In the physical synthesis, high energy, pressure and temperature are used. Biosynthesis of nanoparticles is beneficial and it is advancement over physical and chemical methods

because it is simple and environment friendly and the use of high temperature, pressure, energy and toxic chemicals is not needed. Usually, biosynthesis involves three steps, namely: selection of reducing agent, selection of stabilizing agent and selection of reaction medium.[20]

Metal nanoparticles

Metal nanoparticles are known to act as delivery vehicles and they also exhibit antimicrobial activities. Nanoparticles are majorly synthesized using plant extract, fungi and bacteria.[19] Metal nanoparticles have been synthesized using several plant extracts such as *Tinospora cordifolia* leaf extract, *Aloe vera* extract, *Butea monosperma* leaf extract, *Azadirachta indica* leaf extract, *Sinapis arvensis* seed exudates, etc.[20] Plant-mediated synthesis of metallic nanoparticles is known to be a generally acceptable method for the production of metallic nanoparticles because of the easy accessibility and affordability of plants. The use of plants during biosynthesis is considered to be safe because hazardous chemicals which are unsafe to public health are not released. Plants contain many cellular structures and dynamic solutions that help them to destroy the toxicity of metals.[20] This has led scientist to go into phytoremediation. The mechanism of detoxification by plants includes chelation, exclusion, and immobilization of the metal ions. Plants have the capacity to tolerate limiting concentrations of toxic metals. It was observed that plants can accumulate essential metals such as zinc (Zn), copper (Cu), iron (Fe) in addition to non-essential metals such as aluminium (Al), cadmium (Cd), arsenic (As) and mercury (Hg). The merits of green synthesis of metal nanoparticles led researchers to search for the bio-reduction mechanism of metal ions by plants and also the likely mechanism of formation of metal nanoparticle by plants. Based on the above information, the bioreduction mechanism of metal nanoparticles in plant extract involves three phases. The three phases involved in the bio-reduction mechanism of metal nanoparticles in plants include the activation phase, growth phase and termination phase. During the activation phase, there is a reduction of the metal ions and nucleation of the reduced metal atoms. Nucleation is defined as the method in which nuclei (seeds) serve as templates for crystal growth.[21] The growth phase refers to the spontaneous joining of small nearby nanoparticles into particles of bigger size; followed by an increase in the stability of nanoparticles. The final shape of nanoparticles is formed during the termination phase.

As a result of the easy availability of plants, green synthesis of nanoparticles using plants extracts appears to be an important topic in the field of bio-nanotechnology. Usually, the green synthesis uses plant extracts that is in aqueous form during the production of metal nanoparticles. This is because there is more reducing agent available in the extract than the whole plant.[20] Moreover, green synthesis of nanoparticles is easier and simpler to be carried out since it does not require particular operating conditions when compared to chemical and physical methods. The technique of plant-mediated synthesis of nanoparticles is environmentally friendly since the synthesized products including waste products arise from natural plant extracts. Furthermore, reducing agents and capping agents which are chemicals such as alcohols, sodium borohydride and sodium citrate are flammable, highly hazardous, and difficult to degrade are needed during the chemical and physical methods. It is established that the rate of reduction of metal ions using plant extracts is quicker when compared to microorganisms.[22] The morphology (size and shape) of the biosynthesized nanoparticles using plants could be controlled by altering the P^H. The waste products arising from the biosynthesis using microorganisms might likely be toxic to the environment depending on the kind of microorganism that is used. Nevertheless, the waste products resulting from plant-mediated synthesis of nanoparticles are usually safe to the environment. Following the above mentioned advantages of plant-mediated synthesis of nanoparticles, it could be said that the biosynthesis employing plants appears to be safe, feasible, simple, affordable and effective technique as well as a better option to physical and chemical nanoparticle preparation method and also microbial-mediated method.

Noble metal nanoparticles

Noble metal nanoparticles such as gold nanoparticles (AuNPs), silver nanoparticles (AgNPs) and copper nanoparticles (CuNPs) are drawing attention as a result of their exceptional biological and physicochemical properties.[23] Three things are needed during the green synthesis of metallic nanoparticles namely: metal precursor, reducing agent and capping or stabilizing agent. The metal precursor is gotten from a specific metal salt depending on which metallic nanoparticle that would be synthesized. Several researchers have been able to synthesize metallic nanoparticles using plant extracts.

Gold nanoparticles (AuNPs)

In a study, it was reported that gold nanoparticles (AuNPs) were synthesized using *Polyscias scutellaria* leaf extract.[24] Tetrachloro(hydrido) gold ($HAuCl_4$) was used as the metal precursor. During the synthesis of AuNPs, nine millilitres of 1.0×10^{-4} M $HAuCl_4$ solution was mixed with one milliliter of aqueous fraction of *P. scutellaria*. The mixture produced was irradiated using ultraviolet lamp for two hours. The synthesized results were characterized to confirm the presence of gold nanoparticles using particle size analysis and transmission electron microscopy- selected area electron diffraction (TEM- SAED). The particle size analysis reveals that the synthesized gold nanoparticles had a particle size of 15.49 nm. This size showed that *P. scutellaria* leaf extract had enough strength to reduce gold (III) ion (Au^{3+}) to elemental gold (Au^0). The transmission electron microscopy – selected area electron diffraction (TEM- SAED) analysis indicates that the synthesized AuNPs were spherical having a diameter of 5 – 20 nm.

