



Controlled spontaneous generation of Gold Nanoparticles assisted by dual reducing and Capping Agents

Manish Shrivastava*, Shakti Bala, Sweety Sharma, Anamika Shrivastava

* Department of Chemistry, Banasthali Vidyapith, Banasthali, Rajasthan, 304022, India.

Article history

Received 12th Oct 2017
Received in revised form 18th Nov 2017
Accepted 07th Dec 2017

ABSTRACT

Noble-metal nanoparticles have attracted a great deal of interest by their unique optical, electronic, magnetic, and catalytic properties and intense research efforts are still devoted to develop new synthetic and functionalizing strategies. This extremely active research field was supported by the amazing chemical and physical properties displayed by the metal particles of nanometric size that are markedly

different from those of the corresponding bulk materials. Especially, optical and electronic properties of metal nanoparticles can be easily tuned by modifying their size and shape. Regarding noble metals nanoparticles, gold nanoparticles (Au-NPs) are without contest at the forefront in this research area. Academic interest for Au-NPs, which showed fast growth over the past years, is motivated by the strong surface PR displayed by gold nanoparticles.

KEYWORDS

Gold nanoparticles; Catalytic properties; Nanometric size.

1. INTRODUCTION

During the last decades, gold nanoparticles gained a renewal of interest by finding potential uses in medical diagnostics, imaging, and therapeutic treatments. In these last fields, preparation of Au-NPs with benign reactants is often favored to remove all potential contamination of the colloidal solutions [1-6]. To date, four different classes of biological applications for Au-NPs have been identified: labeling, delivering, heating, and sensing [7-15]. However, the use of gold nanoparticles was not limited to biological applications and Au-NPs were also successfully employed as scaffolds for molecular recognition of elements and molecules [16], in optoelectronics and data storage [17], in nanotechnology with molecular switches [18] and motors [19], or in light-harvesting assemblies [20, 21]. Typically, gold nanoparticles are obtained by chemical reduction of tetrachloroauric acid [22, 23]. However, this conventional approach is based on the use of external chemical reductants that often produce undesired side-products.

Therefore, a series of functionalizing agents for Au-NPs has recently been developed that display a dual role of effective reducing agents of gold salts and of stabilizers, by providing a robust coating to gold nanoparticles, within a unique reaction step. Seven different types of these reducing/ capping agents were investigated to date: microorganisms and bacteria, plants extracts and physiological molecules, inorganic reagents and metal complexes, organic molecules, organic acids and salts, liposomes, and polymers (Table 1). In this review, we propose to focus on these exciting functionalizing agents exerting the dual role of reducing and coating agents and to discuss the precise size-controlled synthesis of Au-NPs using this approach

2. MATERIAL AND METHODS

The generation of stable colloidal suspensions with particles of controlled size and shape requires a real synthetic strategy as well as a perfect knowledge of the intimate relationship existing between the surface of the particles and the stabilizing agent. In this regard, the growth of gold nanocrystals persists as long as the crystallization sites are not blocked by the capping agent and as long as the gold salt is available in the reaction medium. In order to obtain Au-NPs of nanometer size, surfactants are introduced in the

*Correspondence to:

Manish Shrivastava*,
Department of Chemistry, Banasthali Vidyapith,
Banasthali, Rajasthan, 304022,
India. E-Mail: sagermanish1@gmail.com

reaction medium to contain the crystal growth (see Fig. 1). For an efficient entrapment of gold nano-crystals, surfactants should display a higher affinity for the surface of the nanoparticle than the solvent molecules but also subsequently act as a stabilizer preventing the aggregation of the particles. Therefore, coating agents are exerting a critical role by passivating the surface. Among its main characteristics, surfactants should not only exhibit a high solubility in the reaction medium but also induce mutual repulsions between particles. Two basic modes of stabilization can be cited (see Fig. 2). The first one is based on the generation of electrostatic repulsion forces between particles which repel each other by establishing a charged coating at the surface of the particles. The second strategy makes use of nonionic bulky surfactants that generate steric repulsions between particles by forming a sterically hindered coating surrounding the surface of the nano-particles. The high affinity of surfactant molecules for the surface of Au-NPs surfaces finds its origin in the main principles of the coordination chemistry. Molecules of surfactants behave with each individual gold atom at the surface of the particles in a similar way to that observed with ligands and e

lectro-deficient metal ions in metal complexes. Therefore, a prerequisite for surfactants is to possess at least one atom or a functional group exhibiting lone pair electrons that can ensure its binding to the gold particles (see Fig. 3). In the context of this review, surfactants act both as reducing and capping agents.

used. In most cases, natural extracts were often broths obtained from boiled fresh plants leaves. It can be pointed out that all the recent reports concerning the synthesis of Au-NPs via the phytochemical approach were accompanied of investigations examining the cytotoxicity of Au-NPs in terms of proliferation of cells or apoptose [32]. When used in bioreductive synthetic approaches, the concentration of the natural extracts was a crucial parameter for the control of the size and shape of the nanoparticles, as evidenced with apiin [26]. In that case, an increase of the concentration of apiin extract in the reaction medium modified the morphology of the particles.

