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Review

Phytofabricated gold nanoparticles and their biomedical applications

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ABSTRACT

In a couple of decades, nanotechnology has become a trending technology owing to its integrated science collection that incorporates variety of fields such as chemistry, physics, medicine, catalytic processes, food processing industries, electronics and energy sectors. One of the emerging fields of nanotechnology that has gained momentous admiration is nano-biotechnology. Nano-biotechnology is an integrated combination of biology with nanotechnology that encompasses the tailoring, and synthesis of small particles that are less than 100 nm in size and subsequent exploitation of these particles for their biological applications. Though the variety of physical techniques and chemical procedures are known for the nanoparticles synthesis, biological approach is considered to be the preferred one. Environmental hazards and concerns associated with the physical and chemical approaches of nanoparticles synthesis has added impetus and zenith to the biological approach involving the use of plants and microorganisms. The current review article is focused on the synthesis of plant-derived (phytochemical) gold nanoparticles alongside their scope in biomedical applications.

Contents

1. Introduction

Nanotechnology is a combination of two words; nano and technology. The term 'nano' originate from 'nanos'. It is a Greek word that means 'extremely small or dwarf' and refers to one billionth part (10^{-9}). In 2006, American Society for Testing and Materials (ASTM) defined the term 'nanoparticles' as particles having at least two or more dimensions ranging in size from 1 to 100 nm [1]. So, nanotechnology is the application of science that controls matter at molecular level [2]. According to a recent definition put forward by British Standards Institution, nanoparticles (NPs) are the particles with one or more dimensions at nanoscale (with dimensions of the order of 100 nm or less) [3]. At this scale, properties of particles are different from their properties at either atomic or molecular levels. This is because, changes in atomic properties are governed by the law of quantum mechanics and molecular properties governed by the laws of classical physics.

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So, the size of a nanoparticle (1–100 nm) serves as an intermediate state between the atomic and molecular (bulk) states.

This intermediate state thus plays a critical role in deciding its fate in such a manner that not only the synthesized nanomaterial behaves differently from its bulk material but also, it reveals certain unpredicted physical and chemical properties. Such change in the behavior of these nanomaterials is still unexplained by classical laws of physics [4]. The aforementioned changes in physical and chemical properties of the manufactured NPs provides them with characteristic thermal conductivity, catalytic, melting point, biological, sterical, mechanical, electrical and optical properties [5–7].

Variety of techniques devised to produce eco-friendly products (NPs) with less hazardous effects [8]. One of the emerging fields of nanotechnology is referred as nano-biotechnology. Nano-biotechnology engrosses biological standards with the chemical procedures and physical techniques to produce NPs for specified uses. Nano-biotechnology is therefore used as an umbrella term that encompasses the tailoring, synthesis and subsequent exploitation of small particles that are less than 100 nm in size [9].

Gold is one of the biocompatible metals also possessing various effective properties against many diseases. From history, it is known that colloidal gold solutions were used to cure various kinds of infections [10]. Well engineered AuNPs are considered to be of more importance as they offer some unique properties like being, more compatible with living tissues/systems, provide more surface reactivity, very small size, diverse range of shapes, and readily oppose oxidation [11,12]. Fabrication of AuNPs by using plants as natural source has provided a better, environmental friendly approach [13]. For instance, the plant extract of *Aloe vera* has been used to get gold nanotriangles of size ranges from 20 to 50 nm [14]. Similarly, *Nyctanthes arbortristis* flower extract has been utilized to synthesize spherical AuNPs of diameter approximately 20 nm [15]. AuNPs synthesis of various shapes have been reported (like, spherical, triangular, quasispherical, cubic hexagonal, decahedral, isosahedral, and rod shaped) using variety of plant sources such as *Anacardium occidentale* [16], *Camelia sinesis* [17], *Cymbopogon* sp [18], *Geranium* [19], *Vitex negundo* L. [20], *Memecylon edule* [21], and *Cinnamomum camphor* [22].

Thus, advances in the applications of the synthesized NPs can be achieved by adjusting both shape and size of the nanoparticles at nanoscale. Such shape and size dependent properties are the main areas to exploit for researchers nowadays. These characteristic features have helped scientists in developing novel antimicrobial formulations, biosensors, drug delivery protocols, medical imaging, treatment of tumors, nanocomposites and filters, catalytic procedures, computer transistors, electrometers, chemical sensors, wireless electronic memory and logic schemes [22–25].

