

A REVIEW ON GREEN SYNTHESIS OF METAL OXIDE NANOPARTICLES BY LEAF EXTRACT FOR BIOMEDICAL APPLICATIONS IN VARIOUS FIELD

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Abstract

Now a day, metallic oxide nanoparticles (NPs) have appeared as having essential business application. In these nanoparticles, the toxicity has also been an important subject of area of research studies. In this context, for decrease the toxicity levels and facilitating an unhindered application in human consumer products the most important solution is the green synthesis of these particles. The biological synthesis of metal oxide nanoparticles by the usage of microorganisms and plant extraction opens up massive possibilities for the manufacturing of biocompatible and cost-effective particles with potential applications in the healthcare sector. The most critical area that requires attention is cancer therapy. So the nanotechnology has used to intervention of improve the existing present therapeutic practices. Nanoparticles of Metal oxide have been identified as therapeutic agents with an extended half-life and therapeutic index. In These metal oxide nanoparticles has been found lesser immunogenic properties. At present, Nanoparticles of metal oxide synthesized by green synthesis method are the subject of considerable research and analysis for the early detection and treatment of tumours. But their performance in the clinical experiments is yet to be determined now. This review paper provides a detailed description of recent research on the green synthesis of metal oxide nanoparticles. In this area of research, the scientific reports have been specially highlighted on the properties and applications of nanoparticles of oxide of titanium, cerium, selenium, zinc, iron, and copper. This review gives the detailed discussion of the importance of green synthesis of metal oxide nanoparticles. This study will also give new insight of new methods that are cost effective and free from pollution.

Index Terms: Green synthesis, Nanoparticles, Metal Oxide, Cost effective, Nanomaterials

1. INTRODUCTION

Feynman (1960) observed that nanoparticles are excellent because "there is plenty of room at the bottom" [1]. In accordance with his prediction, the technology and science of miniaturisation have created new opportunities for addressing the synthesis, characterisation, and use of nanomaterials in society. Because nanoparticles operate as a bridge between bulk materials and atomic or molecular assemblies, there has been an increase in scientific interest in these small objects. Many well-characterized bulk materials have intriguing nanoscale characteristics. Compared to most materials, nanoparticles' high aspect ratio allows for greater reactivity and efficacy. Researchers have shown their skills throughout time and created unique nano-based materials as well as complements for composites that are nanoscale in size [2-4]. Higher resolution picture capture, numerous nano-sized sensors for environmental pollution, a large number of optoelectronics techniques, and nano-engineered solar applications are all notable and significant uses of nanotechnology. The nanoscale is the subject of nanotechnology. Nanostructures have been around from the origin of life, according to the available evidence [5-7]. The accumulated claims for nanostructured materials

in several domains, such as catalysis, have created a substantial demand for nanotechnology. Materials scientists have found carbon-based materials and mineral elemental blends that have potential optoelectronic and dimensional properties that are greater than most of their complements in recent generations [8-11]. While inorganic nanoparticles are made up of magnetic, noble metal, and semiconductor nanoparticles, organic nanoparticles comprise carbon in the configuration of liposomes, fullerenes, dendrimers, and polymeric micelles [12-15]. Due to the difficulty in accessing their precise characteristics in isolated molecules, metallic NPs are crucial for study [16]. The creation of metallic NPs is a current topic of theoretical and, more significantly, "applied research" in nanotechnology [17]. This review focuses on current research initiatives that deal with environmentally friendly inorganic nanoparticle production, which offers benefits over conventional methods that involve environmentally harmful chemical agents. The current article examines conventional synthetic techniques with an emphasis on new innovations of more environmentally friendly methods to produce metal, metal oxide, and other significant nanoparticles. The production methods and the environmental factors that affect the surface shape, dispersity, and other characteristics of these biosynthesized nanoparticles are

then discussed. The research concludes with a review of the current state of affairs and future projections for the manufacture of nanoparticles using various environmentally friendly methods.

