CHAPTER II

LITERATURE REVIEWS

2.1 Gold nanoparticles

Gold is a bright, too soft, slightly reddish yellow, dense, malleable, solid under standard conditions, transition metal (Depending on the element with which it reacts, it may lose a different number of valence electrons) with the electronic configuration represented by (Xe) $4f^{14}$ $5d^{10}$ $6s^{1}$ and is one of the least reactive chemical elements (Rinehart and Winston, 2005). Since ancient Roman times, gold nanoparticles were used to stain glasses with different colors (Hunt, 1973). In the 1850s, Michael Faraday's investigated the colloidal gold's optical properties (Faraday, 1857). The scattering and absorption of light of the colloidal gold depend on aggregation state, local refractive index, particle size, and shape resulting in different colors (Anderson et al., 1999). Various types of gold nanoparticles has already been used in a variety of applications (Table 2.2) (Link and El-Sayed, 1999). The synthesis and properties of colloidal gold were interesting for scattering and absorption by spherical particles (Sharma et al., 2009; Zeng et al., 2013). Various types of gold nanoparticles are already being used in a variety of applications as shown in Table 2.2. As early as 2500 BC., the ancient Chinese and Egyptians used gold for therapeutic purposes (Daniel and Astruc, 2004).

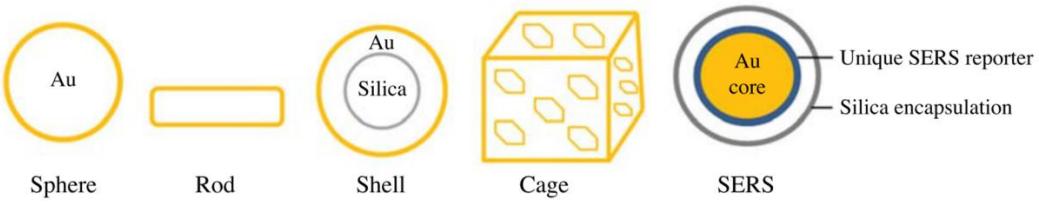

Figure 2.1 Various types of gold nanoparticles (Das et al., 2012).

Gold nanoparticles can easily synthesize in various shapes with sizes ranging from 1 nm to more than 200 nm. The size of gold nanoparticles affects their applications such as the particles size ranging from 2 nm to 15 nm are used in microscopy immunohistochemistry and biomarkers. Chemical sensors, medication delivery, biomarkers, and DNA detection all use particles with sizes ranging from 20 nm to 60 nm. 20 nm to 50 nm particles had the best cellular uptake, whereas 40 to 50 nm particles have the best diffusion into tumor cells. The larger size of gold nanoparticles ranging from 80 to 250 nm is used in optical mammography, electronic devices, forensic science, etc. (El-Sayed et al., 2006).

Table 2.1 The wavelengths of spherical AuNPs depend on size changing (Shah et al., 2014).

Wavelength (nm)	Size of gold nanoparticle (nm)
515	5
520	10
524	20
526	30
530	40
535	50
540	60
553	80
572	100

Gold nanoparticles have the potential for many biomedical applications, due to their large specific surface, high surface activity, good biocompatibility, strong antioxidant property, and suitableness for manipulations at the molecular level (Chithrani et al., 2010; Kong et al., 2017). Gold ionic chemical compounds (gold salts) have been used to relieve TB discomfort and swelling, as well as to halt disease development in people with rheumatoid arthritis, psoriatic arthritis, and bronchial asthma (Rau, 2005; Shaw, 1999). In recent years, colloidal gold nanoparticles are efficient for potential applications depending on their shape and size (Khan et al.,

2014; Mishra et al., 2012; Svedberg and Pedersen, 1940). In general, gold nanoparticles are more recommended than other inorganic nanoparticles for biomedical applications, because of their excellent biological compatibility with human cells (Alanazi et al., 2010; Jain et al., 2006; Shukla et al., 2005), and are easily available for conjugation with various small biomolecules such as amino acids, carboxylic acid, enzymes, proteins (Guglielmo et al., 2010; Wangoo et al., 2008), polyethylene glycol (Khalil et al., 2004), DNA (Kim et al., 2010), RNA (Lee et al., 2009), antibodies (Yang et al., 2009), and peptides (Sun et al., 2008). In addition, these particles can circulate with blood flow and easily reach the targeted site such as the cancer site (Kojima et al., 2010; Ye et al., 2018).