Besides the size and shape dependent properties, the stability of the synthesized NPs is also a major area of research studies. In accordance with Raveendran, choice of solvent, non-toxic synthesizing material and use of reducing agent; that is environmentally safe and non-hazardous; are the three characteristic features important for stability of the fabricated NPs [26].

1.1. Approaches for nanoparticles synthesis

There are two major approaches for the synthesis/construction of NPs; top down and bottom up approaches. Top down approach makes use of physical techniques such as irradiation, arc discharge, diffusion and thermal decomposition. This approach uses grinding and etching techniques to breakdown the bulk material into NPs. While the bottom up approach uses chemical and biological procedures for manufacturing the NPs; as shown in Fig. 1 [27]. This is based upon the assembly of the atoms/molecules into molecular structures with nanometer size range [27]. Chemical processes include chemical reduction, polyol synthesis, seeded growth and electrochemical synthetic methods while biological approach uses biological entities (microorganisms and plants) for the NPs synthesis.

The chemical methods for AuNPs fabrication involves two steps; reduction by reducing agents and subsequent stabilization by the agents. Reduction process uses chemicals such as hydrazine, hydroxylamines, carbon monoxide, polyols, aminoboranes, formaldehyde, acetylene, hydrogen peroxide, hydrogen, citric and oxalic acids, sugars and ono-electronic reducers that contain electron rich transition metal in sandwiched complex forms. The stability of AuNPs is provided by oxygen based ligands, phosphorus ligands, sulfur ligands (e.g. thiolates), nitrogen based ligands, polymers and surfactants (e.g. cetyltrimethylammonium bromide). Presence of stabilizers also avoids aggregation of the synthesized AuNPs [28]. Thus, most of the chemicals used in chemical synthetic procedure are not only flammable and toxic but are also hazardous to the environment. Moreover, the production rate of the synthesized NPs is also low [29,30]. Thus, the toxicity, use of energy, expensive organic chemicals and inefficient production rate limits the applications of the NPs synthesized through chemical routes. Thus arises a need for clean, green, biocompatible, cost effective and ecofriendly approach for manufacturing NPs. While the green synthesis focuses on the use of plant and microorganisms for NPs production. One such approach makes use of microorganisms and plants; shown in Fig. 1 [31,32].

1.2. Chemistry of gold

Gold (Au) exists in six oxidation states on the basis of its high electronegativity; −1, 0, +1, +2, +3 and +4. Mostly, Au forms complexes in auric [Au (III)] and aurous [Au (I)] oxidation states [33]. In an aqueous solution, Au can dissolve by combined action of oxidation and complex formation processes. In the presence of a complex forming ligand, Au (I) and Au (III) can easily form stable complexes. While in the absence of any complex forming ligand in the solution, the solution reduces Au (I) and Au (III) to metallic state [Au (0)]. Not only the complex forming ligand but also the donor atom of the ligand bonded to Au atom is responsible for the stability of the gold complex formed.

Nicol et al., reported two rules for the stability of gold complexes. First rule states that electronegativity of the donor atom increases as the stability of gold complex decreases in such a manner that stable gold halide complexes follows the pattern as: $I^- > Br^- > Cl^- > F^-$. Second rule suggests that Au (III) binds with hard ligands while Au (I) favors the formation of complexes with soft ligands. Thus, Au (I) forms linear complexes with an oxidation state of 2 while Au (III) forms square planar complexes with an oxidation state of 4. As such, the common precursors used for AuNPs synthesis are gold (I) thiosulfate and gold (III)–chloride complex [34].

1.3. Plant mediated synthesis of gold nanoparticles

Gold (Au) has always been a subject of keen interest in primeval times yet its re-creation in the field of evolving nano-technological science has provided it with an increased recognition; especially in the form of self-assembled monolayers (SAMs) and NPs. This review article focusses on plant extract derived gold nanoparticles (AuNPs). Among the variety of synthesized NPs, AuNPs are considered to be the most stable ones. This stability of AuNPs appears as a result of their characteristic optical, electrical, electronic, catalytic, magnetic and biological properties. Also the assembly of AuNPs in material sciences and the behavior of individual particles in the synthesized AuNPs also add further stability to the synthesized NPs. Such potential applications mark