2. Bio/Green Synthesis Method

The physical and chemical processes for the synthesis of metallic nanoparticles have been very diverse, with results showing that process parameters such as temperature or concentration etc. significantly influence particle morphology, stability and physicochemical properties. In addition, the production of nanoparticles using conventional methods involves complex chemical and physical processes that may pose potential risks to ecological damage, cellular toxicity or carcinogenicity [18-19]. This has been caused by the use of substances that are harmful, e.g. organic solvents, reduction agents and stabilisers in order to prevent an unwanted agglomeration of colloids. Some nanoparticles are deadly, as a result of their size, composition, form and external interactions, leading to the occurrence of fatal agents in nanoparticles that may prevent them being used clinically or for medical purposes. Consequently, for the manufacture of nanoparticles it is essential to evolve new, biologically compatible and environmentally friendly green processes [20-22]. Unicellular and multicellular organisms are biological agents that have largely been applied to the synthesis of metal nanoparticles. Bacteria, fungi, seed extracts, algae, diatoms, viruses, yeast and several other more important organisms are a few of the most prominent examples. Various attempts at synthesis of metal nanoparticles in bio factories have been explained by a number of sources in the literature. In order to synthesise biocompatible nanoparticles with a variety of sizes, shapes, compositions, and physicochemical properties, the biological factories serve as safe, non-toxic, and environmentally friendly systems. The majority of living things serve as templates that help biological polymers stabilise the nanostructures. These biopolymers help to increase the biocompatibility of these nanoparticles and avoid their aggregation into clusters. However, extracts from the plant provide a broad range of enzymes and reduceor that help to rapidly synthesise nanoparticles. The plant technique is extremely useful compared to the microorganism, as it does not entail any special, complicated or extensive procedures like isolation, culture development and preservation. Furthermore, for the manufacture of large quantities of nano particles synthesis using a plant is quicker, more cost effective and easier to scale up. Figure 1 shows a schematic representation of the synthesis of nanoparticles using green synthesis.

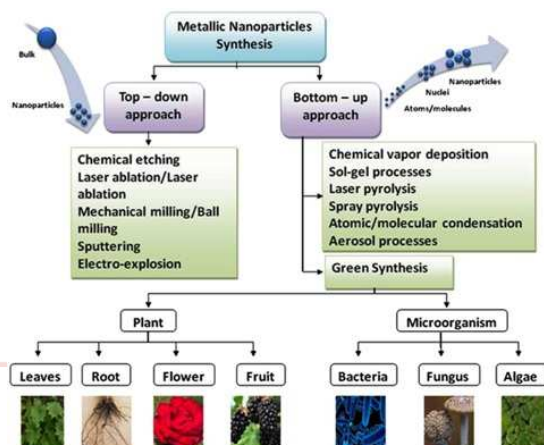


Fig. 1: shows a schematic representation of the synthesis of nanoparticles by green synthesis.

Natural organisms like plants, bacteria, fungi and algae play an important role in sustainable synthesis at times. Natural extracts are capable of acting as a reduction or stabilisation agent [23].

3. Effect of numerous parameters on the Synthesis of Nanoparticles

The nucleation and construction of stabilised nanoparticles are governed by a number of characteristics. For crystalline nanoparticles, which are different in shape and controlled size, a range of claims have been made for their properties such as antioxidant, antimicrobial, anticancer, larvicidal or antibiofilm. The characteristics and magnitude of those features are mostly due to the processing limitations of plant extract, coupled with metal salts response, pH, time of reaction, temperature, concentration of plant extracts into metallic salt as described in this article [24]. Kalimuthu looked at the effects of biomass growth phase on ag nanoparticle synthesis in 2011 [20]. During the stationary phase, it has been observed that an organism *Bacillus* sp. develops a fairly large amount of nanoparticles compared to biomass from different phases. In the stationary phase of bacterial growth, Sweeney et al. demonstrated an intracellularly dense packing of nanoparticles in *E. Coli*[25]. The literature indicates that enzymes and other chemical metabolites have been released during the immobilization phase in order to decrease metal stress which has a positive effect on fungus tolerance. In addition, it was stated that the metal tolerance capacity varies in relation to the type of bacteria and metallic constituents under consideration. For example, in *Aspergillums* sp, it has been demonstrated that nickel is present in the growing medium which results in a longer midlog phase. But in a similar organism, it has been noted that the presence of chromium was found within the medium and prolonged the stagnation phase [26].

