

Green Synthesis of Gold Nanoparticles for Bio-applications

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ABSTRACT

Even though AuNPs were synthesized successfully by chemical approach, synthesizing them by biological methods is becoming important day by day. This is due to the sustainable or green chemistry insight. With this approach, it is likely that bio-synthetically prepared AuNPs will have more biocompatibility; which is more suitable for using them in potential biological applications. Up to now, remarkable works have been done to synthesize the AuNPs using bio-entities such as bacteria, yeast, fungi, plant, fruit extract, peptide and have attained novel results. Contrary to the synthesis by chemical methods, the synthesis by biological systems generally follows non-toxic, moderate processes which occur at ambient temperature and pressure. It has been known that ancient gold colloids had been used for therapeutic and decorative purposes. AuNPs are now widespread used for various applications especially in biology namely labeling, heating, sensing, delivering.

I. Introduction

It is obvious that various gold nanoparticles can be produced by chemical methods [1-6]. But it is now popular to utilize the bio-materials. With the creation of green chemistry that is safe, harmless, and acceptable to the environment methods, biological resources involving a variety of species, including bacteria, fungus, and plants have been used to synthesize the AuNPs [7-19]. Similar to the synthesis by chemical methods, the AuNPs' size and form achieved through bio-route could be controlled by adjusting variables like pH and temperature, the ratio of Au ion to reducing agents and so forth. Some efforts have been done to generate the AuNPs using bacteria. Only a small number of microorganisms have been shown to be capable of selectively reducing particular metal ions [20]. First, Beveridge and Murray showed that AuNPs were formed when exposed to *Bacillus subtilis* [21]. Only a small number of microorganisms

have been shown to be capable of selectively reducing particular metal ions [20]. First, Beveridge and Murray showed that microscopic gold [22]. The reduction of gold ions additionally utilised *Pseudomonas aeruginosa* bacterial cell supernatant [7]. As being shown in this research, with the help of greater control over the size and polydispersity of nanoparticles was achieved using cell filtrate achieved.

Shape-control AuNPs has been attained using the filamentous cyanobacterium *Plectonema boryanum* UTEX 485. With different reaction conditions, cubic AuNPs or octahedral platelets were formed [23]. The mechanisms of gold bioaccumulation by cyanobacteria have also been documented.

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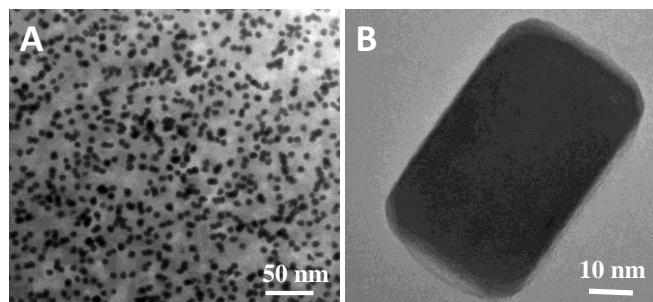


Figure 1. TEM images of synthetic spherical and rectangular gold nanoparticles in (A) from Bay leaves.

Spherical AuNPs in the range of 10-50 nm were using a bacteria called *Brevibacterium casei* to produce and stabilise [24].

Thermomonospora sp., an actinomycete, has been observed to produce reduced the gold ions extracellularly with a much improved polydispersity [25]. In the same year, Ahmad et al. efficiently synthesised monodisperse by doing the reduction on the same substance AuNPs [26]. The reaction was thought to be caused by an enzymatic process and they concluded that the monodispersity maybe as a result of harsh biological circumstances, including the alkaline and slightly raised temperature utilised for the synthesis. Along this line, Additionally, yeast strains have been identified based on generation of AuNPs. According to reports, *S. cerevisiae*, or baker's yeast, biosorbs and converts Au^{3+} into elemental gold [27]. Similar intracellular formation of gold nanoparticles with spherical, triangular, and hexagonal morphologies was seen throughout the cell of the yeast *Pichia jadinii* (*Candida utilis*) [8, 28]. *Yarrowia lipolytica* NCIM 3589, a tropical marine yeast, also produced gold nanoparticles linked to cell walls. Gold ions were reduced in a pH-dependent way [29]. Good monodispersity and well defined gold nanoparticles can be obtained by fungi. Since it is known that fungi produce higher levels of proteins, it is possible to scale up the synthesis. Furthermore, fungi are economic viability and ease in handling biomass. In 2001, Mukherjee et al. achieved the highly monodispersed and well defined AuNPs using the fungus *Verticillium* sp. [9]. The geranium plant's leaves contain an endophytic fungus called *Collitotrichum* sp. that is employed to create stable AuNPs in a variety of shapes [11]. Polypeptides and enzymes were the reducing agent in this fungus. Growth conditions are crucial for the fungi's ability to synthesise AuNPs. When gold ions were incubated with the *Trichothecium* sp. under stationary conditions, extracellular AuNPs were created meanwhile intracellular AuNPs formed under shaking conditions

[30]. Recently, Gold nanoparticles were created using the *Volvariella volvacea*, an edible straw mushroom fungus extract [31]. In this work, AuNPs were found to be of different shapes and hexagonal structures with sizes ranging from 20 to 150 nm were attained.

