



“The Gold Nano Particles: A Novel Drug Delivery”

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2. ABSTRACT

In every field of life, nanotechnology has an impact. Researchers expend their interests on gold nanoparticles synthesis as they provide superior properties for various types of applications. Different physical and chemical methods have synthesized conventionally nanoparticles that have a negative impact on the environment. Due to their unique properties, small size and high area-to-volume ratio, gold nanoparticles show special advantages in this field among nanoparticles. Because of their inert nature, stability, high dispersity, non- cytotoxicity and biocompatibility, these particles have been widely used in various biomedical applications and drug delivery systems. This paper shows the comparison and survey of all the methods. Gold nanoparticles are widely used in many fields As preferred materials for their unique optical and physical properties, such as surface plasmon oscillations for labeling, imaging, and sensing. Recently, many advancements were made in biomedical applications with better biocompatibility in disease diagnosis and therapeutics. Au-NPs could be prepared and conjugated with many functionalizing agents, such a polymers, surfactants, ligands, derailments, drugs , DNA, RNA, proteins. Peptides and oligonucleotides. This review addressed the use of gold nanoparticles and the surface functionalization with a wide range of molecules expanding and improving gold nanoparticles in targeting drugs for photothermal therapy with reduced cytotoxic effects in various cancers gene therapy and many other diseases.

Keywords: Gold nanoparticles, Nanotechnology, drug delivery, biomedical Applications, cytotoxicity, cancer, drug delivery.

3. INTRODUCTION

In recent years, nanotechnology has become one of Physics, Chemistry, Engineering and Biology's most important and exciting front lines. It shows great promise to give us many breakthroughs that in a wide range of applications will change the direction of technological advances. The nanotechnology research area is interdisciplinary, covering a wide range of topics ranging from nanoparticles

catalyst chemistry to quantum dot laser physics. As a result, researchers need to go beyond their expertise in

any particular area to appreciate the wider implications of nanotechnology and learn how to contribute to this exciting new field. Particles of 1-100 nm size are called nanoparticles, whether dispersed in gaseous, liquid, or solid media. Because NPs are larger than individual atoms and molecules but smaller than bulk solids, materials in the regime of nanometers size show an intermediate behavior between that of a macroscopic solid and that of an atomic or molecular system.

Nanotechnology is based on the recognition that particles below the size of 100 nm convey new properties and behavior to nanostructures built from them. The electronic structure, conductivity, reactivity, temperature melting and mechanical properties were all observed to change when particles are smaller than a critical size. The behavior's dependence on the particle sizes can enable one to develop their properties. The properties of nanometer- dimensional materials differ significantly from those of atoms and bulk materials. There are three major factors responsible for these differences: the high ratio of surface to volume, the effect of quantum size and the interactions of electrodynamics.

All nanoparticles irrespective of their chemical constituents have extremely high surface- to-volume ratios. Thus, the nature of the NP surface dominates many of the physical properties of nanoparticles such as solubility and stability

The first use of gold as money occurred around 700 B.C., when Lydian merchants produced the first coins (Gimeno, 2008). The use of gold for medicinal purposes dates back to 2500 BC to the ancient Chinese and Egyptians. In medieval Europe, numerous recipes for gold elixirs existed. In the 17th and 19th century gold was used to treat fever and syphilis.

4. GOLD NANAO PARTICLES

Gold nanoparticles properties differ from their bulk form because bulk gold is yellow solid and inert in nature, while gold nanoparticles are red wine solution and are reported to be antioxidant. Inter particle interactions and assembly of networks of gold nanoparticles play a key role in determining the properties of these nanoparticles. Gold nanoparticles have different

sizes ranging from 1 nm to 8 μm and have different shapes such as spherical, sub octahedral, octahedral, decahedral, multiple twined, multiple twined, irregular shape, tetrahedral, nanotriangle, Nano prism, hexagonal platelets and nanorods (Figure 1). Triangular shaped nanoparticles show attractive optical properties compared to spherical shaped nanoparticles among all these shape