3.1: Effect of pH and Concentration of Precursor

Another important parameter affecting the sizes of nanomaterials in chemical synthesis protocols is reported to be the molar ratios of reactants. It is known that products in chemical synthesis may be directly affected by the concentration of reactants. For this purpose, Perumal Karthiga showed that it is possible to systematically regulate the shape of silver nanocrystalline biosynthesize by applying silver nitrate and lemon leaf extracts with different concentrations of reactants [27]. The pH was also stated to have a profound effect on the reduction reaction of the metallic ions. Pandian's analysis revealed the influence of different pH conditions on CdS nano crystallite synthesis by *Brevibacterium* species [28]. The alkaline pH has generally allowed accessible functional groups to be incorporated into the reaction mixture, thus enhancing nucleation and NP formation. It was previously demonstrated that the alkaline environment helps to produce different NPs in association with protein molecules, all of which are carboxylic acids [29]. The pH stability of the biosynthesized nitrogen is checked by Kowshik. The acidification of nanocrystallites resulting from pH 7 to 6 has been found to cause agglomeration and formation of crystals [30]. In another study, the number of Ag NPs synthesized from the bark extract of *Cinnamon zeylanicum* increased with cumulative concentrations of bark extract and higher pH values than 5 and above. Moreover, nanocrystals have been diluted from the solution due to a pH value of less than 6. Biomass production methods for metalmetallic nanospheres with ordered micronucleated structures and programmed functionalities are essential in basic research as well as practical applications, because of their decreased toxicity, reduced pollutant output and energy conservation. Microorganisms, as effective biofactories, have a significant ability to biomineralize and bioreduce metal ions, which can be obtained as nanocrystals of varied morphologies and sizes. The safety and sustainability of the production of nanospheres is improved by an increase in their synthesis [31].

3.2: Effect of Temperature

In numerous studies, the temperature has been shown to have a major influence on nanocrystal morphology and distribution. A large number of studies in the literature indicate that higher temperature conditions are associated with reduced nanoparticles size. For example, when the reaction temperature was raised from 25⁰ C to 60⁰ C, researchers reported a decrease in size of Ag nanoparticles biosynthesized at 35 nm to 10 nm [32]. Sweet orange peel extract was used as a starting point for biosynthesis. When the reaction temperature increased, the reaction rate and particle formation rate increased, although the average particle size decreased and the

particle change rate increased as the temperature increased. In the same context, consideration must also be given to the heat tolerance profile of the biomaterial which is being taken into account for its synthesis. Many researchers report the production of heat shock proteins by microorganisms at elevated temperatures that help to synthesise nanoparticles [33].

4. Applications of Nanoparticles

A schematic representation of the synthesis methods and applications of Nanoparticles discussed in this review is shown in Figure 2. The synthesis of NPs using extracts of leaves (plant) and/or bark provides more extensive applications in biotechnology [34], sensors [35], medicine [36], catalysis [37], optical devices [38], coatings [39], drug delivery [40], water remediation [41], and agriculture [42]. NPs have micro and nanomolar sensitivity, making them capable of being measured with an imaging instrument that allows for the image to be interpreted as well as therapeutic or administration of drugs [43]. There are different biomedical uses for the NPs of various dimensions. In addition, for the use as orthopaedic implant materials, NPs have been loaded onto TiO₂ nanotube implants. Figure 2 shows the different applications of green synthesis nanoparticles.

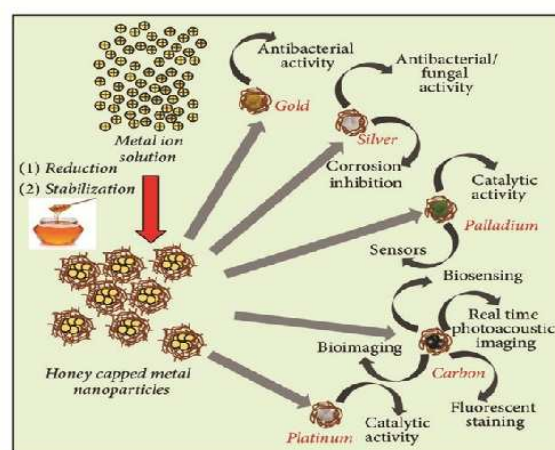


Fig. 2: Applications of green synthesis nanoparticles.