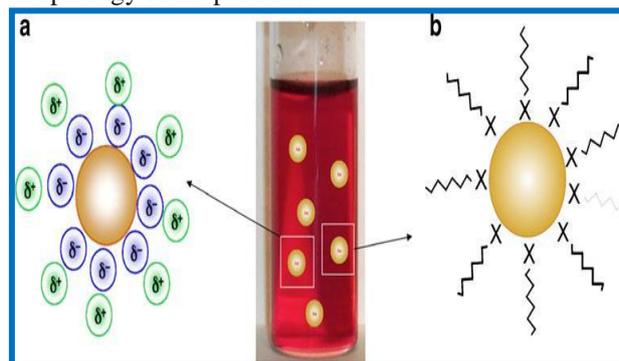


Figure. 2 Both possible modes of stabilization of gold nanoparticles. a Stabilization by

3. RESULTS AND DISCUSSION

Electrostatic repulsions

Contrarily, when purified phyllanthin [25], Cinnamomum camphora leaf [37] or edible mushroom *Volvariella volvacea* [38] extracts were employed, progressive increase of the concentration successively produced hexagonal, triangular, and spherical shape forms. Recently, cell-free mycelial extract of *Rhizopus oryzae* enabled the selective preparation of particles of different shapes (spheres, triangles, hexagons, pentagons, stars, and wires) simply by manipulating the key-growth parameters (gold salt concentration, pH of the solution, and reaction time) [39]. By fine-tuning the reaction conditions, synthesis of gold nanoparticles at pH=7 and 30°C for 6 h produced well-dispersed and essentially spherical particles with an average size of 9.52 ± 0.26 nm whereas the same reaction performed at pH=10 and higher concentration of the gold solution for 10 h furnished spherical particles of 50 to 70 nm diameter. Even if highly controlled syntheses of spherical nanoparticles have recently been reported [39], most of these approaches provided relatively polydispersed Au-NPs. The temperature was also determined as a critical parameter for controlling the size and shape of Au-NPs. An elevation of the temperature resulted in a decrease of the average particle size with extracts from black Darjeeling tea leaves, for which the diameter of the particles evolved from 35 to 24 nm [24]. In another example, when the

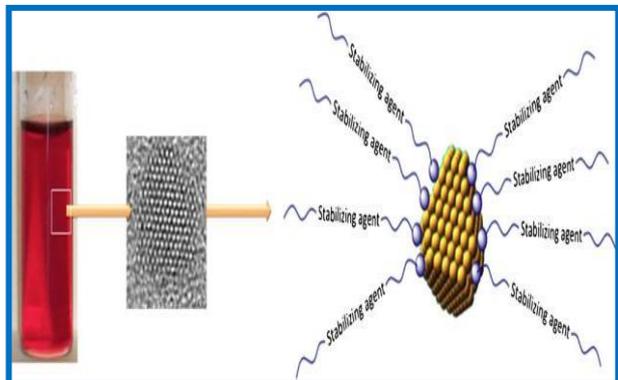


Figure.1 A colloidal solution of Au-NPs and the schematic representation of a nanoparticle stabilized by a stabilizing agent

Plants extracts and physiological molecules

Among all reported reducing/capping agents, plants extracts were seen as a possible eco-friendly approach for the synthesis of Au-NPs (see Fig. 4). Phytochemicals coming from black Darjeeling tea leaves [24], phyllanthin [25], apiin from henna leaves [26], leaf extract of *Terminalia catappa* [27], *Emblica officinalis* (Indian Gooseberry) fruits [28], *Tamarindus indica* leaf [29], plants extracts from *Mucuna pruriens* [30], cell-free extract of *Rhodospseudo-monas capsulata* [31], Korean red ginseng root (*Panax ginseng* C.A. Meyer) [32], leaves extracts of *Centella asiatica* [33], coriander [34], *Aloe vera* [35], or a waste product of the wine industry, i.e., red grape pomace [36] were notably

temperature was increased in the presence of leaf extract of lemongrass, the morphology of the resulting particles changed from triangular to spherical [40]. Authors also demonstrated the shape-directing role of halide ions in the growing process since Cl^- ions promoted the growth of nanotriangles at room temperature, whereas I^- ions favored the formation of spherical nanoparticles in the same conditions. The cooperative reduction of phytochemicals issued for soybean extracts efficiently reduced sodium tetrachloroaurate in aqueous media and produced particles of relatively small size (15 ± 4 nm) [41]. In this interesting example, saccharides (sucrose and stachyose) from soybean were synergistically used to reduce the gold salt whereas proteins (isoflavones and phyto-estrogens) of soybeans provided a strong coating to the particles, thus preventing their sintering. When red grape pomace, a waste product of the wine industry, was used as a reducer, high concentration of polyphenolic compounds enabled to reduce and stabilize quasi-monodisperse spherical particles [36]. The same experience performed with the red wine-produced quasi-spherical Au-NPs in the 10–30 nm range with a few rods, evidencing a lower concentration of polyphenols in wine compared with pomace. Recently, another polyphenol-based natural plant extract, bayberry tannin, also served as a reducing agent and stabilizing agent of Au-NPs in water [42]. By using strict synthetic conditions and by markedly increasing the concentration of bayberry tannin, particles with a mean diameter as small as 1.8 ± 0.3 nm were obtained. Common specificity of polyphenols in tannins is that their molecular backbone is generally composed of rigid aromatic rings functionalized by multiple ortho-phenolic hydroxyl groups. Reaction with Au(III) enables the oxidation of the phenolic hydroxyls to the corresponding benzoquinones. More precisely, reduction of Au(III) is initiated by the formation of five-membered ring chelates between the electrophilic metal ion and the phenolic hydroxyls which inductively decompose upon oxidation to the corresponding benzoquinones. Enzymatic activity was also envisioned as another bio-based method for the synthesis of metal nanoparticles. In this aim, enzymatic activity of α -amylase for the synthesis of Au-NPs was investigated [43]. Interestingly, if authors tested other enzymes, the reduction process of the parent cationic salt was only observed with pure α -amylase and EcoRI and activities of enzymes were maintained after their anchor-age to Au-NPs. Careful structural analyses of both enzymes revealed the presence of free SH groups in the side chain of cysteine, certainly involved in the reduction process, and not detected on the other enzymes. Interestingly, thiol groups were positioned on the opposite side of the enzymatic site therefore retaining the biological activity of both enzymes after attachment to Au-NPs.