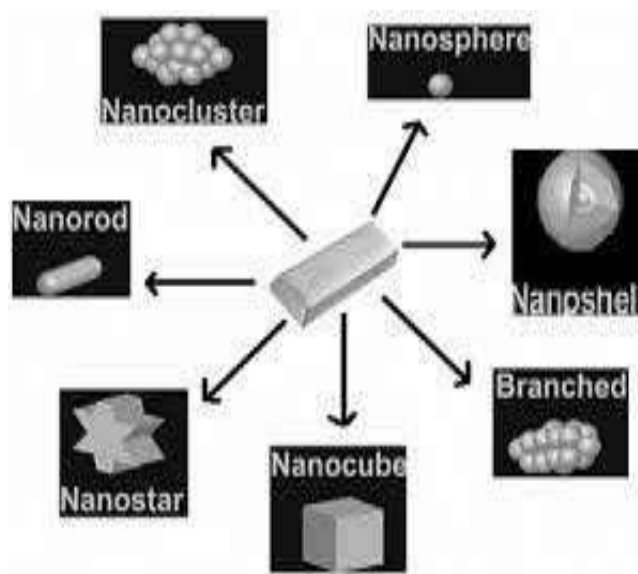


Figure 1: Various shapes of gold nanoparticles

5. Properties of Gold Nanoparticles

Gold nanoparticles (AuNPs) are being extensively researched as well as used for the diagnosis of tumors along with therapy due to their exceptional fundamental properties. AuNPs' inherent features, as well as the interrelationships between these traits, must be thoroughly investigated to make them more appropriate for tumor detection and treatment.

Physical Properties:

Physical properties of nanoparticles include “color, density, melting temperature, tensile strength, and electrical conductivity”, which are affected due to their size, structure, and surroundings. Physical properties like elasticity can differ significantly when a material's size approaches the nanoscale scale. Due to significant internal compressive stress, the mechanical properties of gold clusters are $\frac{2}{3}$ that of bulk gold, according to various studies, indicating the possibility of ultra-hard materials.

Catalysis and Chemical Properties:

AuNPs, varying from other nanoparticles, might create strong chemical interactions with groups containing S and N. As a result, AuNPs can be affixed to a broad range of chemical ligands or polymers having certain functionalities. AuNPs have excellent “biocompatibility, targeting, and drug delivery capabilities” thanks to these surface changes.

Optical And Electronics Properties:

AuNPs have unique optical characteristics that make them excellent dyes for sensing, imaging, and labeling. Regardless of the size and shape of the nanoparticles, the AuNPs solution absorbs a lot of light and changes color. Gold nanoparticles' surroundings, size, and physical qualities all have an impact on how nanoparticles engage with light. The fluctuating electric field propagating near the colloidal nanoparticles interacts with free electrons, causing the electronic charge resonance and the coordinated oscillation of the visible light frequency.

6. CHARACTERISTICS OF GOLD NONOPARTICLES

The synthesis of gold nanoparticles can be preliminary characterized by noticing the color change of the solution. Gold nanoparticles have wine red color while the bulk gold is yellow solid. This color effect occurs as gold nanoparticles absorb and scatter light with extraordinary efficiency caused due to surface plasmon resonance (Suresh et al., 2015). This color change of gold nanoparticles was first noticed by Faraday (1857) and he suggested that, these colors are formed due to the presence of suspended gold particles in the solution. However, the color change depends on the size and shape of gold nanoparticles. Different sizes and shape of gold nanoparticles possess different color change. For example, gold nanosphere suspension (of particle size less than 100 nm) can have a dark, intense reddish color, purple or blue color for large size particles. Though, the synthesis of gold nanoparticles can be preliminary characterized by the color change of the solution.

- i. UV-Vis spectroscopy UV-Vis spectroscopy is one of the simplest methods used for characterization of gold nanoparticles synthesis due to the fact that gold nanoparticles exhibit a strong UV-Vis absorption band (caused due to surface plasmon resonance) that is not present in the spectrum of the bulk metal (Stuart et al., 2005). Their strong interaction with light occurs because the conduction electrons on the metal surface undergo a collective oscillation when they are excited by light at specific wavelengths (Deene and Lingappa, 2013). Gold nanoparticles have an absorption maximum ranging from 515 nm-572nm.
- ii. Elemental analysis the elemental analysis, electronic state and chemical characterization can be carried out by using energy dispersive spectrum (EDS), energy dispersive X ray (EDX) and X-ray photoelectron spectral (XPS) techniques.
- iii. Microscopy the microscopy techniques used for characterization of gold nanoparticles includes scanning electron microscopy (SEM), field emission scanning electron microscopy (FESEM) and atomic force microscopy (AFM). Scanning electron microscopy (FESEM) and atomic force microscopy (AFM) are used for detection of surface characters of gold nanoparticles while transmission electron microscopy (TEM) (Figure6) helps to elucidate gold nanoparticles size and morphology.