4.1. Anti-Inflammatory Properties of Nanoparticles

A wide range of NPs based on metals, like silver, gold, copper and iron oxide, have been demonstrated to be highly effective in the fight against inflammation. In this review, a mechanism for the development of anti-inflammatory properties in neutrophils has been demonstrated. The mechanism of nano particles in the anti-inflammatory system is shown in Figure 3. Swelling is the immediate response of the body to internal damage, contagion, hormone imbalance, and failure of internal

structures or external features, such as an attack by pathogenic bacteria or an external element. In this way, it triggers overweight, food allergies or interactions with ecological contagions. Adjuvant receptors that can detect biochemical signals are found in differentiated resistant cells. Cellular and tissue damage brought on by an imbalance in the signals regulating inflammation is what leads to swelling [44]. Muscles initiate an inflammatory response in response to damage or infection, which mobilises macrophages and killer cells [45,46]. The important role in self-modifying inflammatory processes is the macrophage. Macrophages are large, mononucleated phagocytes produced in the bone marrow and originate as moveable white blood cells (WBCs) called monocytes in the bloodstream [47]. In a number of tissues, those monocytes are then moved to different places where they become macrophage. There are two types of macrophages: M2 macrophages, which are alternately activated as an anti-inflammatory response and support the remodelling of the swollen tissues and organs, and M1 macrophages, whose production promotes inflammation [48-49]. By overpowering cellular and tissue damage through phagocytosis, macrophages cause swelling and cause inflammation by activating activation signals in the macrophages.

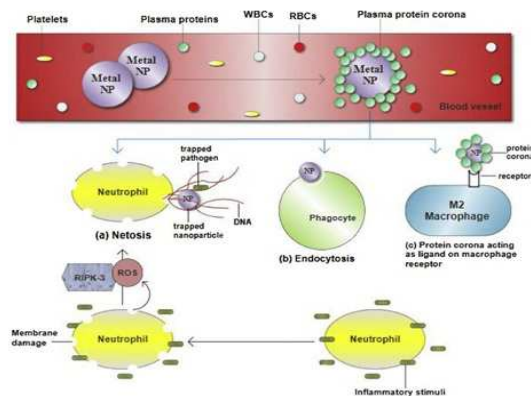


Fig. 3: The mechanism of nano particles in the anti-inflammatory system.

4.2: In Therapeutics

NPs serve as the ultimate platform for biomedical uses and therapeutic interventions. Cancer is a notorious and deadly disease and still stands as one of the principal health issues of the 21st century. Therefore, there is an urgent need for the use of anticancer drugs. Current advances in cancer therapy have been slow to differentiate between cancer and normal cells, and have not produced a complete anti-cancer response [50]. Recent research has shown that metal oxides such as zinc and copper NPs have considerable potential for anti-cancer medicine,

especially when used in conjunction with other anticancer agents [51-52]. Cerium nanoparticles CeO NPs comprised of a cerium core and attached to an oxygen lattice, have demonstrated tremendous potential for treating patients with cancer or other diseases. *Abelmoschus esculentus* (L.) pulp extract was used to make silver nanoparticles (Ag NPs), which have demonstrated potential therapeutic benefits and effectiveness in killing Jurkat cells in vitro. The anticancer activity of Ag NPs was found to be strongly associated with higher levels of reactive oxygen species (ROS) and reactive nitrogen species, with a loss of integrity in the mitochondrial membrane [53]. A liver cancer cell line (HepG2) was used to test the anti-cancer efficacy of Ag NPs made from *Punica Granatum* leaf extract (PGE). The results demonstrated that the PGE Ag NPs had a greater ability to kill cancer cells. A schematic image showing how an Ag NP kills cancer cells is shown in Figure 4. Yet another report by Saratale showed that Ag NPs synthesized from the common medicinal plant dandelion (*Taraxacum officinale*) had a high cytotoxic effect against HepG2 [54]. In addition, the anticancer activity of different types of cancer cells B16: mouse melanoma cell line A549: human lung cancer cell line and MCF7: human breast cancer cell lines have been demonstrated by an AgNP developed with *Oxalis scandens* leaf extract [55].

Recently, the ability of iron oxide NPs to function as both magnetic and photothermal agents for cancer therapy has been demonstrated. The double action has been found to induce complete apoptosis mediated cell death. Furthermore, these iron oxide nanoparticles can be combined with laser therapy, showing complete regression of tumour cells in vivo [56]. Studies show that glioblastoma cancer cells were killed by photothermal treatment utilising green synthesised iron oxide nanoparticles that were loaded with the medication temozolomide and exposed to near-infrared light [57]. When the ICG was free, this photothermal action effectively decreased the breast cancer cell line MCF7 [58]. Geetha synthesised gold nanoparticles from the *C. guianensis* flower in 2013 and investigated their antileukemic cancer activity [59]. Without using a capping agent, Fazal reported greenly synthesised anisotropic and cytocompatible gold nanoparticles and investigated their efficacy along with photothermal treatment [60].

