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How to use Green Technology to Enhance Antioxidant Efficiency of Plant Extracts: A Novel Strategy

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Abstract

Nanotechnology is a rapidly growing science of producing and utilizing the nano-sized particles. It was necessary to develop another non-toxic and environmentally friendly procedure for production of nanoparticles by mean of green technology to avoid production of the hazardous chemicals (sodium borohydride, sodium citrate, ascorbate, elemental hydrogen, Tollen's reagent, N,N-dimethyl formamide and poly (ethylene glycol) block copolymers) produced during the chemical preparation. The metal nanoparticles (MNPs) (silver, gold, platinum, copper and zinc oxide) were biosynthesized through the reaction with plant extract by bio-reduction mechanism. Among all noble MNPs, the silver nanoparticles (AgNPs) are non-toxic and gained boundless interests due to their characteristic properties in addition to their significant antibacterial, antifungal and anti-inflammatory effects.

The UV-Vis Spectrophotometer, X-Ray Diffractometer (XRD), Atomic Force Microscopy (AFM), Fourier Transform Infrared (FT-IR) Spectroscopy, Dynamic Light Scattering (DLS), Energy Dispersive X-ray Spectroscopy (EDX), Scanning Electron Microscope (SEM), Field Emission Scanning Electron Microscope (FESEM) and Transmission Electron Microscope (TEM) are considered as the most widely used techniques for characterization of the synthesized nanoparticles.

Incorporation of the AgNPs into the plant extracts enhanced the antioxidant properties due to increasing the total polyphenolic compounds which exhibit more antioxidant potentials and possesses significant cytotoxicity and free radical scavenging activity than the crude ones. It was revealed that deposition of the nanoparticles was greatest in liver followed by blood, spleen, kidney, lungs, brain, reproductive organs, thymus and heart. Removal of the nanoparticles from the body through renal clearance is considered as a multifaceted process. The review concluded that it is necessary for undergoing further studies to evaluate the deleterious effects that may be occurred as a result of administration of the nanoparticulated extracts.

Keywords: Nanotechnology; Green technology; Metal nanoparticles; Silver nanoparticles; Renal clearance

Introduction

Nanotechnology is defined as a rapidly growing science of producing and utilizing particles at the nano-scale. It is well known that the nano-sized particles exhibit physicochemical and biological properties differ in fundamental and valuable ways from those of individual atoms and molecules [1,2]. Incorporation of metal nanoparticles (MNPs) into polymeric matrices is considered to be one of the most promising solutions to their inherent stability problem. It showed valuable properties in many practical applications [3].

Nanomedicine is defined as utilization of submicron size (<1 um) modules for treatment and diagnosis of various chronic diseases. Synthesis of nanoparticles eco-friendly is considered as building blocks of the forthcoming generations for monitoring and control of biological system [4]. During preparation of nanoparticles, different organic and inorganic reducing agents, such as sodium borohydride, sodium citrate, ascorbate, elemental hydrogen, Tollen's reagent, N,N-dimethyl formamide and poly (ethylene glycol) block copolymers are used for reduction of metal ions in aqueous and non-aqueous solutions [5,6]. These chemicals are toxic and led to non-ecofriendly by-products. This may be the reason which leads to the biosyntheses of nanoparticles via green route that does not employ toxic chemicals [7].

Due to formation of these hazardous chemicals during the chemical preparation of nanoparticles, it was necessary to develop other high-yield, low cost, non-toxic and environmentally friendly procedures [8,9]. Generally, there are two approaches involved in synthesis of silver nanoparticles (AgNPs), either from "top to bottom" approach or a "bottom to up" approach (Figure 1) [7].

Bera TK et al. stated that butylated hydroxyl toluene, tertiary butylated hydroquinone and gallic acid esters are the most common synthetic antioxidants that have been restricted and suspected to cause or prompt negative health effects and may lead to cancerous diseases. Consequently, the recent studies have been directed to search in the medicinal plants to select the most suitable one to be utilized for biosynthesis of AgNPs from a silver nitrate ($AgNO_3$) solution by mean of green technology. Then, the nano-extract used for therapeutic purposes as it does not involve any harmful chemicals. In addition, various natural materials like plants, bacteria, fungi, yeast are used for AgNPs synthesis [10-12].

