



Exploration of plant derived nanoparticles for human healthcare

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Abstract

Nanomaterials may be considered as one of the most promising commodities especially in the field of healthcare, drug-gene delivery, environment, electronics, etc. One of the major investigation revealed applications of nanoparticles and its effect is totally varied with the phases, sizes, and morphologies of these particles. Thus, governed synthesis of nanomaterial with unfamiliar framework has gained much attention. With further improvement, nanoparticles synthesized from medicinal plant products and may provide potential and valuable end products with numerous applications in many fields providing a superior, ecofriendly alternative for harsh and toxic rules, practiced till date. Recently, nanotechnology was gaining more importance in the field of plant science, due to the need to develop miniaturized efficient systems pertaining to improve its seed germination including its growth and protect the plant due to abiotic and biotic stresses. Now a day, major challenge for researchers using plant products as a promising cure for various infectious diseases. In literature, more than 3000 medicinal plant species are reported and showed various immunopharmacological properties but these crude extracts are not proven to be specific and even the doses are not well-defined. Various efforts were taken by researchers to improve the therapeutic effect against infectious diseases from these natural compounds in the form of nanoparticles extracted from medicinal plants and showing some promising results for human healthcare.

Keywords: Nanomaterials, considered, commodities, nanoparticles

Introduction

Nanotechnology is a field of science that deals with the synthesis of particles ranging in nanometres and these particles, synthesized with controlled size, shape and dispersity are called nanoparticles (Ismail *et al.*, 2018) ^[9]. Nanoparticles have many properties of functioning in different ways and have various applications in the areas of medicine, development of surgical nanodevices, nutrition and energy. Generally, it has created remarkable advantage in pharmaceutical industry for curing various diseases caused by bacteria and viruses, especially the production of nanomedicines which are making a huge impact in health care sector in treating infections (Nuzhina *et al.*, 2019) ^[16]. Therefore, researchers are considering eco-friendly synthesis of nanoparticles (Subhapiya and Gomathipriya, 2018) ^[23] as the building blocks of future generations to further control the spread of chronic diseases. In addition, nanoparticles have also played a vital role in agriculture industry like increasing the agriculture potential for improving the fertilization processes (Velmurugan *et al.*, 2013) ^[25]. Though, not all, but some metals like silver, gold and platinum and their oxides such as zinc oxide based nanoparticles has been occupying the centre stage till now and the reason behind it is that they are inert within themselves and most importantly can facilitate their surrounding chemical reactions (Raj *et al.*, 2018) ^[18]. Several methods are introduced for the synthesis of metallic nanoparticles which are physical, chemical, enzymatic and biological, among which the biological method of synthesis has paved more attention as it reduces the use of toxic substances and has also proven to be one of the good methods due to slower kinetics, a better manipulation and most importantly because of their eco-friendly procedures (Ventola, 2017) ^[26]. Recently, the plant mediated

nanoparticle synthesis has derived more attention because of its applications in various fields due to their physio-chemical properties (Raj *et al.*, 2018) ^[18]. Plant crude extract contains primary and secondary metabolites such as phenolic acid, flavonoids, alkaloids and terpenoids which are responsible for the reduction of ionic to formation of bulk metallic nanoparticles by their constant involvement in the redox reactions (Marshlin *et al.*, 2019) ^[13]. The use of plant extracts for nanoparticle synthesis is most favourable because of short process of maintaining the cell cultures. The different parts of plants like stems, roots, seeds, calli, peels, flowers and leaves are used for synthesis of metallic nanoparticles (Marshlin *et al.*, 2019) ^[13]. Based on the facts presented, the review focuses on the nanoparticles derived by the use of plants as it is a less toxic method that can be used for further mediating green synthesis of the metallic nanoparticles. The plants extracts are used either in the green synthesis of the metallic nanoparticles or conjugated with the latter (Rashmi *et al.*, 2017) ^[17].

The metallic nanoparticles play a crucial role in cancer therapy as they provide better targeting and gene silencing. The phytochemical-conjugated metal nanoparticles are being used in the procedure of drug delivery as they enhance aqueous solubility of the plant-based drug and deliver it efficiently to the target site (Gnanavel *et al.*, 2017) ^[5].

Although there are a number of benefits of the metallic nanoparticles, yet there are peculiar loopholes also. The prominent disadvantage includes increased toxicity levels caused by accumulation of the metallic nanoparticles both in the body and in the environment.