Table 2.2 Shapes of gold nanoparticles and their applications (Khan et al., 2014).

Shape	Size (nm)	Application	Reference
Nanorod	2-5	Photothermal therapy and drug delivery	(Guo et al., 2014)
Hollow particle	25	Photo-electronics, cancer therapy, and catalysis	(Ganeshkumar et al., 2012)
Triangular particle	3.85-7.13	Highly effective against *K. pneumonia* and *E. coli*	(Murawala et al., 2014),
Faceted particle	50-100	Reproducible, Effective, and stable large area substrates for near infra-red surface-enhanced Raman spectroscopy	(Papasani et al., 2012)
Nanocage	50	Effective molecular contrast agent for non-linear endomicroscopy imaging and in vivo medical applications	(Giljohann et al., 2010), (Bisker et al., 2012)
Nanocube	50	Refractive-index sensing and field enhancement applications	(Pissuwan et al., 2011)

The applications in the field of optoelectronics, biological and chemical sensing, biomedical imaging, biological tagging, DNA labeling, photothermal therapy (Alanazi et al., 2010), photoacoustic imaging (Kim and Jon, 2012), catalysis, tracking and drug delivery (Tedesco et al., 2010), cancer antigen and cancer therapy (Guo et al., 2014; Mishra et al., 2012). For medical applications, gold nanoparticles are used for the diagnosis and therapy of cancer cells and microorganisms, and important in HIV therapeutics, and are also being used as target delivery of compounds such as drugs, genes, and proteins (Bowman et al., 2008; Li et al., 2006; Mody et al., 2010).

2.2 Synthesis of gold nanoparticles

Various methods for synthesizing gold nanoparticles have been developed. The general method for synthesizing AuNPs consists of physical, chemical, and biosynthesis methods (Papasani et al., 2012). The methods for producing gold nanoparticles can be classified into two categories, the “top-down” and “bottom-up” techniques (Eustis and el-Sayed, 2006). The top-down technique is a physical method that requires the matter removal from the bulk iron oxide material divided into nanoparticles, such as electron beam lithography and photolithography (Sun et al., 2006). The bottom-up technique is a chemical or an electrochemical that involves the assembly of atoms (produced by ion reduction) into preferred nanomaterials, such as sol-gel processing.(Heidari et al., 2014; Xinghua Sun et al., 2013), photochemical (Jin et al., 2001), nanosphere lithography (Pileni, 1997), templating (Hall et al., 2001), electrochemical, sonochemical (Okitsu et al., 2005), and thermal reduction techniques (Magnusson et al., 1999). The shape and size of gold nanoparticles can be generated using both top-down and bottom-up techniques (Figure 2.2). The morphology of nanoparticles depends on synthesis processes such as the formation of nuclei, growth, aggregation, and absorption of impurities. Whereas the particle size of nanoparticles is influenced by varying factors, such as pH value, temperature, reaction conditions, the reactants concentration, impurities, the nature of the solvent, etc. (Chen et al., 2005; Eustis and el-Sayed, 2006). Compilation of TEM images with various shapes of gold nanostructures synthesized by various methods are shown in Figure 2.3.

