Chapter 2

Review of Literatures on Noble Metal Nanoparticles: Properties and Applications

“Prepare for the unknown by studying how others in the past have coped with the unforeseeable and the unpredictable.”

-George S. Patton
“Nanotechnology in medicine is going to have a major impact on the survival of the human race.”  
- Bernard Marcus

2.1. Introduction

The unique optical property of the noble metal nanoparticles has made them a potential candidate in the nanotechnology field. Zijlstra et al. have demonstrated a DVD disk having storage capacity of 10 terabytes, approximately 2000 movies of conventional size [1]. This is possible because of the superior optical properties of randomly oriented gold nanorods embedded in the disk. As the metal nanoparticles show size and shape dependant optical properties, Zijlstra and coworkers used optical spectrum and different polarization directions to store data. The enhancement in the optical and photothermal properties of noble metal nanoparticles e.g., AgNPs, gold nanoparticles, Pb nanoparticles etc., arises from resonant oscillation of their free electrons in the presence of light, also known as localized surface plasmon resonance (LSPR). The plasmon resonance can either radiate light (Mie scattering), a process that finds great utility in optical and imaging fields, or be rapidly converted to heat (absorption); the latter mechanism of dissipation has opened up applications in several new areas.

So here, this chapter is divided into following parts. Some historical evidences of use of AgNPs along with other noble metal nanoparticles are given at first. The overview of various properties of AgNPs is described further. Finally, we highlight some recent applications based on properties of AgNPs.

2.2. Historical Perspective

In ancient time, silver was considered more precious than gold and symbol of purity. Hippocrates proclaimed that silver contained medicinal properties and could cure multiple maladies 10. Since silver was publicized to have antiseptic properties, Phoenicians used silver vials for food storage to help prevent spoilage. Ravelin (1869) and von Nageli (1893) had done pioneering work in the study of anti-bacterial properties of silver [2]. Based on silver a
number of products commercialized throughout the 20th century like Katadyn, Movidyn, Argyrol, Alagon, Tetrasil, etc. [3]. Prior to the wide spread use of antibiotics, during World War I silver compounds were used to help prevent infection.

History tells about the use of these noble metals in stained glass to produce the beautiful colors of drink cups, such as the Lycurgus cup [4], or ancient windows, for example, in the Altenberg dome near Cologne in Germany [5]. The early alchemist tried to produce portable gold, “the elixir of life” as they considered gold as indestructible and have enormous medicinal importance [6]. The German bacteriologist Robert Koch discovered in 1890 that low concentrations of potassium gold cyanide, K[Au(CN)2] had antimicrobial activity against the tubercle bacillus. From thereafter gold is introduced in modern medicine [7]. During the Vedic period (1000BC-600BC) in ancient India, the use of gold, in the form of swarna bhasma (meaning, gold ash), is suggested for medicinal purposes started [8].

In1856, Faraday had hypothesized that the color of ruby glass and its aqueous solutions of gold (mixed with either SO3 or phosphorus), is due to finely divided gold particles [9]. Stoke had different opinion about the existence of a purple gold oxide, apparently prompted Faraday’s famous electrical discharge method for preparing aqueous gold colloids [10]. It is noteworthy that Faraday did not have a quantitative theoretical framework, but seems to have based his postulate on an intuitive understanding of highly reflective metals and scattering processes.

Gustav Mie’s 1908 paper represents the first rigorous theoretical treatment of the optical properties of spherical metal particles [11, 12]. Mie’s theory yielded extinction coefficients for nanoscopic gold particles which compared well with the experimental spectra of gold sols and unlike Maxwell-Garnett theory, was applicable to spheres of any size. Mie scattering theory is applied today to a variety of systems, including nonmetal particles. His basic approach has also been adapted to other shapes, such as cylinders [13] and ellipsoids [14].
In 1727, a German professor, John Herman Schulze first revealed that on exposure to light silver salts turned into black. Silver salts then after were further explored and were for many years the critical component of photographic plate. Platinum was discovered on the alluvial sands of the Pinto River in Columbia and confirmed as new metal by Italian-French scientist Julius Caesar Scaliger who concluded that the metal was not silver and in fact a new element [15]. In 1845, Michel Peyrone synthesized cisplatin (platinum-containing anti-cancer drugs) [16] and Alfred Werner, in 1893, elucidated the structure of cisplatin whereas Rosenberg studied the antitumor activity of cisplatin. After successful studies and trials, in 1978 the US by the Food and Drug Administration approved the use of cisplatin as anticancer drug.