There's a lot of free energy in these particles which causes the agglomeration of particles making them ineffective for delivering drugs. Because of such limitations, there is an

ongoing search for other nanomaterials making the future of the metallic nanoparticles a dubious one in cancer therapy.

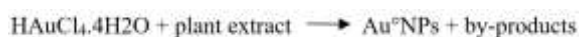
Mechanism of Nanoparticle Synthesis

The most specific yield source for nanoparticle synthesis is the plant biodiversity. Several methods like physical methods including plasma arcing, ball milling, thermal evaporate, spray pyrolysis, ultra-thin films, pulsed laser desorption, lithographic techniques, sputter disposition, layer by layer growth, molecular beam epitaxy and diffusion flame synthesis of nanoparticles; chemical methods such as electrodeposition, sol gel process, chemical solution deposition, chemical vapour deposition, soft chemical method, Langmuir Blodgett method, catalytic route, hydrolysis, co-precipitation method and wet chemical methods (Gan *et al.*, 2012) [3] and biological methods are introduced but because of the adverse effects of physical and chemical methods, the biological method for nanoparticle synthesis is applied as it is eco-friendly in nature (Yuan *et al.*, 2017 [27]; Singh *et al.*, 2018) [22]. Plants with an increased genetic variability possess a variety of molecules in the form of coenzymes, vitamins based intermediates, and plants metabolic materials such as phenolic compounds, alkaloids and sterols which can reduce metal ions of nanoparticles in a single step. With an increasing demand of nanoparticles, the nanoparticle synthesis from the plant extract has derived researchers' interest in the recent years (Hasan *et al.*, 2017) [7]. The use of plant extracts has increased much because they are believed to act as reducing agents and stabilizing agents in the nanoparticle synthesis (Mubarak *et al.*, 2011) [14]. In the synthesis of nanoparticles, the plant extract is directly mixed with a solution of metal salts at room temperature. After the completion of the reaction within a few minutes, as a result of biochemical reduction, the metals convert from monovalent or divalent states to zero-valent states, which is indicated through the colour change in the media vessel. The last step includes the stabilization which occurs by natural capping that preserves the natural structures of nanoparticles.

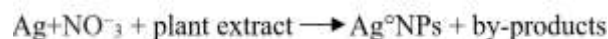
Green Synthesis and Metallic Nanoparticles

Medicinal plants are used and applied for the green synthesis of metallic nanoparticle (gold (Au); silver (Ag); platinum (Pt); copper oxide, CuO; zinc oxide, ZnO). In literature, medicinal plants showed medicinal and clinical importance but now explored for green synthesis of metallic nanoparticles (Kumar *et al.*, 2014 [11]; Ghosh *et al.*, 2015) [4]. Some of the metallic nanoparticles are given below-

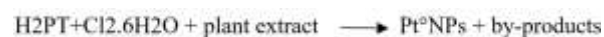
- **Gold (Au):** The plant extract contains different biomolecules such as proteins, sugars, amino acids, enzymes and other traces of metals. These metabolites are involved in the bio-reduction process. The proposed reaction was Au ion reduction into metallic Au nanoparticles in the presence of metabolites and redox enzymes (Halder *et al.*, 2017) [6]. The reaction is as following.



- **Silver:** The biochemical reduction of AgNO₃ reacts with plant solution that leads to the formation of AgNPs by the following reaction (Avoseh *et al.*, 2017) [1].



- **Platinum:** Platinum is involved in the following reaction (Tahir *et al.*, 2017)



- **Copper:** The copper nanoparticles are synthesized from the plant extracts and reduction mechanism was proposed by Devipriya and Roopan, 2017



- **Zinc Oxide:** A typical procedure was involved in ZnO nanoparticles production, the zinc nitrate was dissolved in the aloe plant extract to produce nanosized particles. The method is as follows (Mahendra *et al.*, 2017)



Examples of Nanoparticles Isolated From Medicinal Plants

Now a day, these pathogenic micro-organisms considered as one of the biggest threats in today's world. All these microbes i.e. extracellular or intracellular are getting more resistant against antibiotics. This may happen due to the existence of biofilm layer above the micro-organisms. These biofilms may help us in order to treat infectious disease induced through various pathogenic micro-organisms. Generally, these pathogenic micro-organisms may effect human's life directly or indirectly e.g. formation of plaque in our teeth may cause tooth decay is due to the formation of bacterial biofilm. In general, protection of these micro-organisms is mainly due to biofilms and cause infectious disease. Various studies were conducted and proved that medicinal plant products are more effective in treating disease caused through microbes. Active components were isolated and purified from medicinal plant products may help in the treatment of infectious disease (Nuzhina *et al.*, 2019) [16]. One of the biggest threats or problem is due to antibiotics because most of them are not able to penetrate through the biofilm. A lot of efforts were taken and tried to solve this problem pertaining to convert antibiotics in nanoparticle size. In other words, nanoparticles have high power of penetrating as compared to antibiotics which may help them to controlling microbial growth (Iravani, 2011). Various studies were conducted and most familiar examples are given below-