The synthesis of particles in the sub-100 nm size regime was not only limited to plants extracts but was also investigated from the point of view of living plants. The

first report concerning this biosynthetic approach for the stabilization of spherical Au-NPs was published in 2002 by Gardea-Torresdey et al. with living alfalfa plants [44]. When alfalfa plants were grown in an AuCl_4^- rich environment, gold uptake from solid media by the plants occurred and growth of Au nanoparticles inside the plant was evidenced. Discrete nanoparticles of 2–20 nm in diameter were obtained. This synthesis of Au-NPs related from phytomimic strategies [45], paved way for further investigations [46, 47]. Desert willow (*Chilopsis linearis*) [45] and leguminous shrub (*Sesbania drummondii*) [48] displayed high capabilities to uptake gold from a gold-enriched medium and particles were obtained with sizes ranging from 2.9 to 17.2 Å and 6 to 20 nm, respectively. The size of the particles could be drastically reduced to 0.55 nm in the case of *C. linearis* by adding thiocyanate ions in the reaction medium [49]. Unequivocally, all these studies demonstrated the involvement of proteins, polyphenols, and carbohydrates in the growth process and the stabilization of Au-NPs in living organisms, even if the elucidation of the exact mechanisms involved in the growth of the nanoparticles needs much more experimentations for a complete understanding.

Microorganisms and bacteria

Microorganisms have also been studied for the stabilization of nanoparticles (see Fig. 5). The biosynthesis of spherical Au-NPs by microorganisms has emerged as a safe and reliable alternative competing with the conventional chemical syntheses. The regulation of crystal morphology by proteins is also the central feature that governs the formation of hard tissues such as bones, teeth and mollusk shells. Bacteria are well-known to exhibit high metal reducing capacities and to stabilize particles by biosorption. Notably, carboxylic groups in the cell wall are strong sorption sites for metals [50]. The reducing properties of bacteria are highly pH-dependent [51–57] and reduction of gold salts is reported under aerobic and anaerobic conditions. Concerning this living approach, Beveridge and co-workers demonstrated for the first time in 1980 that Au-NPs could be readily precipitated within bacterial cells of *Bacillus subtilis* with particles sizes ranging from 5 to 25 nm [50, 58]. Then, a number of different genera of fungi were investigated in the effort of developing efficient size-controlled syntheses. Mesophilic anaerobic bacterium *Shewanella* algae was able to reduce a gold salt within 30 min at 25°C and pH=7 with the assistance of hydrogen gas as an electron donor. Spherical Au-NPs of 10–20 nm were obtained in the periplasm space. The authors demonstrated the exceptional reducing ability of *S. algae* as the reducing power of 3.2×10^{15} cells/m³ of the microbial solution at 25°C was comparable to that of a 20-mol/m³ aqueous solution of citric acid at 50°C. Similarly, native *R. oryzae* strain furnished well-dispersed particles (with an average diameter of 10 nm) with no conspicuous agglomeration. Nanoparticles formed on the mycelia surface were stable up to 6 months. Through severe adjustments of the experimental conditions, filamentous

fungus *Aspergillus niger* exclusively formed spherical Au-NPs in alkaline (4 nm) and neutral (18 nm) media by means of proteins localized on the fungal cell walls. Other bacteria such as *Rhodobacter capsulatus*, *R. capsulata* [57], actino-mycete *Rhodococcus* species, *Escherichia coli*, *Desulfovibrio desulfuricans*, *Lactobacillus* strains, *Fusarium oxysporum*, *Pyrobaculum islandicum* and other hyperthermophilic Fe(III)-reducers, and *Brevibacterium case* were also used to synthesize nanoparticles intra- or extracellularly. The determination of the amino acid sequences of polypeptides involved in the reduction mechanism of Au(III) in living microorganisms was performed with one of the simplest organisms known in nature, i.e., *E. coli*. Careful examination of the proteins revealed the presence of polypeptides that accelerate the rate of colloid appearance by the presence of a catalytic site that functions by acid catalysis and participate to the alteration of the crystal shape. In the presence of these “accelerators,” specific direction of crystal growth were favored and other structures such as thin and hexagonal crystals were found in addition to nanospheres. The first use of eukaryotic organism, *Verticillium sp.* (AAT-TS-4), was reported in 2001 and generated Au-NPs with an average diameter of 20 nm, the smallest particles being located on the cell walls and the largest ones within the fungal cells. In the case of Au-NPs synthesized using the endophytic fungus *Colletotrichum sp.*, isolated from geranium leaves, particles were predominantly spherical and aggregated into larger irregular structures with no well-defined morphology. The shape was only poorly controlled using this microorganism. Review of the literature revealed that algae have been only scarcely explored as living nanofactories. Au-NPs with good monodispersity were obtained with marine alga *Sargassum wightii* and small spherical particles ranging from 8 nm were obtained. This selectivity was comparable to that observed with the extremophilic actinomycete *Thermonospora sp.* Keeping in mind the biological perspectives, less attention has been paid to molecules from biological origin. However, sodium salts of the amino acids conjugates of bile salts successfully produced gold clusters surrounded by a shell of amino acids. Presence of amino and carboxylic groups on amino acids (taurine and lysine) formed anchoring points that strongly bind to the surface of the nanoparticles. Interestingly, an increase of the concentration of amino acids leads to the formation of small particles (4 to 30 nm) which ripen to form larger particles such as triangles and hexagons. Similarly, bovine serum albumin provided small Au-NPs of 2 nm after 12 h of reaction which slowly evolved to form nanoplates after 48 h of reaction. Previously, investigation on three different proteins, namely, bovine serum albumin, Rituximab and Cetuximab revealed that bovine serum albumin was the only protein of the three able to reduce the gold salt to form gold nanotriangles. A series of cholesteryl phenoxy hexanoate mesogens were also investigated and the influence of the