2.3. Properties of Noble Metal Nanoparticles

2.3.1. Optical Properties

Metal nanoparticles exhibit unique shape and size-dependent optical properties. In particular, the extinction spectra of noble metal nanoparticles are dominated by localized surface plasmon resonance (LSPR). These resonances are attributed to a coherent excitation of the conduction band electrons, excited by means of an electromagnetic field. In the presence of the oscillating electromagnetic field of the light, the free electrons of the metal nanoparticle undergo a collective coherent oscillation with respect to the positive metallic lattice. The general case of an interaction between an electromagnetic field and a spherical metal nanoparticle is schematically depicted in figure 2.1. The field in the nanoparticle is in homogeneous and its optical response is rather complex [17].
Figure 2.1 Schematic of plasmon oscillation for a sphere, showing the displacement of the conduction electron charge cloud relative to the nuclei [15]

Large number of atoms present on the surface of nanoparticles contributes electron cloud on the surface of nanoparticles. As shown in the figure 2.1, the movement of these free electrons under the influence of the electric field vector of the incoming light leads to a dipole excitation across the particle. This induces positive polarization charge on cationic lattice. This charge acts as a restoring force, and brings back electron cloud to its original position, thus causing the oscillations of the electron cloud. In this manner a dipolar oscillation of electrons is created (called plasma oscillation) with a certain frequency called plasmon frequency. The surface plasmon resonance is a collective excitation mode of the plasma localized near the surface. However, the resonance frequency of the surface plasmon is different from an ordinary plasma frequency. If the frequency of the excitation light field is in resonance with the frequency of this collective oscillation, even a small exciting field leads to a strong oscillation [18, 19].

The rigorous calculations made by Mie are traditionally referred to as the Mie theory. The theory of light scattering by small spheres was already
developed, but it was Mie who applied it to the scattering and absorption of metal spheres. Mie theory describes characteristic light absorption of spherical metal nanoparticles which demonstrates that the absorption does not strongly depend on the particle size in the size range of 3 to 10 nm. The particles start showing size dependence of the plasmon resonance band below the size limit of 10 nm and ultimately disappear for particles of size less than 2 nm. This is attributed to the decreasing validity of the free electron gas model assumption [20, 21].

The electric field intensity and the scattering and absorption cross-sections are all strongly enhanced at the LSPR frequency [22] which for gold, silver, and copper lies in the visible region [22, 23]. Since copper is easily oxidized, gold and silver nanostructures are most attractive for optical applications. The ability to integrate metal nanoparticles into biological systems has had greatest impact in biology and biomedicine. Due to the plasmonic properties of gold and silver nanostructures, they are being utilized for biodiagnostics, biophysical studies, and medical therapy.

2.3.2. Catalytic properties

Metal nanoparticles like silver, palladium and gold have attracted a great interest in scientific research and industrial applications, due to their unique large surface-to-volume ratios. Catalytic activity of usually work on the surface of metals, the metal nanoparticles have been considered as promising materials for catalysis, which have much larger surface area per unit volume or weight of metal than the bulk metal. The size of the nanoparticle is one of the most important factors in the catalytic activity. As surface-to-volume ration increases the catalytic activity of the metal nanoparticles increases which ultimately increases with decrease in the size of the nanoparticles. Pd and Ag nanoparticles can be used for the hydrogenation of oxygen-containing olefins and epoxidation of ethylene with oxygen, respectively [24]. Thus, metal nanoparticles have been demonstrated for homogeneous and heterogeneous catalytic activity. The catalytic activity is also shape dependent phenomenon as
the shape of the nanoparticle changes the surface-to-volume ratio also changes which causes the exchange of electrons. The hydration of acrylonitrile was catalyzed by Cu-Pd bimetallic nanoparticles [25] and like that plenty of bimetallic have been studied for the catalytic activity.

2.3.3. Electronic properties

Metal nanoparticles show different electronic properties below certain size limit. There will be change in electronic distribution in metal which may transform some metal into semiconductor at nanometer scale. For example, gold nanoparticles act as quantum dot below certain size range [26]. Coulomb blockade is important and interesting effect that occurs when nanoparticles embedded between metal-insulator-metal junctions show charging of differential capacitance or charging at low temperature even at zero bias. This effect is a result of extremely small capacitance of the metal nanoparticles [27].