- **Aloe barbadensis Miller:** It is commonly known as Aloe vera from which silver, gold and zinc oxide nanoparticles are synthesized. *Aloe vera* leaf extract has a medicinal value as it acts as a medicinal agent with various properties including an antibacterial effect. In literature, *aloe vera* constituents are reported in leaves (lignin, hemicellulose and pectins) and used these constituents especially for the reduction of silver ions to produce as silver nanoparticles (AgNPs; spherical shape) and showed antimicrobial activity (Sangeetha *et al.*, 2011) [20]. These nanoparticles also showed some significant effect on gram negative bacteria i.e. *E.coli* and gram positive bacteria i.e. *S. aureus*. In addition, Biogenic gold nano-triangles are also synthesized.

Through simple procedure using *Aloe vera* leaf extract as the reducing agent. This procedure controls the size of the gold nano-triangle and thereby handles their optical properties such as plasmon resonance. The antibacterial and antifungal activities of the zinc oxide nanoparticles from *Aloe vera* also show a maximum inhibitory effect against bacterial strains like *S. aureus*, *S. pyogenes*, *P. aeruginosa*, *E. coli* and *S. typhi* and inhibition of fungal strain like *A. niger*.

- **Azadirachta indica:** It is commonly known as neem from which silver and platinum nanoparticles are synthesized. Flavonoids and terpenoids present in neem leaf extract acts as a reducing as well as a capping agent. It shows highest antimicrobial activities against gram negative bacteria *E.coli*. In literature, addition of silver salt (AgNO_3) solution in aqueous neem leaf extract and its colour change from pale yellow to yellowish brown and then finally to dark brown colour. In contrast, using neem leaf extract, platinum nanoparticles also produced from chloroplatinic acid which on heating changes the colour from light yellow to black, indicating the formation of platinum nanoparticles having a size between 5-50 nm in diameter. Terpenoids present in the leaf extract stabilizes the nanoparticles (Shukla *et al.*, 2012) ^[21].
- **Tamarindus indica:** commonly known as Tamarind where gold and silver nanoparticles are synthesized using fruit extract. The extract taken out of fruit plays a dual role of reducing agent and capping agent for the synthesis of AgNPs. The formation of spherical shape AgNPs is readily confirmed by X-ray diffractometry (XRD), field emission scanning electron microscope (FE-SEM), and high-resolution transmission electron microscope (HR-TEM) while the presence of face-centred cubic (FCC) silver is confirmed by XRD studies and the average crystallite size of AgNPs is calculated to be around 6nm in diameter (Jayaprakash *et al.* 2017) ^[10].
- **Plumbago Zeylanica:** commonly called as White leadwort or Chitrak and belongs to the Plumbaginaceae family. For the synthesis of silver nanoparticles from aqueous extract of *Plumbago zeylanica* considered as one of the simplest assay or friendly environmental method using UV-visible spectrophotometer (446 nm) (Roy and Bharadvaja, 2019) ^[19]. In literature, synthesized silver nanoparticles were determined through SEM image and confirmed it's spherical in shape. So, these silver nanoparticles showed importance in biomedical field and reported advantages in terms of cost effective and compatible for medical and pharmaceutical applications.
- **Catharanthus Roseus:** To develop a novel approach for the green synthesis of silver nanoparticles using aqueous leaves extracts of *Catharanthus roseus* (*C. roseus*) showed immunity against malaria parasite (*Plasmodium falciparum*). In short, these nanoparticles from medicinal plant especially leave may be used for biomedical and nanotechnology based industries (Mukunthan *et al.*, 2011) ^[15].

Conclusion

Overall, these medicinal plants may be considered as one of the vital sources for the synthesis of nanoparticles. So, various methods are applied for synthesis of naturally

occurring metallic nanoparticles and also showed its effectiveness against various infectious diseases. Use of these medicinal plants for the synthesis of nanoparticles is quite the novel leading to truly 'green chemistry' route. In short, nanoparticles are mainly synthesized and provide potential and valuable end products with numerous applications.

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