functional group on the meta-position of the phenyl ring was determined. The self-reduction of HAuCl_4 was only observed for mesogens bearing amino and carboxylic acid groups. Amino-substituted mesogens ensured the formation of Au-NPs with an average size of 12–16 nm whereas carboxy-substituted mesogens stabilized small Au-NPs with size ranging from 2 to 6 nm.

Organic molecules

Macrocycle cucurbit[7]uril was used to form spherical Au-NPs in the presence of sodium hydroxide. Interestingly, the nanoparticles thus obtained showed strong catalytic activities for the reduction of 4-nitrophenol in the presence of NaBH_4 . Similarly, reaction of HAuCl_4 with thiacalix[4]arene produced nanoparticles whose shapes were finely tuned by controlling the addition of HAuCl_4 . This macrocyclic approach was also transposed to cyclic oligosaccharide β -cyclodextrin which formed spherical Au-NPs only in aqueous solutions free of dodecyltrimethylammonium bromide. The organic molecule acting as reducing agent is indeed oxidized during the synthetic process. An illustration is given by hydroquinone that is oxidized in benzoquinone during the synthesis of Au-NPs. The stabilization of Au-NPs by benzoquinone proved to be highly pH-sensitive and stable nanoparticles were only obtained while maintaining the pH below 4. Previously, a more sophisticated hydroquinone derivative, i.e., 2,3,5,6-tetrakis(morpholinomethyl)hydroquinone produced spherical Au-NPs with aggregates as large as 170 ± 17 nm. The preparation of water-soluble Au-NPs is of utmost importance for various applications, for example for biological applications, and several amines were investigated for this purpose. Remarkably, oleylamine (9-octadecenylamine) enabled to form and stabilize well-dispersed Au-NPs by means of an intermediate Au-amine complex which undergoes a rapid thermal decomposition in water to produce Au-NPs. Notably, the size of the particles was strongly affected by the amine concentration, and only scarcely by the reaction time. A careful survey of the literature showed that other amines such as aliphatic amines (hexadecylamine, tree-type multiple-head amine bis(amidoethyl carbamoyl)octadecylamine), and aromatic amines (4-hexadecylaniline, bis(2-(4-amino phenoxy)ethyl)ether (DAEE)) were also investigated to prepare Au-NPs in aqueous and organic solutions. Interestingly, in the case of DAEE, the stabilization of Au-NPs was ensured by the polymer resulting from the oxidative polymerization of the diamine compound. For all the amines previously cited, Au-NPs with a narrow size distribution were characterized, except for bis(amidoethyl-carbamoyl)octadecylamine which produced Au-NPs with a very broad size distribution (20 to 250 nm). 4-Aminothiophenol was also used as reducing and surface passivating agent for the preparation of organically capped gold nanoparticles. The influence of the solvent in the reduction process was evidenced by the fact that the reduction only occurred in a mixture of high dielectric solvents such as N,N-dimethylformamide (DMF) and water, whereas no

reduction was observed in water or in DMF. The morphology of the Au-NPs proved to be also strongly pH dependent. If no reduction was observed for pH above 12, highly acidic medium provided particles of different morphologies. Interestingly, nearly spherical Au-NPs of small size (3 nm) in a chain-like arrangement could be obtained under careful control of the reaction conditions. Small-sized nanoparticles (4.5 nm) were also characterized with dodecylaminomethanol as a reducer by electrospraying a gold precursor solution into the reductive solution of surfactant at room temperature. In this novel and versatile approach, the reduction of Au(III) into Au(0) occurred upon oxidation of dodecylaminomethanol into dodecylaminomethanoic acid which subsequently decomposed into dodecylamine and formaldehyde. The main drawbacks of this method were the resulting broad size distribution of the spherical nanoparticles (5 to 20 nm) and the weak shape control obtained during the synthesis since other structures such as icosahedra, decahedra, and hexagons were additionally observed. It has to be noticed that when dodecylaminomethanol was previously employed as reducing and capping agent by the same authors using the conventional wet synthetic approach, Au-NPs of small size (3.9 ± 0.5 nm) were obtained, thereby showing the crucial role of the method employed in the size dispersity. More surprisingly, Tween 80 or polysorbate 80, which is a nonionic surfactant and emulsifier derived from polyethoxylated sorbitan and oleic acid often used in foods, acted as reductant for a gold salt precursor in aqueous medium. The control of the size of the particles was achieved by adjusting parameters such as the temperature or the concentration of both reagents. Tween 80 yielded extremely small-sized Au-NPs at 4°C even in the absence of light (1.48 ± 0.02 nm) and a linear correlation between the temperature and the size could be clearly established. Further investigations concerning the reduction mechanism showed that the main factor determining the formation of Au-NPs was the presence of ethylene oxide units in the main chain. As previously postulated by Barnickel et al, authors attributed the reductive ability of poly(ethylene oxide) to the formation of hydroperoxides with the oxygen from the air, thus producing highly reductive species. The authors also discussed the potential contribution of the terminal OH groups of the poly(ethylene oxide) POE chain in the reduction process. Such contribution of the OH groups in the reduction process was also investigated with β -D-glucose. By simply adjusting the pH, β -D-glucose rapidly reduced Au(III) at ambient temperature under basic conditions. In addition to spherical Au-NPs, a few triangular particles were also observed. The authors clearly established the crucial role of the five hydroxyl groups in the complexation process of β -D-glucose to Au-NPs. The pH dependence of the reduction process was plausibly explained by generating highly reductive and electron-rich hydroxylates anions under basic conditions. The nanoparticles thus obtained displayed unusual and