2.3.4. Melting point

Many physical properties of materials, especially the melting point, change as the physical size of the material approaches from the micro to nanoscale [28]. Changes in melting point occur due to a much larger surface-to-volume ratio of nanoscale material than bulk materials, altering thermodynamic and thermal properties. The melting temperature also decreases as the metal particle size decreases. The melting point is also marginally depending on shape of the metal nanoparticles. The melting point decrease with the large surface-to-volume ratio. The surface areas of nanoparticles in different shape will be different even in the identical volume, and the area difference is large especially in small particle size.
2.4. Applications of Noble Metal Nanoparticles

![Figure 2.2. The schematic of the various applications of noble metal nanoparticles in the therapeutics, imaging, diagnosis](image)

Metal nanoparticles due to the varies physical, chemical and biological properties also size and shape dependent phenomenon have potential application in vast area like antimicrobial agents, therapeutic, imaging, diagnostic, catalysis, environmental decontamination etc., (figure 2.2). The following section will briefly cover the various metal nanoparticles used in various applications.

### 2.4.1. Antimicrobial properties

Among noble metal nanoparticles, silver, copper and gold have been studied extensively for antimicrobial activity against pathogenic microorganisms [29]. High surface areas to volume ratios with unique physicochemical properties of noble metal nanoparticles are contributing effective antimicrobial activities [30]. Lots of burden on the economy for the developing countries is rising due to the production cost of traditional antibiotics [31]. Also, microorganisms are developing resistance against these antibiotics. So continues development in the traditional antibiotic is required desperately. The biological synthesis method of metal and metal oxide
nanoparticles have been explored since few years. So the production cost of these materials is too less than chemical antibiotics. It is also demonstrated that the rate of acquiring resistance to the nanoparticles is slower as compared to conventional antibiotics [32]. Antimicrobial mechanisms of nanomaterials include: 1) photocatalytic production of reactive oxygen species (ROS) that damage cellular and viral components, 2) damaging the bacterial cell wall/membrane, 3) disruption of energy transduction, and 4) inhibition of enzyme activity and DNA synthesis [30, 33-35]. Figure 2.3 shows the brief mechanisms of antimicrobial activity of metal nanoparticles.

![Figure 2.3. Schematics of antimicrobial mechanisms of AgNPs [39]](image)

The antibacterial property of silver has been used since antiquity. Silver in the forms of metallic silver, silver sulfadiazine, and silver nitrate has been used for burn wound treatment and disinfection of catheters, dental instruments, and bacterial infection control [36]. Using after discovery of antibiotics in the 1940s silver become out of favor to treat bacterial infections [37]. The clinical use of silver is now under extensive research as antibiotics-resistant bacteria are emerging and showing less or no response to conventional antibiotics [38]. AgNPs among other metallic NPs have proven to be the most
lethal against viruses, bacteria, and other eukaryotic microorganisms [39]. The respiratory chain and cell division are affected by AgNPs which finally lead to cell death [40]. The antimicrobial activity of AgNPs is oppositely allied to size and shape [41]. Amalgamation of AgNPs with antibiotics such as penicillin G, erythromycin, amoxicillin, and vancomycin, resulted in improved and synergistic antimicrobial effects against Gram-positive and Gram-negative bacteria [42, 43]. AgNPs have been used in fabrics, textiles, surgical masks and medical devices, gels and lotions [44]. Irreversible pigmentation in the skin (argyria) and eyes (argyrosis) with also other toxic effects like irritations, organ damage, and blood count change are the possible adverse effects due to prolonged exposure of Ag+ ions [45]. On the other hand, metallic silver appears to have a minimal risk to health and AgNPs are recommended to be non-toxic in some studies [46], but concentration-dependent adverse effects of AgNPs on the mitochondrial activity are also report. So AgNPs to be used as the sole antimicrobial agent against diseases is required to undergo thorough study of effects to mammalian and other animal cells.

Near-infrared (NIR) light-absorbing AuNPs, nanoshells, nanorods, and nanocages have been demonstrated to kill bacterial growth via irradiation with focused laser pulses of suitable wavelengths [47]. AuNPs have strong attraction towards negatively charged cell membrane of microorganisms which is the main cause of the antimicrobial activity of the AuNPs [48], which was also supported by the observation that cationic particles were found to be slightly toxic while anionic particles were not. AuNPs conjugated with antimicrobial agents and antibodies have been investigated to obtain selective antimicrobial effects. For example, Au NPs conjugated with anti-proteinA antibodies for the selective killing of S. aureus, which target the bacterial cell surface, was reported [49]. Laser induced hyperthermia caused formation of the bubble which is used for the selective killing of the bacteria [50]. Effective inhibition of antibiotic resistant microorganisms with the conjugation of antibiotic is demonstrated [51]. Therefore, AuNPs can be promising adjuvants for antibiotic
therapy in treating serious bacterial infections with minimal adverse effects as AuNPs have been demonstrated to be less toxic to mammalian cells.