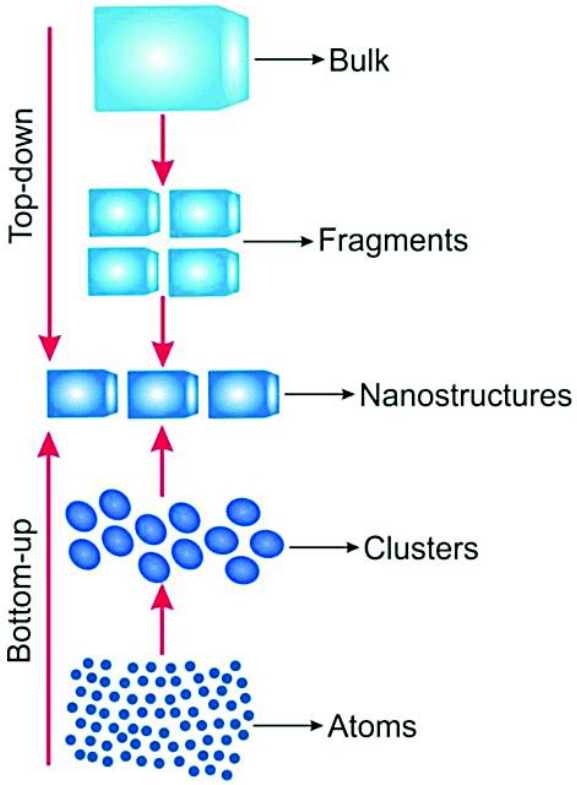

Figure 2.2 The schematic representation of the top-down and bottom-up technique for nanoparticle preparation (Galstyan et al., 2018).

2.3 Biological synthesis of nanoparticles by *Streptomyces*

Streptomyces is the largest genus of Actinobacteria. *Streptomyces* species are capable of producing secondary metabolites such as vitamins, immunosuppressive, and antibiotics. Bacterial interactions with inorganic materials are well known (Bosecker, 1997). Actinobacteria have resistance to harmful heavy metals due to chemical detoxification, which includes the movement of ions via ATPase membrane proteins or chemiosmotic cation or proton anti-transporters, as well as solubility changes (Bruins et al., 2000). In comparison to intracellular production, extracellular production of metallic nanoparticles has many applications in diverse fields such as optoelectronics, sensor technology, electronics, and bio-imaging (Bao et al., 2003; Narayanan and Sakthivel, 2010).