somewhat unexpected catalytic properties for the reduction of 4-nitrophenolate into 4-aminophenolate with the mild reductant NaBH₄. Honey, whose main ingredient is the monosaccharide fructose, was also investigated as an eco-friendly route to generate Au-NPs. However, the presence of numerous other potential reducing agents such as vitamin C, glucose, sucrose, proteins, and enzymes did not allow to clearly determine the origin of the reduction process. Honey-mediated biosynthesis yielded mainly triangular nanoparticles mixed with spherical nanoparticles with a mean diameter of 15 nm. Notably, addition of a large excess of honey, compared with Au(III), inverted the ratio of nanotriangles and nano-spheres. Recently, a fluorophore-substituted amine 1-pyrenemethylamine acted as a strong coating agent for Au-NPs following an auto-reduction pathway based on the electrostatic interaction of the amine with the gold salt followed by a reduction process promoted by the protonated amine. The authors clearly showed that the shell around the metal core of the particles was composed of unpolymerized 1-pyrenemethylamines. Similarly, when luminol was used as reducing/capping agent, results indicated that residual luminol and the corresponding oxidation product 3-aminophthalate both coexisted on the surface of Au-NPs without any formation of polymer. The size of the nanoparticles decreased while increasing the concentration of luminol and an extremely low stability of the colloidal solutions was observed for pH values under 3. Later, for a better understanding of the exact role of amines in the reduction process, an extensive study was performed on 14 amines.

Organic acids and salts

Due to the remarkable reducing capabilities of amines, amino acids and their derivatives were also studied for the synthesis of Au-NPs (see Fig.). Lauroyl glucose, lauroyl fructose, and lauroyl ascorbate formed spherical Au-NPs with sizes depending on the nature of the amino acid. Lauroyl glucose and lauroyl fructose furnished spherical Au-NPs with core sizes ranging from 168 to 226 nm while smaller particles were obtained with lauroyl ascorbate (35 to 48 nm). Other amino acids such as tyrosine, alkylated tyrosine, aspartic acid, tryptophan, glutamic acid, and tryptophan-containing peptide amphiphiles were also identified as molecules able to reduce chloroaurate ions under mild experimental conditions in aqueous medium. Surprisingly, the shape of the particles formed with alkylated tyrosine dramatically changed when the spontaneous reduction occurred at the liquid-liquid interface or at the liquid-air interface. Very polydisperse nanospheres (5 to 100 nm) were obtained in the first case whereas nanoribbons and nanosheets were obtained in the second one. When tryptophan was used as reducing/capping agent, the resulting nanoparticles exhibited a polymer coating issued from intermolecular reactions between indole groups of the oxidized tryptophans. In this study, polymerization of tryptophan was shown to occur through the secondary

amine of the indole groups resulting in some degree to cross-linkage of the Au-NPs. In the case of glutamic acid, gold nanospheres obtained via a controlled $\text{HAuCl}_4/\text{glutamic acid}$ molar ratio slowly formed nanochains by linear aggregation of the particles through an oriented attachment mechanism. This promising polymerization opens up the possibility to form, in a simple manner, numerous polymer-embedded nano-particles. Concomitantly, other authors carried out a comparative study with four amino acids, i.e., lysine, tyrosine, tryptophan, and arginine. When Au-NPs were prepared under similar conditions, the smallest particles were obtained with lysine (6 ± 2 nm in diameter), the largest ones with tryptophan (60 ± 5 nm in size) and intermediate size of particles with arginine (10 ± 5 nm). Surprisingly, examination of the particles obtained with tyrosine showed the presence of both spherical and rod-shaped particles. More recently, Au-NPs were also prepared with L-tyrosine, glycyl-L-tyrosine and L-arginine as peptides in alkali medium starting from potassium tetrabromoaurate as the precursor of gold. If L-tyrosine and glycyl-L-tyrosine stabilized spherical particles with diameters comprised between 5 and 40 nm, L-arginine stabilized particles of different morphologies. Interestingly, by mixing L-tyrosine and glycyl-L-tyrosine in the same reaction, and varying the ratio from 0% to 100%, Au-NPs with average

Particles were almost spherical in shape and a better control of the nucleation process was obtained since particles ranged from 10 to 20 nm. The mean diameter of the lipid-based colloids decreased with increasing the temperature as a result of a faster nucleation kinetic. However, the amount of Au-NPs per vesicle was low (only two particles per ethosome) and the synthesis of Au-NPs at higher concentration of salt resulted in multipod clusters and bunches within the ethosomes. The authors rejected the probability of a self-reduction process within the ethosomes and they concluded that the reduction was carried out by water molecules with the phosphatidylcholine lipid acting as a catalyst.