2.4.2. In therapeutics

Versatile noble metal nanoparticles are agents with a variety of biomedical applications and sensitive diagnostic assays [50], radiotherapy enhancement, and thermal ablation [51, 52], as well as gene delivery and drug [53, 54]. In addition, noble metals NPs have been projected as non toxic carriers for drug and gene-delivery applications [55]. Theranostic application is the major advantage of noble metal nanoparticles where they are being explored to use as simultaneous diagnostic as well as therapeutics purpose.

It is necessary to use designed and engineered NPs especially in therapy that can be targeted to tissues of interest, also can produce specific, desired effects. The function of AgNPs as antibacterial agents has been well established. Anti-viral properties of biologically formed AgNPs are more effective than chemically synthesized AgNPs [56]. Vero cells co-incubated with AgNPs were reported to prevent plaque formation after being infected with the Monkey pox virus [57] Metallic nanoparticles have also been described as a possible HIV preventative therapeutic [58]. Metallic nanoparticles have also been effective antiviral agents against herpes simplex virus, influenza, and respiratory syncytial viruses [59]. The potential therapeutic application of noble metal nanoparticles represents an attractive platform for cancer therapy in a wide variety of targets and clinical settings. It is shown that “naked” gold nanoparticles inhibited the activity of heparin-binding proteins, such as VEGF1and bFGF in vitro and VEGF induced angiogenesis in vivo [60]. Dalton’s lymphoma ascites (DLA) cell lines co-incubated with AgNPs displayed a dose dependent toxicity through activation of caspase-3 and inhibition of cellular proliferation. Furthermore, tumor bearing mice injected with AgNPs demonstrated a reduction of ascites production (65%) and tumor progression compared to the sham treated mice [61] which have been shown to have applications in cancer treatment. Human
colon carcinoma cells (HT29) showed a dose and time dependent response when exposed to platinum nanoparticles (Pt-NP) [62].

Gold nanoparticles have shown potential as intracellular delivery vehicles for antisense oligonucleotides [63] and for therapeutic siRNA by providing protection against RNAses and ease of functionalization for selective targeting [64] have emerged as a powerful and useful tools to block gene function and for sequence-specific posttranscriptional gene silencing, playing an important role in down regulation of specific gene expression in cancer cells. Metallic nanoparticles may offer an advantage in radiotherapy area by utilizing their excellent optical properties, surface resonance, and wavelength tunability. For example X-ray irradiation, gold nanoparticles can induce cellular apoptosis through the generation of radicals which can be used as therapy without harming the surrounding healthy cells [65]. The surface size of AgNPs enhances the thermal sensitivity of glioma cells. Pioneering work by Pitsillides illustrated that the surface plasmon resonance (SPR) of nanoparticles is easily exploited for photo-dynamic therapy (PDT) anti-cancer therapy [66]. El-Sayed group demonstrated that AuNPs are effective PDT agents and could “seek and destroy” cancerous cells [67].

The metallic nanoparticles have been demonstrated promising as PDT and hyperthermic agents for the treatment of cancer. Rapid heating of metallic nanoparticles occurs on the application of magnetic field. The gold particles by the oscillating magnetic field produce electric currents [68]. The heat generation occurs due to eddy which dissipates into the surrounding from nanoparticles, causing thermal ablation [69]. Figure 2.4 is demonstrating the treatment of cancer using metallic nanoparticles by inducing hyperthermia with the aid of radiotherapy. The toxicity of metallic nanoparticles to the normal tissue or cells is the major concern of the use of metallic nanoparticles for the use of cancer hyperthermia.
Figure 2.4. Therapeutic application of noble metal nanoparticles by the induction of hyperthermia with the assists of radiotherapy [64]