In addition, gold nanoparticles (AuNPs) have been synthesized using *Mimosa tenuiflora* bark extract.[25] The filtrate of *Mimosa tenuiflora* served as the reducing agent during the synthesis. The metallic precursor used was tetrachloroauric acid ($HAuCl_4$). Fifteen grams of the plant bark was cut into pieces and kept in 100 ml flask. Seventy millilitres of 99 % pure ethanol and 30 ml of ultrapure water were added. It was then closed with aluminium. This was left at room temperature for fifteen days. The mixture was filtered using 8 µm of Whatman filter paper. It was later filtered with 0.20 µm of acrodisc. Two different concentrations of the metallic precursor (5.3 mM and 2.6 mM) were used in the synthesis. Using a 50 ml tube, 1.6 ml of the plant extract was added. This was followed by the addition of ultrapure water to make it up to 6 ml. Finally, the metallic precursor solution was added. There was immediate stirring using the vortex at 3000 rpm for ten seconds. The synthesis was carried out at 25 °C. The change in the colour of the mixture shows the presence of AuNPs. The most abundant biomolecules in *Mimosa tenuiflora* extract were flavone sakuranetin, tannin, triterpenoids saponins, N,N-dimethyltryptamine alkaloid and chalcones. TEM micrograph reveals the diversity in the shape of the AuNPs. The shape of the AuNPs was determined by the relationship between the differences in the gold precursor concentration and plant extract. The average sizes of the AuNPs when the metallic precursor was used at different concentrations of 5.3 mM and 2.6 mM during AuNPs synthesis were 40 nm and 150 nm respectively.

Silver nanoparticles (AgNPs)

Silver nanoparticles (AgNPs) were synthesized using *Azadirachta indica* leaf extract.[26] During this synthesis, silver nitrate acted as the metallic precursor while the plant extract served as both the reducing and capping agent. Twenty grams of cut leaves of *A. indica* were mixed with 200 ml of double distilled water using a beaker. The mixture was boiled for thirty minutes. The mixture was cooled and filtered using Whatman number one filter paper. The plant extract was stored at 4 °C for further experimental studies. One hundred millilitres of 1 mM solution of silver nitrate were prepared using an Erlenmeyer flask. One millilitre of the plant extract was added to 10 ml of silver nitrate solution. The solution was incubated in a dark chamber to reduce photo-activation of silver nitrate at room temperature. The colour change of solution from colourless to brown indicates the reduction of silver ion (Ag^+) to elemental silver (Ag^0). This colour change is a confirmation of the presence of silver nanoparticles. The TEM analysis reveals that the silver nanoparticles were spherical and homogenous. The average diameter of the synthesized AgNPs was 34 nm. The antibacterial activities of the synthesized AgNPs were evaluated using the disc diffusion method. The synthesized AgNPs had efficient antibacterial activities against *S. aureus* and *E. coli*.

Moreover, silver nanoparticles (AgNPs) were also synthesized using *Catharanthus roseus* leaf extract.[27] Silver nitrate served as the metallic precursor while the plant extract served as both reducing and stabilizing agents. Ten grams of washed and cut leaves of *C. roseus* were mixed with 100 ml of sterilized double distilled water using Erlenmeyer flask. The mixture was boiled for five minutes. The plant extract was filtered using Whatman number one filter paper and stored at -15 °C for further experimental procedure. The filtrate was added to 1 mM silver nitrate solution using an Erlenmeyer flask. There was formation of brown-yellow solution which confirms the presence of AgNPs. The SEM analysis shows that the AgNPs were spherical having an average size from 35 – 55 nm. X-ray diffraction analysis revealed that the AgNPs were crystalline in nature. The synthesized AgNPs exhibited antiplasmodial activity against *P. falciparum*.

Copper oxide nanoparticles (CuONPs)

Copper oxide nanoparticles (CuONPs) were synthesized using *Gloriosa supereba* leaf extract.[28] Cupric nitrate served as the metallic precursor while the plant extract served as both the reducing and stabilizing agents. Dried leaves of *G. superba* were collected, powdered, sieved and extracted using the soxhlet extraction method. Deionized water was used during the extraction for 72 hours. The filtrate was concentrated at 40 ± 5°C with the aid of a rotary flash evaporator. It was then dried to obtain a crude extract (15.50 g) using hot air oven at 50 – 60 °C. An aliquot portion of the extract (0.1 g/ml) was used during the synthesis of copper oxide nanoparticles. One millilitre of the plant extract was added to 2.32 g of cupric nitrate in solution combustion method. An aliquot portion of double distilled water was added to obtain homogenous mixture. The mixture was constantly stirred for about ten minutes. The CuONPs obtained were stored for further experimental studies. TEM analysis showed that the CuONPs were spherical. The size of the nanoparticles was seen to be in the range of 5 – 10 nm. The antibacterial activities of copper oxide nanoparticles were evaluated using agar well diffusion method. It was evaluated against Gram positive bacteria (*S. aureus*) and Gram negative bacteria (*E. coli*, *K. aerogenes* and *P. desmolyticum*). CuONPs showed significant antibacterial property against all the bacterial strains.