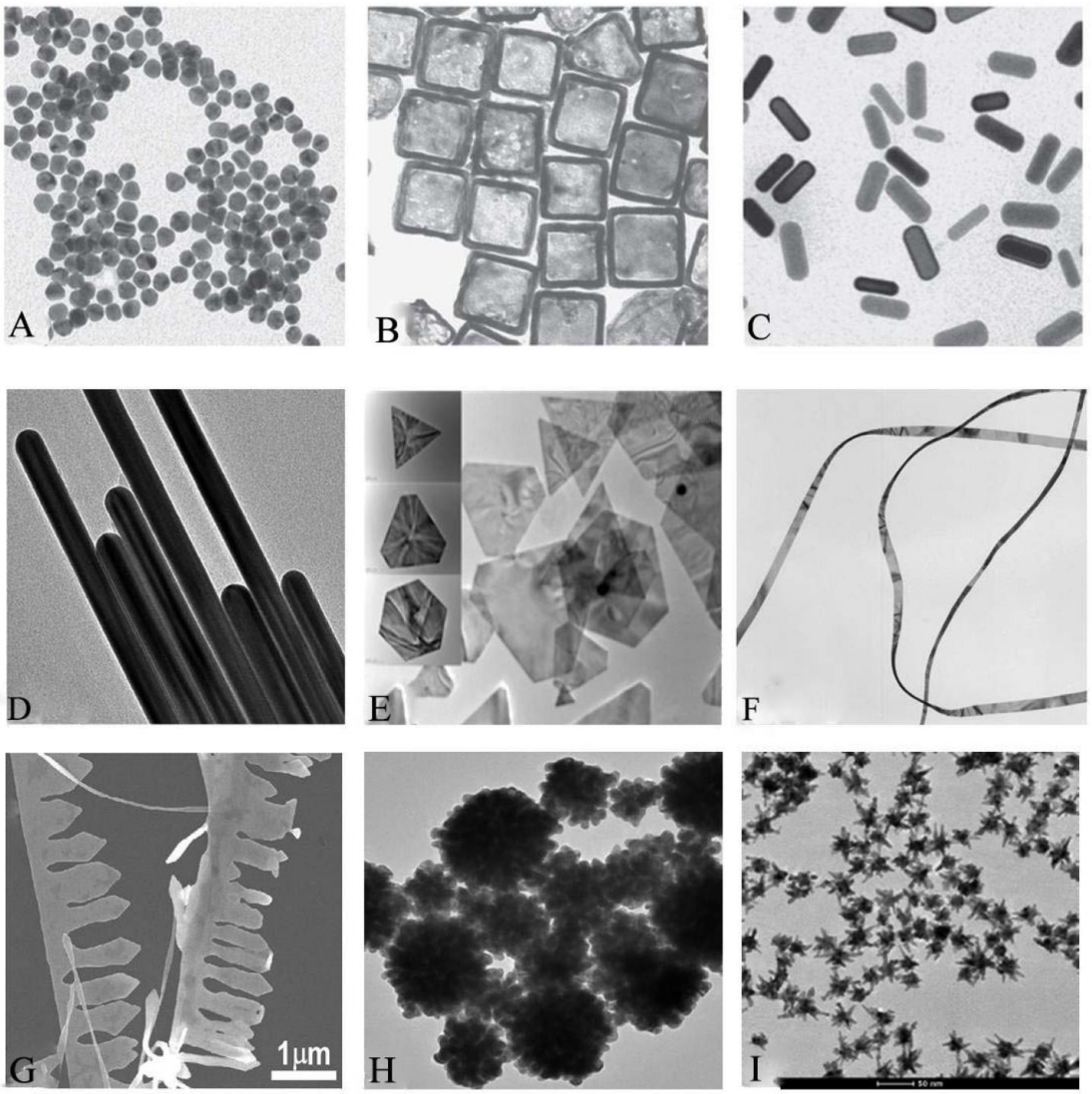

Figure 2.3 Compilation of TEM images with various shapes of gold nanostructures synthesized by various methods. (A-I) Represents the TEM image of the gold nanostructures consisting of (A) gold nanospheres (Cho et al., 2011), (B) gold nanocages (Cho et al., 2011), (C) gold nanorods (Cho et al., 2011), (D) gold nanowires (Kim et al., 2008), (E) gold nanoplates (Liu et al., 2005), (F) gold nanobelts (Zhao et al., 2008), (G) gold nanocombs (Zhao et al., 2008), (H) gold nanoflowers (Li et al., 2010), and (I) gold nanostars (Yuan et al., 2012). (Source: (Shah et al., 2014).

Khadivi et al. (2012) reported the biosynthesized gold nanoparticles using extracellular production of *Streptomyces griseus*. After 48 hours, the XRD and UV-visible spectra of the mixture containing *S. griseus* and 1mM $HAuCl_4$ revealed the formation of gold nanoparticles. The image of TEM revealed spherical gold nanoparticles with an average particle size of 50 nm (Khadivi et al., 2012).

Zonooz et al. (2012) reported biosynthesis of gold nanoparticles by *Streptomyces* sp. The formation of gold nanoparticles was monitored using UV-visible spectroscopy. Moreover, the nanoparticles of gold were characterized using SEM, TEM, and XRD. The result shown shows a spherical shape with the average particle size ranging from 10 to 30 nm (Zonooz et al., 2012).

Sadhasivam et al. (2012) described how *Streptomyces hygroscopicus* assisted in the biosynthesis of multidimensional gold nanoparticles. The control of the key growth parameters, such as reaction time and pH of the solution, resulted in multidimensional gold nanoparticles. The spherical gold nanoparticle has a diameter of 10 to 20 nm (Sadhasivam et al., 2012).