2.4.3. In diagnostics and imaging

Due to the strongly enhanced LSPR, noble metal nanoparticles scatter light very strongly at the LSPR frequency, making them very promising for optical imaging and labeling of biological systems [49]. While scattering and absorption are competing processes, the relative contribution of scattering increases rapidly with increase in the nanostructure volume. Dark-field microscopy shows (right) HSC cancer cells clearly defined by the strong LSPR scattering from (top) gold nanospheres and (bottom) gold nanorods bound specifically to the cancer cell surface, whereas (left) HaCat healthy cells have (top) gold nanospheres and (bottom) gold nanorods randomly dispersed without specific binding (figure 2.5). The scattering color (LSPR frequency) of the nanospheres and nanorods can be clearly distinguished. While the scattering from a 10-nm gold nanoparticle is negligible, an 80-nm gold nanoparticle offers scattering 5 orders of magnitude larger than the typical
emission from a dye. Such highly enhanced cross-sections offer sensitive and highly contrasted imaging allowing use of the much simpler but powerful dark-field microscopy [64].

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<th>HaCat healthy cells</th>
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<td><img src="image1" alt="HaCat healthy cells" /></td>
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**Figure 2.5.** Molecular-specific imaging of cancer using metal nanoparticle / anti-EGFR conjugates [21]

The noble metal nanoparticles can be used for the simultaneous actuation and tracking *in vivo* along with their therapeutic capabilities. Most noble metal nanoparticles for *in vivo* imaging and therapy have been designed to strongly absorb in the near infrared (NIR) so as to be used as effective contrast agents whereas at NIR biological components minimum light absorption [46]. The use of PEG-coated AuNPs for *in vivo* computed tomography CT contrast agent was shown to increase image contrast, which allows to reduce the radiation dosage needed, allow to overcome the limitations of conventional contrast agents (e.g., iodine-based compounds), such as short imaging times due to rapid renal clearance, renal toxicity, and vascular permeation [46]. In photoacoustic
imaging (PAI) and photoacoustic tomography (PAT), Au-nanocages enhanced the contrast between blood and the surrounding tissues by up to 81%, allowing a more detailed image of vascular structures at greater depths [69].

2.4.4. In catalysis and environmental decontamination

Noble metals and bimetallic nanoparticles have shown their potential use for the environmental application in conversion of hazardous chemical compound to less toxic or non-toxic one. Liu et al. reported hydrodechlorination of monochlorobenzene in the presence of colloidal platinum nanoparticles stabilized on polyvinylpyrrolidone (PVP) [70]. Silver/gold (Ag/Au) bimetallic nanoparticles have also been reported as being effective for dehalogenation processes. Using an underpotential deposition-redox placement technique, Zhou used Ag/Au bimetallic nanoparticles as the cathode in the electrochemical reduction of benzyl chloride [70]. Platinum/palladium (Pt/Pd) bimetallic nanoparticles, iron/silver (Fe-Ag) and gold/platinum (Au-Pt) are increasingly being investigated for dehalogenation and it is expected that with optimization of reaction conditions [70].

A number of contaminants such as lead and pesticides are affecting water supplies globally due to their widespread use; pollutants of geochemical origin such as arsenic and fluoride are currently found in selected countries. It is quite evident that pesticides contain highly toxic recalcitrant groups and hence are extremely difficult to break through normal synthetic routes of degradation. A useful example of size-dependent catalysis has been demonstrated through AgNPs-catalyzed reduction of nitrophenol to aminophenol [66]. Contaminants such as pesticides are removed through homogeneous or heterogeneous chemistry. A remarkable example is the catalytic oxidation of CO with supported gold nanoparticles [71]. One of the interesting application areas of noble metal nanoparticles in drinking water purification is the sequestration of heavy metals. The first studies of the interaction of metal ions with noble metal nanoparticles were in the early 1990s [71]. Noble metal nanoparticles have extensively studied for the detection of
heavy metals and pesticides in the drinking water [72]. In addition, the biggest class of contaminants affecting drinking water is microorganisms. Every year, 1.8 million people die from diarrheal diseases (including cholera); 90% are children under five, mostly in developing countries. Worldwide, 1 billion people lack access to safe drinking water, 2.4 billion to adequate sanitation. Improved water supply reduces diarrhea morbidity by 6% to 25%; improved sanitation reduces it by 32%. As discussed earlier, the antimicrobial activity of the AgNPs has been top priority of the researcher which is now also being used for the decontamination of water from pathogenic species [72].

2.5. Summary

The present chapter deals with some historical and theoretical background of the noble metal nanoparticles. Due to their unique size and shape dependent optical properties, metal nanoparticles have potential applications in medicine and environmental field. This chapter gives some glimpse of the properties, and applications of the noble metal nanoparticles in various fields including health care and environmental decontamination.
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