In another study, copper oxide nanoparticles (CuONPs) were synthesized using *Ocimum basilicum* leaf extract.[29] Copper sulphate pentahydrate was used as the metallic precursor while the plant extract served as both reducing and capping agent. Ten grams of leaves were added to 100 ml of distilled water. It was boiled for ten minutes. The mixture was allowed to cool and filtered using Whatman number one filter paper. The filtrate was refrigerated for further studies. One hundred millilitres of copper precursor were treated with 10 ml of the aqueous plant extract. It was stirred magnetically for four hours. The synthesized nanoparticles were centrifuged and washed twice using double distilled water. Copper oxide

nanoparticles were collected and dried in an oven at 60 °C. From the UV – Visible absorption spectrum, copper oxide nanoparticles showed an absorption peak between 280 nm and 300 nm. This spectrum shows the presence of CuO only because there was no other measurable peak noticed. The SEM image revealed that the synthesized CuONPs were spherical and well dispersed. The antibacterial activity of the synthesized copper oxide nanoparticles was examined against both Gram – positive (*S. aureus*) and Gram – negative (*E. coli*) bacteria using disc diffusion test. The antibacterial test results showed that *E. coli* was more susceptible to copper oxide nanoparticles when compared to *S. aureus*.

Biosynthesis can be divided into three groups depending on the source of raw materials such as:

a. biomolecules

b. microorganisms

c. plant extracts

Synthesis using biomolecules as the templates

Different biomolecules such as nucleic acids, viruses, diatoms and membranes were utilized as templates to synthesize nanoparticles. It is known that DNA is a biomolecular template which has a strong affinity with transition metal ions. Gold nanoparticles formed when DNA hydrogel was made and crosslinked before including transition metal ions (e.g. Au(III) metal ions) to DNA macromolecules.[11]There is a reduction of Au(III) which leads to the formation of gold (Au) atoms and metal clusters that eventually develop into gold nanoparticles on the chain of DNA.

Synthesis using microorganisms

Actinomycetes, algae, fungi, yeast and prokaryotic bacteria are widely used as bio-reactors for the synthesis of nanoparticles. Massive scientific efforts were put in place to develop this technique of producing diverse nanoparticles (Palladium, Gold, Silver, Cadmium sulfide, Titanium dioxide, etc). By the aid of enzymes generated by cellular activities of microorganisms, microbes grab target ions from their surroundings and then convert the metal ions into the element metal. This type of synthesis can be grouped into either extracellular or intracellular synthesis of nanoparticles depending upon the site of nanoparticle synthesis.[30] The intracellular synthesis of nanoparticles deals with the conveying of metal ions into the microorganism's cell in the presence of enzymes to form nanoparticles. In the extracellular method, there is the entrapping of metal ions on the surface of the microbial cells in the presence of enzymes. In the bacterial biomass, bacteria use a number of enzymes, anionic functional groups, etc to reduce the interacting metal ions.

Synthesis using plant extracts

The green synthesis of nanoparticles using plant extracts is one of the non-toxic, rapid, very effective and ecofriendly methods. The green synthesis has been used to synthesize nanoparticles of noble metals and metal oxides. Different plant biometabolites could aid in the synthesis of nanoparticles based on their role as reducing and capping agents.[31] The reducing agents include the following: terpenoids, tartaric acid, tannic acid, amino acids, sequiterpenes, saponin, secondary metabolites, reducing sugars, citric acid, flavonoids, quercetin, protein, peptide, phenolics, hydrogenase, heterocyclic compounds and functional groups (amines, alcohols, ketones, sulfhydryl and carboxyl acids). On the other hand, the capping agents are tannic acid, pralines, tartaric acid, peptides, extracellular proteins, functional groups (aldehydes, carboxylic acid, alcohols, ketones, sulfhydryl and amines), enzymes and citric acid.

CONCLUDING REMARKS

Nanoparticles are potential drug delivery system that could be used to encapsulate drugs so as to ensure site specific targeting, improved efficacy and reduced adverse effects. The conventional drug delivery systems exhibit several challenges such as lack of site specific targeting, wastage of drugs, and untoward side effects. Nanotechnology is predicted to be the technology that could be used to circumvent the challenges posed by the conventional drug delivery systems. The different methods used in the synthesis of nanoparticles have been discussed including their advantages and disadvantages. The most rewarding research in the synthesis of nanoparticles is through biosynthesis or green synthesis because of its simplicity, affordability, availability, and its environmentally friendly characteristics. The mechanism of formation of metal nanoparticles by plants was highlighted. The possible toxic effects of nanoparticles need to be explored.

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Source of Support: The author(s) received no financial support for the research, authorship, and/or publication of this article.

Conflict of Interest: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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