Gopal et al. (2013) reported the actinobacteria-mediated synthesized gold nanoparticles using the *Streptomyces* sp. VITDDK3 cell-free supernatant. The UV-visible spectra (550 nm) were used to characterize the gold nanoparticles. XRD pattern analysis revealed peaks corresponding to Au metal diffraction at (111), (200), (220), and (311). SEM analysis was used to determine the shape of nanoparticles, which had an average size of 90 nm. Moreover, the antifungal activity of these synthesized gold nanoparticles was tested using the agar well diffusion method. The antifungal activity was demonstrated against *Microphyton gypseum* (10 mm) and *Trichophyton rubrum* (13 mm) (Gopal et al., 2013).

Karthik et al. (2013) reported the synthesis of gold nanoparticles via *Streptomyces* stain LK-3. Gold nanoparticles of these methods were found with an average particle size ranging from 5 to 50 nm. Gold nanoparticles were developed by *Plasmodium berghei* (ANKA (PbA)) for the treatment of infected mice. The ANKA (PbA) affected the infected mice, delaying the rise in parasitemia compared with PbA infection for 8 days post-infection and increasing the 85% survivability of the mice. During the gold nanoparticles treatment in PbA infection, the histomorphological

analysis showed no changes in the tissues of the liver and spleen for 8 days post-infection. The result confirmed the down-regulation of TNF-α and up-regulation of TGF-β in serum and tissue level in ANKA (PbA) compared to PbA infection. Based on the results of the anti-malarial activity, they suggested the synthesized gold nanoparticles using *Streptomyces* sp. LK-3 revealed a potential source for drug development of anti-malarial (Karthik et al., 2013b).

Ibrahim et al. (2016) reported biosynthesized gold nanoparticles using extracellular of *Streptomyces* sp. as a stabilizing /capping/reducing bio-agent and chloroauric acid ($HAuCl_4$) as a precursor. The gold nanoparticles sizes ranged from 4 to 13 nm. They studied UV-blocking for viscose knitted and cotton fabrics surface modification using O_2-plasma, followed by treatment with gold nanoparticles and gold nanoparticles combined with ZnONPs or TiO_2NPs to provide different functional properties, specifically antibacterial properties (Ibrahim et al., 2016).

2.4 Antibacterial activity of gold nanoparticles

Antibiotics improved medicine by permitting the bacterial infections treatment that were previously thought to be incurable. Unfortunately, many bacteria have developed resistance to the antimicrobial drugs now in use (Shah et al., 2014). Gold nanoparticles are inorganic metals known for potential antimicrobial activity against Gram-negative and Gram-positive bacteria (El-Batal et al., 2013). Green synthesis methods of gold nanoparticles showed antibacterial activities in various fields.

Balagurunathan et al. (2011) used *Streptomyces viridogens* stain HM10 to synthesize gold nanoparticles. The average particle size was between 18 and 20 nm. The antibacterial activities of gold nanoparticles were demonstrated in a well-diffusion method against Gram-negative (E. coli) and Gram-positive (S. aureus) bacteria (Balagurunathan et al., 2011).

Sadhasivam et al. (2012) studied the biogenic synthesis of multidimensional gold nanoparticles using cell-free supernatants of *Streptomyces hygroscopicus.* They have demonstrated the antibacterial properties of metallic gold nanoparticles by using a minimal inhibitory concentration assay. The MTT assay was used to

determine the minimum inhibitory concentrations (MIC) of the biosynthesized gold nanoparticles. Growth inhibition studies were used to test the antibacterial activity of gold nanoparticles against Gram-negative and Gram-positive bacteria such as *Escherichia coli* KACC 10005, *Staphylococcus epidermidis* KACC 13234, *Enterococcus faecalis* KACC 13807, *Salmonella typhimurium* KACC 10763, *Staphylococcus aureus* KACC 13236, *and Bacillus subtilis* KACC 14394 (Sadhasivam et al., 2012).

Ibrahim et al. (2016) used marine *Streptomyces* sp. as reducing agents and chloroauric acid ($HAuCl_4$) as a precursor to biosynthesize gold nanoparticles. According to the results, the addition of gold nanoparticles to activated fabric samples significantly improved antibacterial activity against Gram-negative (*E. coli*) and Gram-positive (*S. aureus*) bacteria (Ibrahim et al., 2016).