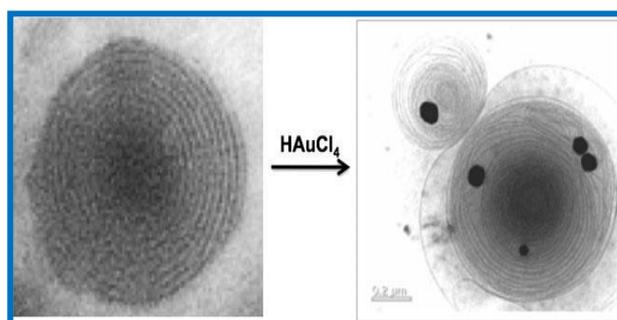


Figure4. Liposomes before and after encapsulation of Au-NPs

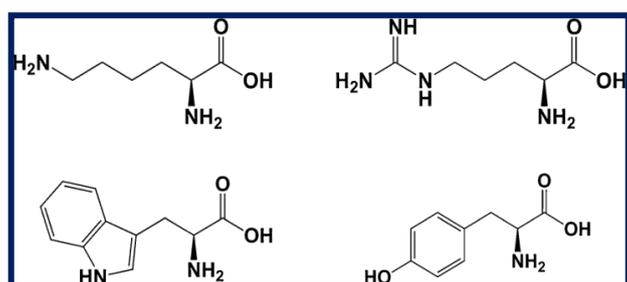


Figure3. Examples of amino acids commonly used for the synthesis of Au-NPs

Liposomes

With the growing need of clean and nontoxic synthetic approaches, the focus also turned towards liposomes for the synthesis of spherical Au-NPs (see Fig. 7). The first article concerning the reduction of Au(III) by liposomes was reported in 1993 with egg yolk phosphatidylcholine as the phospholipid. Ten years later, self-reduction of HAuCl_4 was also studied within onion-type multilamellar vesicles made of monoolein. In this last case, Au-NPs polydisperse in size and shape were obtained and sphere-like and elongated particles were observed. The authors suggested that the reduction of Au(III) occurred via the oxidation of the terminal CH_2OH group of the monoolein into acid. Recently, Hernando et al. reported the spontaneous in situ synthesis of gold nanoparticles within ethosome bilayers, still based on phosphatidylcholine as the lipid.

Metal complexes and inorganic systems

Recent researches have also concerned a limited number of inorganic systems acting as reducing and stabilizing agent. Notably, carbon nanofibers and silica Nanotubes were decorated by Au-NPs of small size. Reduction of the noble-metal salt by carbon nanofibers was attributed to the strongly reductive functional groups on the outside surface. Interestingly, no Au-NPs were found in the solution, illustrating that the reduction process was only occurring inside the nanofibers even if TEM analyses later proved that Au-NPs were localized in the interior and at the surface of the nanofibers. This strategy enabled, in a second step, to fill silica nanotubes with Au-NPs by forming the nanotubes around the carbon nanofibers used as a template. In the final step, pyrolysis at 550°C removed the carbon nanofibers, thus leading to pure silica nanotubes embedded with noble-metal nanoparticles. C_{60} dianion was also used to reduce tetrachloroauric acid. Contrarily to neutral C_{60} , C_{60}^{2-} is an electron-rich species that displays a strong reducing ability toward numerous organic functional groups ($\text{N}-\text{N}^+$, $\text{C}=\text{C}-\text{EWG}$ (where EWG is electron withdrawing groups) and $\text{C}=\text{O}$ bonds). When opposed to a gold salt, spontaneous reduction occurred and Au-NPs with a mean diameter of 17 nm were obtained. The presence of aggregates is also observed with an average size of 100 nm resulting from the strong carbon-carbon interactions. Finally, the strong affinity of C_{60} molecules for gold metal and the tendency of fullerenes to self-aggregate ensured that

every gold nanospheres were loaded with fullerenes. To date, only two metal complexes were reported to reduce HAuCl₄ and to stabilize Au-NPs thus formed .

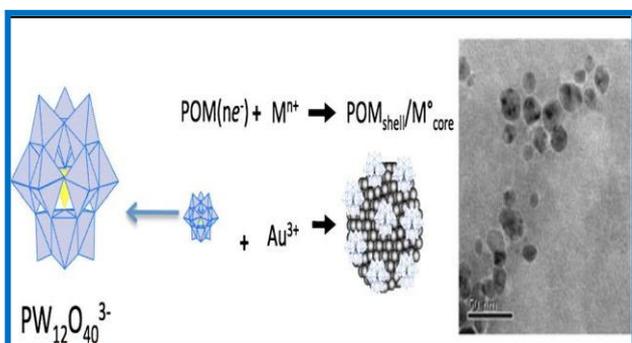


Figure 5 TEM image of Au-NPs stabilized by polyoxometalate PW₁₂O₄₀³⁻

CONCLUSION

A careful survey of the literature concerning all agents exerting the dual function of reducing agent for gold salts and stabilizing agent for Au-NPs clearly shows the predominance of the nature in this field, at least in terms of number of papers. However, this approach often provides polydisperse and poorly characterized Au-NPs made with unreliable and variable materials. This approach is also not necessarily a guarantee of Green chemistry or biocompatibility as molecules present during the synthesis might prove to be toxic to humans. Concerning the chemical approach, apart from all the acids, carboxylates and polymers widely investigated, few other reagents are available and it can be surprising that, to date, only two metal complexes have shown the ability to both reduce Au(III) and stabilize and functionalize the Au-NPs thus formed. However, these reducer-free approaches elegantly ensure the formation of Au-NPs, usually free of byproducts. Additionally, there is still a real improvement needed for these single-reagent methods in order to reach a higher degree of control in the size and shape of the Au-NPs considering the growing demand of well-defined Au-NPs, for instance in electronics and biology. Open Access This article is distributed under the terms of the Creative Commons Attribution License which permits any use, distribution and reproduction in any medium, provided the original author(s) and source are credited.