4.3: In Drug Delivery Systems

The effectiveness of using commercially available ocular drug delivery systems to treat infections in the frontal part of the eye is low. Nanoparticles have been designed for use in the manufacture of eye drops and injectable solutions. Nanoparticles have good pharmacokinetic properties, no specific toxic effects, pharmacodynamics,

immunogenicity and biorecognition which increase the effectiveness of drugs that are carried with nanoparticles [61]. Chitosan based polymeric nanoparticles can act as drug carriers, paving the way for the growth of numerous dissimilar colloidal delivery vehicles. These nanoparticles are capable of crossing biological barriers and protecting macromolecules such as peptides, oligonucleotides, proteins, and genes from degradation of biological media, enabling the delivery of drugs or macromolecules to the target site, followed by a precise release of the drug or macromolecules to the target site [62]. Nanoparticles are a promising strategy for the controlled delivery of a drug against human immunodeficiency virus (HIV) named lamivudine, which acts as a potent and selective inhibitor of type 1 and type 2 HIV [63]. Superparamagnetic iron oxide nanoparticles (SPIONs), together with the drug, have been used for site-specific delivery of drugs. The drug can readily bind to the SPION surface and can be guided with an external magnetic field to the desired site, where the nanoparticles can enter the target cell and deliver the drug [64]. The biosynthesized Ag nanoparticles from *Hybanthus enneaspermus* leaf extract were discovered to be efficient reducing agents with substantial promise for remotely activated medication delivery, antibacterial coatings, and wound dressings [38].

4.4: Medical Diagnosis, Imaging, and Sensors

In the field of drug delivery systems and MRI imaging, as well as in MIP hyperthermia for diagnosis and therapy with cancer, iron oxide nanoparticles have been given a great deal of attention [65]. In Sentinel Lymph Nodes (SLNs), critical data on the evolution of fatal cancer can be obtained with a simple imaging technique. It is due to their specific wavelength absorption in the near infrared region, minimal size and swift lymph movement that nucleated carbon nanomaterials derived from Food grade honey can be effectively deployed for SLN imaging. There is great potential for rapid resection of the SLN and also reducing complications in axillary investigations by means of low resolution MRI techniques, which could be used more frequently than currently with other types of scans [66]. Using grape juice, a chemical free hydrothermal process with high water stability, low toxicity and superior stability was used in the synthesis of Fluorescent Carbon Nanoparticles. These nanoparticles can be used for exceptional fluorescent probes in the cellular imaging process and may serve as an emerging alternative to standard quantum dots [68].

5. CONCLUSIONS

The acceptance of green synthesis promises not only to avoid secondary conservational contamination but also to reduce manufacturing costs. Nonetheless, to contribute to the development of this field there remain gaps in research that need to be tackled. Current research on

green synthesis has led to the formation of NPs with a series of geometrical structures, but there is still an urgent need for methods that will allow more complex forms and clearer surface areas. Researchers studying green synthesis may also explore novel features that differ from the majority material of their materials by altering the crystal-like structure of greener NPs. Nanotechnologies have been developed as an attractive tool that can change the course of a variety of fields. To synthesize and use materials with novel properties, it is a technology that operates on the nanometre scale and deals with atoms, molecules, and macromolecules approximately in the range of 1 to 100 nm. It has attracted great interest because it does not involve any harmful chemicals in its synthesis process, which is used to synthesize NPs via the bio green route. Thus, promising materials that could lead to new areas of clinical, energy and environment research can be generated from the Synthesis of Bio Green Nitrogen Phosphorous. The treatment of cancer and the use of nanotechnology in order to improve current health care practices are among the areas where attention is needed. The use of conventional chemotherapeutics is frequently constrained by the negative side effects they produce because cancer is one of the main causes of death and morbidity globally. For effective cancer treatment, the need for a novel strategy to deal with this situation is of great importance. They are also effective agents of bioremediation and have been used in wastewater treatments. Nanotechnology is currently being used in a variety of areas and provides the basis for an important strategy aimed at addressing many problems.

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