Plant crude extract is rich in the secondary metabolites (phenolic acid, flavonoids, alkaloids and terpenoids) which are mainly responsible

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for the reduction of ionic into bulk metallic nanoparticles formation. Moreover, these metabolites are constantly involved in the redox reaction to synthesize nano-sized particles [13]. The plant extracts act as reducing and capping agents for synthesis of nanoparticles [14]. They are able to be scaled up for large-scale nanoparticle synthesis [15]. Synthesis of the plant-mediated nanoparticles is preferred because it is cost-effective, environmentally friendly, a single-step method for biosynthesis process and safe for human therapeutic use. Different plant extracts have been studied to be used for synthesis of MNPs in different sizes and shapes [16,2]. Nanocomposites are a combination of two or more organic or inorganic components in which one or more phases with nanoscale dimensions are embedded in a metal, ceramic or polymer matrix. They exhibit a significant proportion of the properties of both constituents such that a better combination of properties is realized. In addition, the constituent phases must be chemically dissimilar and separated by a distinct interface.

Synthesis of AgNPs was extensively studied employing chemical and physical methods, but development of the reliable technology to produce nanoparticles is an important aspect of nanotechnology [1]. It was reported that the AgNPs are of particular interest due to their peculiar properties and wide applications. They are used as anti-inflammatory to treat infections in open wounds and chronic ulcers in addition to its effective role in treatment of brucellosis [17,18].

The biological effectiveness of the AgNPs attributed to its ability to increase the proportionately associated with increasing the specific surface area as a result of increasing their surface energy and catalytic reactivity. Various methods have been used for synthesis of AgNPs, like chemical and photochemical reduction, electrochemical techniques and radiolysis methods [19].

The AgNPs were synthesized by reduction of aqueous $AgNO_3$ into AgNPs during the exposure to plant extracts and could be easily monitored by using UV-visible spectrophotometer. Incorporation of AgNPs into the plant extracts enhanced the antioxidant activity at lower concentrations [20]. It was demonstrated that the biosynthesized nanoparticles effectively controlled oxidative stress, genotoxicity and apoptosis related changes and this might be attributed to the increased total phenolic compounds and total flavonides [21]. Polyphenols are the most biologically active classes of secondary plant metabolites that are structurally characterized by presence of one or more phenol units. They play an effective role in preventing chronic diseases owing to their antioxidants potentials [22,23]. Furthermore, [24] reported that incorporation of AgNPs increased concentration of the polyphenolic compounds with respect to the native extract (without AgNPs).

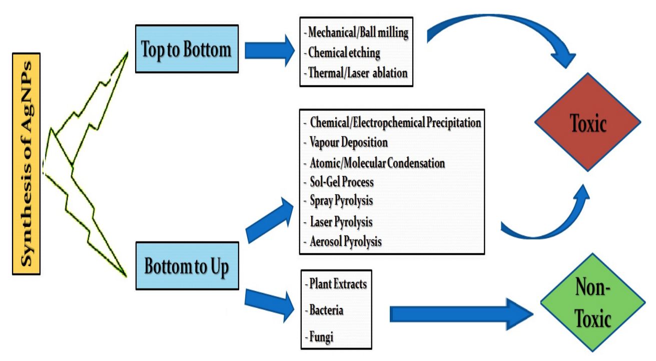

Figure 1: Different approaches for synthesis of silver nanoparticles.

It is worth to mention that MNPs (silver, gold, platinum, copper and zinc oxide) were biosynthesized through the reaction with plant extract by bio-reduction mechanism. Among all noble MNPs, the AgNPs gained boundless interests due to their characteristic properties in addition to their significant antibacterial, antiviral, antifungal and anti-inflammatory effects. It is well known that silver is a nontoxic inorganic agent. It is to kill about 650 types of diseases caused microorganisms. It exhibits vital functions as an antiseptic and displays a broad biocidal effect against various microorganisms through disruption of their unicellular membrane thus disturbing their enzymatic activities [25]. Furthermore, synthesis of AgNPs using plant extracts revealed that the nanoparticulated extracts were economic and cost effective. In addition, this technique provide healthier work places, communities, protecting human health and environment, leading to less waste and more safe products [26,27]. As illustrated in Figure 2, silver nitrate ($AgNO_3$) reacts biochemically with plant extract leading to formation of AgNPs through the reaction suggested by [28]. The reaction time is considered as very effective factor affecting the prepared AgNPs. As revealed in Figure 3, color of the reaction mixture changed within 10 min. during green synthesis of AgNPs [29].

The UV-Vis Spectrophotometer, X-Ray Diffractometer (XRD), Atomic Force Microscopy (AFM), Fourier Transform Infrared (FT-IR) Spectroscopy, Dynamic Light Scattering (DLS), Energy Dispersive X-ray Spectroscopy (EDX), Scanning Electron Microscope (SEM), Field Emission Scanning Electron Microscope (FESEM) and Transmission Electron Microscope (TEM) are considered as the most suitable techniques used widely for characterization of the synthesized nanoparticles.