7. ADVANTAGES & DISADVANTAGES OF GOLD NANOPARTICLES: ADVANTAGES:

- i. Gold nanoparticles is simple for diagnosis.
- ii. It is non-toxic to human beings.
- iii. It is less invasive.
- iv. It provides increased contrast for diagnosis oral cancer.
- v. It does not photo blinking which is inherent to many other fluorophores.
- vi. As compared to other metallic nanostructures, AuNP provide advantages of their simple and fast preparation and bioconjugation.
- vii. It is smaller in size.
- viii. It have a higher surface area.
- ix. lose dose required.
- x. It can be administered via different routes

DISADVANTAGES:

- i. It leads to acute or chronic toxicity.
- ii. Optical signals of AuNPs may not be as strong as quantum dot.
- iii. It exhibits difficulties like biocompatibility, in vivo kinetics, and tumor target efficiency.

8. SYNTHESIS OF GOLD NANOPARTICLES:

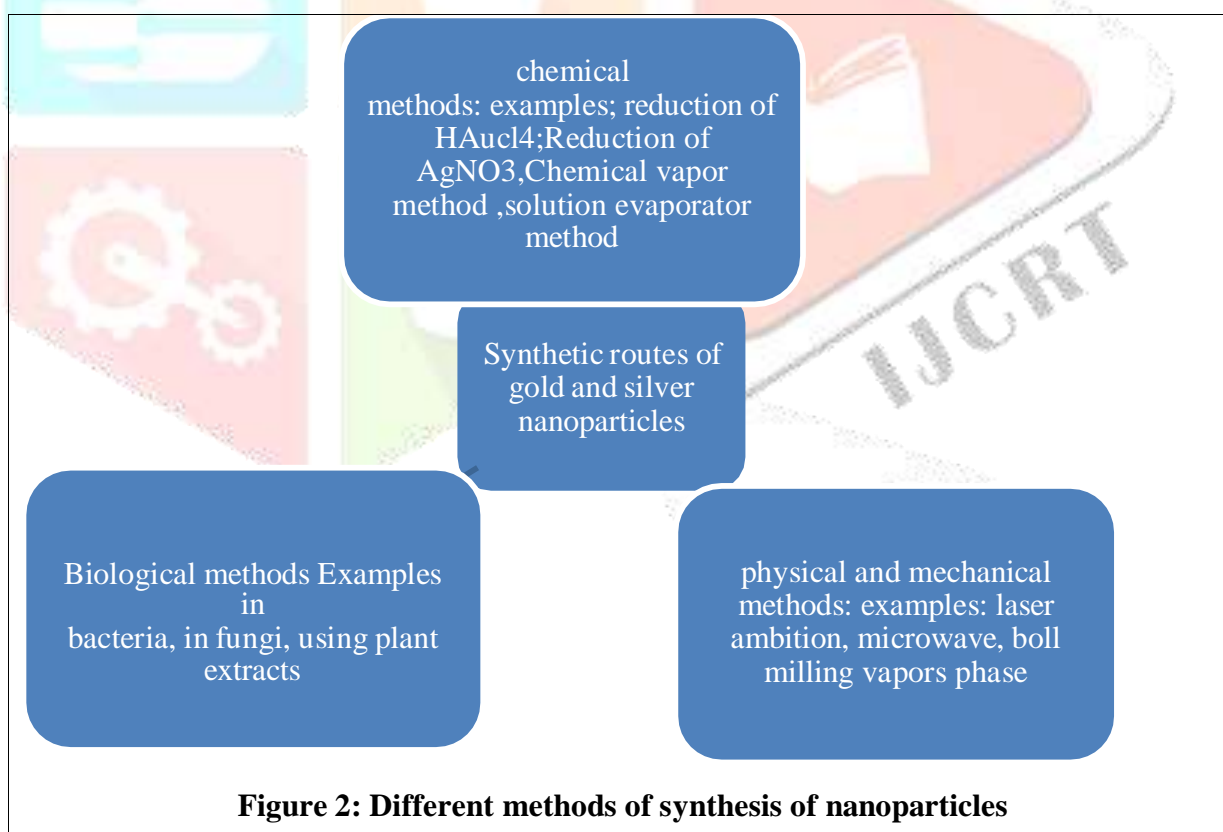
Faraday (1857) was a pioneer to introduce nanotechnology and specifically colloidal gold suspensions. He used phosphorous to reduce gold chloride to gold nanoparticles. Further, Turkevich et al. (1951) developed a method for the synthesis of gold nanoparticles. He used hot chloroauric acid for the synthesis of nanoparticles using a small amount of sodium citrate solution. The nanoparticles formed by this method are stable as citrate acts as a reducing and capping agent simultaneously. Brust et al. (1994; 1995) introduced another new method where gold nanoparticles were synthesized in an organic solvent rather than water. In this technique, chloroauric acid in TOAB (tetraethylammonium bromide) solution is reduced by means of NaBH_4 (sodium borohydride) in a toluene solution. In this method sodium borohydride act as a strong reducing agent while TOAB acts as catalyst and capping agent. At present, there are several methods for synthesizing nanoparticles, which are classified into the top-down and bottom-up approach. In top-down approach, a bulk solid material is broken into many nanoscale pieces (which includes methods like irradiation, arc discharge, thermal decomposition, diffusion, etc.,) while in bottom-up processes, nanoparticles are synthesized atom by atom (which includes methods like chemical reduction, seeded growth, polyol synthesis method, electrochemical synthesis, and biological entities for fabrication of nanoparticles