CONFLICT OF INTERESTS

The authors declare that there is no conflict of interests regarding the publication of this paper.

REFERENCE

1. Valden M, Lai X, Goodman DW (1998) Onset of catalytic activity of gold clusters on titania with the appearance of nonmetallic properties. *Science* 281:1647
2. G (2004) Nanostructures and nanomaterials. Imperial College Press, London.
3. MA, Lee T (eds) (2003) Molecular nanoelectronics. American Scientific Publishers, Valencia.
4. Barnes WL, Dereux A, Ebbesen TW (2003) Surface plasmon subwavelength optics. *Nature* 424:82
5. Tang ZT, Kotov NA (2005) One-dimensional assemblies of nanoparticles: preparation, properties, and promise. *Adv Mater* 17:951
6. Hartland GV (2004) Measurements of the material properties of nanoparticles and nanorods by time-resolved spectroscopy. *Phys Chem Chem Phys* 6:5263
7. Xia YN, Halas NJ (2005) Shape-controlled synthesis and surface plasmonic properties of metallic nanostructures. *MRS Bull* 30:338.
8. Shankar SS, Rai A, Ankamwar B, Singh A, Ahmad A, Sastry M (2004) Biological synthesis of triangular gold nanoprisms. *Nat Mater* 3:482
9. Raveendran P, Fu J, Wallen SL (2003) Completely "green" synthesis and stabilization of metal nanoparticles. *J Am Chem Soc* 125:13940
10. Kattumuri V, Katti K, Bhaskaran S, Boote EJ, Casteel SW, Fent GM, Robertson DJ, Chandrasekhar M, Kannan R, Katti KV (2007) Gum arabic as a phytochemical construct for the stabilization of gold nanoparticles: in vivo pharmacokinetics and X-ray-contrast-imaging studies. *Small* 3:333
11. Kim D, Park S, Lee JH, Jeong YY, Jon S (2007) Antibiofouling polymer-coated gold nanoparticles as a contrast agent for in vivo X-ray computed tomography imaging. *J Am Chem Soc* 129:7661
12. Chen YS, Hung YC, Liao I, Huang GS (2009) Assessment of the in vivo toxicity of gold nanoparticles. *Nanoscale Res Lett* 4:858
13. Homberger M, Simon U (2010) On the application potential of gold nanoparticles in nanoelectronics and biomedicine. *Phil Trans R Soc A* 368:1405
14. Uboldi C, Bonacchi D, Lorenzi G, Hermanns MI, Pohl C, Baldi G, Unger RE, Kirkpatrick CJ (2009) Gold nanoparticles induce cytotoxicity in the alveolar type-II cell lines A549 and NCIH441. *Particle and Fibre Toxicology* 6:18

15. Sperling RA, Rivera Gil P, Zhang F, Zanella M, Parak WJ (2008) Biological applications of gold nanoparticles. *Chem Soc Rev* 37:1896
16. Drechsler U, Erdogan B, Rotello VM (2004) Nanoparticles: scaffolds for molecular recognition. *Chem Eur J* 10:5570
17. Lee JS (2010) Recent progress in gold nanoparticle-based non-volatile memory devices. *Gold Bull* 43:18
18. van der Molen SJ, Liao J, Kudernac T, Agustsson JS, Bernard L, Calame M, van Wees BJ, Feringa BL, Schoonenberger C (2009)
19. Light-controlled conductance switching of ordered metal–molecule–metal devices. *Nano Lett* 9:76
20. Pollard MM, ter Wiel MKJ, van Delden RA, Vicario J, Koumura N, van den Brom CR, Meetsma A, Feringa BL (2008) Light-driven rotary molecular motors on gold nanoparticles. *Chem Eur J* 14:1161
21. Reetz MT, Helbig W, Quaiser SA (1996) In: Furstner A (ed) *Active metals*. VCH, Weinheim, p 279
22. Mackowski S (2010) Hybrid nanostructures for efficient light harvesting. *J Phys Condens Matter* 22:193102
23. Daniel MC, Astruc D (2004) Gold nanoparticles: assembly, supramolecular chemistry, quantum-size-related properties, and applications toward biology, catalysis, and nanotechnology. *Chem Rev* 104:293
24. Brust M, Walker M, Bethell D, Schiffrin DJ, Whyman R (1994) Synthesis of thiol-derivatised gold nanoparticles in a two-phase liquid–liquid system. *J Chem Soc Chem Commun* 801
25. Nune SK, Chanda N, Shukla R, Katti K, Kulkarni RR, Thilakavathy S, Mekapothula S, Kannan R, Katti KV (2009) Green nanotechnology from tea: phytochemicals in tea as building blocks for production of biocompatible gold nano-particles. *J Mater Chem* 19:2912
26. Kasthuri J, Kathiravan K, Rajendiran N (2009) Phyllanthin-assisted biosynthesis of silver and gold nanoparticles: a novel biological approach. *J Nanopart Res* 11:1075
27. Kasthuri J, Veerapandian S, Rajendiran N (2009) Biological synthesis of silver and gold nanoparticles using apiin as reducing agent. *Colloids Surf B Biointerfaces* 68:5
28. Gankamwar B (2010) Biosynthesis of gold nanoparticles (green-gold) using leaf extract of terminalia catappa. *E-J Chem* 7:1334
29. Ankamwar B, Damle C, Ahmad A, Sastry M (2005) Biosynthesis of gold and silver nanoparticles using emblica officinalis fruit extract, their phase transfer and transmetallation in an organic solution. *J Nanosci Nanotech* 5:1665
30. Ankamwar B, Chaudhary M, Sastry M (2005) Gold nano-triangles biologically synthesized using tamarind leaf extract and potential application in vapor sensing. *Syn React Inorg Metal Org Nano Metal Chem* 35:1
31. Arulkumar S, Sabesan M (2010) Biosynthesis and characterization of gold nanoparticle using antiparkinsonian drug mucuna pruriens plant extract. *Int J Res Pharm Sci* 1:417
32. He S, Zhang Y, Guo Z, Gu N (2008) Biological synthesis of gold nanowires using extract of rhodospseudomonas capsulata. *Biotechnol Prog* 24:476
33. Leonard L, Ahmmad B, Okamura H, Kurawaki J (2011) In situ green synthesis of biocompatible ginseng capped gold nanoparticles with remarkable stability. *Colloids Surf B Biointerfaces* 82:391
34. Kumar Das R, Bhusan Borthakur B, Bora U (2010) Green synthesis of gold nanoparticles using ethanolic leaf extract of centella asiatica. *Mat Lett* 64:1445
35. Badri Narayanan K, Sakthivel N (2008) Coriander leaf mediated biosynthesis of gold nanoparticles. *Mat Lett* 62:4588
36. Chandran SP, Chaudhary M, Pasricha R, Ahmad A, Sastry M (2006) Synthesis of gold nanotriangles and silver nanoparticles using aloe vera plant extract. *Biotechnol Prog* 22:577
37. Baruwati B, Varma RS (2009) High value products from waste: grape pomace extract—a three-in-one package for the synthesis of metal nanoparticles. *ChemSusChem* 1:1041 Huang J, Li Q, Sun D, Lu Y, Su Y, Yang X, Wang H, Wang Y, Shao W, He N, Hong J, Chen C (2007) Biosynthesis of silver and gold nanoparticles by novel sundried cinnamomum camphora leaf. *Nanotechnology* 18:105104
38. Philip D (2009) Biosynthesis of Au, Ag and Au–Ag nano-particles using edible mushroom extract. *Spectrochimica Acta Part A* 73:374
39. Das SK, Das AR, Guha AK (2010) Microbial synthesis of multishaped gold nanostructures. *Small* 6:1012
40. Rai A, Singh A, Ahmad A, Sastry M (2006) Role of halide ions and temperature on the morphology of biologically synthesized gold nanotriangles. *Langmuir* 22:736
41. Shukla R, Nune SK, Chanda N, Katti K, Mekapothula S, Kulkarni RR, Welshons WV, Kannan R, Katti KV (2008) Soybeans as a phytochemical reservoir for the production and stabilization of biocompatible gold nanoparticles. *Small* 4:1425
42. Huang X, Wu H, Liao X (2010) One-step, size-controlled synthesis of gold nanoparticles at room temperature using plant tannin. *Shia B* 12:395