The XRD as well as TEM considered the most significant technique to examine structural properties of the fabricated nanomaterials. As suggested by [26], it was found that formation and stability of the reduced AgNPs were monitored in the colloidal solution by UV-Vis spectrophotometer analysis. Mean of AgNPs diameter was calculated from the XRD pattern according to line width of the plane, and the refraction peak, using Scherrer's equation. AFM showed the irregular shapes of AgNPs. The FT-IR spectroscopy confirmed the presence of protein as the stabilizing agent surrounding the AgNPs. Moreover, it affirmed the role of plant extract as a reducing and capping agent of silver ions.

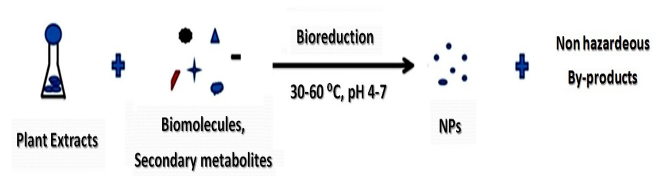

Figure 2: The proposed mechanism of biological synthesis of nanoparticles.

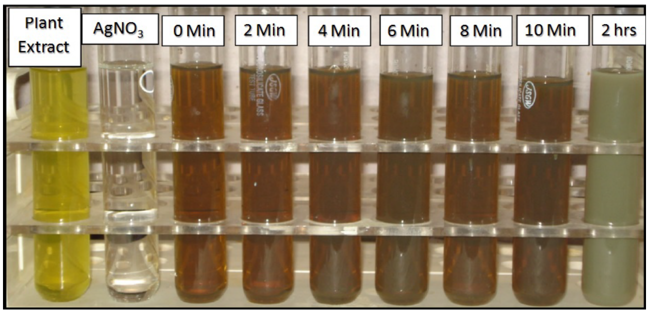

Figure 3: Color change in the reaction mixture within 10 min.

Ibrahim reported that the X-ray diffraction revealed the crystalline nature of AgNPs. The SEM and FESEM showed the spherical shaped and monodispersed nanoparticles. TEM confirmed the spherical nature and the crystallinity of nanoparticles. The average size of nanoparticles was 23.7 nm as determined by DLS. The EDX analysis showed the peak in silver region confirming presence of elemental silver. Furthermore, antimicrobial activity of the silver bio-nanoparticles was performed by a well diffusion method [30].

The recent studies documented that silver plant nano-extracts showed possible applications through enhancing the antioxidant properties after incorporation of AgNPs into the plant extract. This was attributed to increasing the active phytoconstituents which exhibit more antioxidant potentials and possesses significant free radical scavenging activity than the crude extracts. This was supported through increasing number of peaks that represent the phenolic compounds in the nanoparticulated extracts. Thereafter, the nanoparticulated extracts found with increased cytotoxicity against growth of human cancer cells compared to the crude ones. In addition, enhancement of total polyphenolic compounds found to be related to the total antioxidant capacity, iron reducing power and free radicals scavenging activity and hence increasing the anticancer activity through lowering growth of the cancer cells [24]. For these reasons, the AgNPs were incorporated into different extracts prepared recently from Moringa oleifera leaves, Bauhinia variegate leaves and Croton tiglium seeds to be utilized for treatment of chronic diseases like cancers and diabetes.

Although it was revealed that deposition of the nanoparticles was greatest in liver followed by blood, spleen, kidney, lungs, brain, reproductive organs, thymus and heart; whereas the 50, 100 and 250 nm particles were deposited in liver followed by spleen and blood [31], the practical studies emphasized that oral administration of the silver nanoparticulated extracts caused no obvious toxicity in the experimental animals [32]. Kidneys are capable of rapidly removing molecules from the vascular compartment. The renal excretion represents a desirable pathway for removal of nanoparticles with minimal catabolism from the body to avoid the possible side effects. Removal of the nanoparticles from the body through the renal clearance that is considered as a multifaceted process involving glomerular filtration, tubular secretion, and finally elimination of the molecule through urinary excretion [33]. Notably, the previous studies did not evaluate the direct clearance and did not measure urine particle losses, so kidney particle levels reflect nanoparticles present in the kidney at the time of harvesting rather than levels that may have been cleared by the kidneys. However, the predominance of accumulation of nanoparticles in liver suggested that the hepatobiliary system was the primary site for agent clearance for nanoparticles from 10-250 nm [32]. Therefore, it is necessary for undergoing further studies to evaluate the deleterious effects that may be occurred as a result of administration of nanoparticles alone or as nanoparticulated extracts.

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