II. Literature Review

While the golden helmets and Nebra disc first emerged in Central Europe in the second millennium B.C., gold was only unearthed nearby the Varna Necropolis in Bulgaria around five thousand years ago. The ancient colloidal gold was used for both aesthetic and treatment purposes. Gold was used to make the ornaments or artifacts in antiquity in Egypt and China. The Lycurgus cup, which dates to the fourth century, is one of the famous specimens. "Drinkable gold" was also famous for curing various diseases over the centuries such as heart problems, tumors, dysentery. A scientific report on the synthesis of red-colored AuNPs from the reduction of an aqueous solution of chloroaurate ($AuCl_4^-$) using phosphorus in CS_2 was made by Michael Faraday in 1857 [1]. Over the past years, a great deal of researches for preparing AuNPs has been reported and reviewed. The publications of this subject has increased considerably especially after the reports by Schmid and Brust et al. [2]. There are various ways to synthesize the AuNPs normally starting from commercial $HAuCl_4$. The most popular method to generate the AuNPs, which is still preferably used nowadays for exchanging appropriate ligands of biological interests, is citrate reduction of $HAuCl_4$ in water. This method was introduced in 1951 by Turkevitch et al. [3]. It gives the AuNPs of about 20 nm. Recent modifications of this method have shown better size distribution and size control. A practical preparation of AuNPs capping with sodium 3-mercaptopropionate was reported in which citrate salt and an amphiphile surfactant were simultaneously added. The size could be tuned by varying the ratio between stabilizer and gold [4]. The most efficient stabilisers for capping the AuNPs were thiolates, which are based on the robust Au-S link between the soft acid Au and thiolate base. Other stabilisers that were tested included ligands, surfactants, polymers, dendrimers, and others. Mulvaney and Giersig were the first to report on the stabilisation of AuNPs by alkanethiols with various chain lengths in 1993 [5].

In comparison to chemical synthetic methods biosynthetic methods are appreciable for their easy and less toxic synthetic pathway and due to their great utility in therapeutic field [21-29]. Recent years, It has

been established that plants are a good source for AuNP production. According to Armendariz et al., *Avena sativa* (Oat) biomass produces AuNPs of varying sizes [12]. The pH dependence of the reduction has also been investigated. Smaller nanoparticles between 25 and 85 nm were produced in greater proportions at pH 3 and pH 4 compared to larger nanoparticles between 25 and 85 nm at pH 2.

In a different study, triangular gold nanoprisms were produced by reducing AuCl₄⁻ ions in a single step at room temperature using lemongrass (*Cymbopogon flexuosus*) plant extract [32]. Many fruit extracts have been employed as reducing agents, expanding the number of plants that have the potential to produce AuNPs. In their study, Sharma J. et al. demonstrated a straightforward biomodulation method using tomato (*Lycopersicon esculentum*), apple (*Malus domestica*), and lemon (*Citrus limonia*) extracts to create a variety of gold structures, including spherical, marigold-like, and triangular plates [18].

A few publications have also shown how algae may be used to synthesise AuNPs. Singaravelu et al. used a methodical strategy to investigate *Sargassum wightii*'s synthesis of AuNPs. In contrast to other biological processes, this is the first case in which a marine alga has been employed to produce very stable extracellular AuNPs quickly [33].

III. Future Prospects

Though it is of much interest to use fruit extracts or their mixture to generate nanoparticles, the precise control of the sizes and shapes of such nanoparticles are still not visible, due to the complexity in composition of fruit extracts. Hence, it is necessary to investigate the dominant components of those fruits in order to gain better understanding of the synthesis mechanisms.

Moreover, it is believed that detailed investigations of anticancer drug- Au nanoparticles conjugates are crucial from the synthesis point of view.

Finally, in vivo test is needed for the investigation of the therapeutic efficiency of anticancer drug-Au nanoparticles conjugates.

IV. Conclusion

A few publications have also shown how algae may be used to synthesise AuNPs. Singaravelu et al. used a methodical strategy to investigate *Sargassum wightii*'s synthesis of AuNPs. In contrast to other biological

processes, this is the first case in which a marine alga has been employed to produce very stable extracellular AuNPs quickly [33]. These particles were described using a variety of analyses, including UV-Visible, TEM, XRD, FTIR, XPS, and SERS. The outcomes showed that a special self-sustaining process is involved in the synthesis of AuNPs with fruit extracts, and that a variety of nanoparticle forms may be produced simply by modifying various bio-additives. In addition, the results of extremely low toxicity exhibit the potential of using these nanoparticles in biological and medical applications.

In addition, easy preparation method to generate Au-anticancer-drug conjugate were also demonstrated. By varying the concentration of auric ion, AuNPs with different shapes were derived. The binding of anticancer-drug molecule on AuNP surface was studied by different analytical techniques. The conjugates provide alternative drug formulation of anticancer-drug for cancer therapy. The attachment of anticancer-drug molecule on AuNP surface was investigated using different analytical techniques. By integrating AuNPs into drug composition rather than considering them as purely drug carriers, the conjugate exerted better in vitro cytotoxic activity to human choriocarcinoma JAR cell line in comparison with pure anticancer-drug.

In general, the results from cytotoxic tests suggest that Au-anticancer drug have improved therapeutic effect for different cancers. In some cases not only Au-anticancer-drug conjugates but also gold nanoparticles synthesized from fruit extract exhibited high efficacy in LDH and MTT test.

IV. References

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