43. Rangnekar A, Sarma TK, Singh AK, Deka J, Ramesh A, Chattopadhyay A (2007) Retention of enzymatic activity of α -amylase in the reductive synthesis of gold nanoparticles. *Langmuir* 23:570
44. Gardea-Torresdey JL, Parsons JG, Gomez E, Peralta Viddea J, Troiani HE, Santiago P, Yacamán MJ (2002) Formation and growth of Au nanoparticles inside live alfalfa plants. *Nano Lett* 2:397
45. Rodriguez E, Parsons JG, Peralta-Videa JL, Cruz-Jimenez G, Romero-Gonzalez J, Sanchez-Salado BE, Saupe GB, Duarte-Gardea M, Gardea-Torresdey JL (2007) Potential of *Chilopsis linearis* for gold phytomining: using XAS to determine gold reduction and nanoparticle formation within plant tissues. *Int J Phytoremed* 9:133
46. Arya V (2010) Living systems: eco-friendly nanofactories. *Dig J Nanomater Bios* 5:9
47. Kumar V, Yadav SK (2009) Plant-mediated synthesis of silver and gold nanoparticles and their applications. *J Chem Technol Biotechnol* 84:151
48. Sharma NC, Sahi SV, Nath S, Parsons JG, Gardea-Torresdey JL, Pal T (2007) Synthesis of plant-mediated gold nanoparticles and catalytic role of biomatrix-embedded nanomaterials. *Environ Sci Technol* 41:5137
49. Gardea-Torresdey JL, Rodriguez E, Parsons JG, Peralta-Videa JR, Meitzner G, Cruz-Jimenez G (2005) Use of ICP and XAS to determine the enhancement of gold phytoextraction by *Chilopsis linearis* using thiocyanate as a complexing agent. *Anal Bioanal Chem* 382:347
50. Beveridge TJ, Murray RGE (1980) Sites of metal deposition in the cell wall of *Bacillus subtilis*. *J Bacteriol* 141:876
51. Tsuruta T (2004) Biosorption and recycling of gold using various microorganisms. *J Gen Appl Microbiol* 50:221
52. Brown S, Sarikaya M, Johnson E (2000) A genetic analysis of crystal growth. *J Mol Biol* 299:72

ABOUT AUTHOR



Dr. Manish Shrivastava is Assistant Professor (Chemistry), Department of Chemistry Banasthali University, Rajasthan. He obtained his Graduation, Post graduation and D. Phil (PhD) degree from University of Allahabad, Allahabad. He has published over 20 research paper in International Journals, eight proceedings in national conference. At present time it is work in field of nanocatalyst, catalyzed organic synthesis and water treatment. At present time six students going to research work under the supervision and two students awarded the PhD degree under the supervision. Dr. Shrivastava presented research paper in numerous International and National conferences.