9. METHODS FOR SYNTHESIS OF GOLD PARTICLES:

Different methods for the synthesis of gold nanoparticles have been developed and these methods follow the same rules as other particle preparation methods. General methods for gold nanoparticles synthesis include chemical, physical, and biological methods, terkovich method, seeding growth method, electrochemical method, green method described below

i. Physical Method:

The π -irradiation technique is one approach to Au / NPs synthesis with a uniform size of 5-40 nm and high purity using polysaccharide alginate as a stabilizer. By reducing agents such as citric acid and a binding agent such as cetyltrimethylammonium bromide (CTAB), the microwave irradiation technique was used to prepare Au / NPs. In addition, Au / NPs are prepared with heat or photochemical reduction and HAuCl_4 reduction with citrate, tartrate and malate. For the synthesis of gold-polyethylene glycol nanoparticles by polymerization reactions of size 10-50 nm, a common method of photochemical reduction has been recorded. In addition, the radical formation of glycol diacrylate coated with polyethylene glycol by UV reaction reduces gold salt.



ii. Chemical Method:

In general, the chemical reduction method used to prepare AuNPs includes two main parts:

- a) Reduction of agents such as borohydrides, formaldehyde, aminoborans, hydrazine, hydroxylamine, polyols, citric and oxalic acids, hydrogen peroxide, carbon monoxide, sugars, sulfide testers, hydrogen, acetylene and electronic reduction agents including electron-rich transition metal sandwich complexes;
- b) Stabilization with agents such as trisodium citrate dihydrate, sulfur ligands (including thiolates),

phosphorus ligands, oxygen-based ligands, nitrogen-based ligands (including heterocyclic compounds), dendrimers, polymers and surfactants (including cetyltrimethylammonium bromide). In order to avoid particle aggregation, some sort of stabilizing agent is usually added. Gimenez et al proposed a method for synthesizing gold nanoparticles supported by an insoluble thiolated chitosan derivative by reducing HAuCl_4 by means of thiolated chitosan (QTDT) as a reduction and coupling agent for gold nanoparticles in order to use the synthesized QT / Au nano as a good catalyst to reduce methylene blue.

iii. Turkevich method:

One of

the most popular techniques for AuNPs synthesis is based on reducing HAuCl_4 by citrate in water, which Turkevich designed first in 1951. The HAuCl_4 solution is boiled in this method and the trisodium citrate dihydrate is then quickly added under vigorous stirring to the boiling solution. The solution's color changes from light yellow to wine red after a few minutes. This is the result of the method in AuNPs with a diameter of about 20 nm. Citrate ions play a double role in this technique, as they both stabilize and reduce agents.

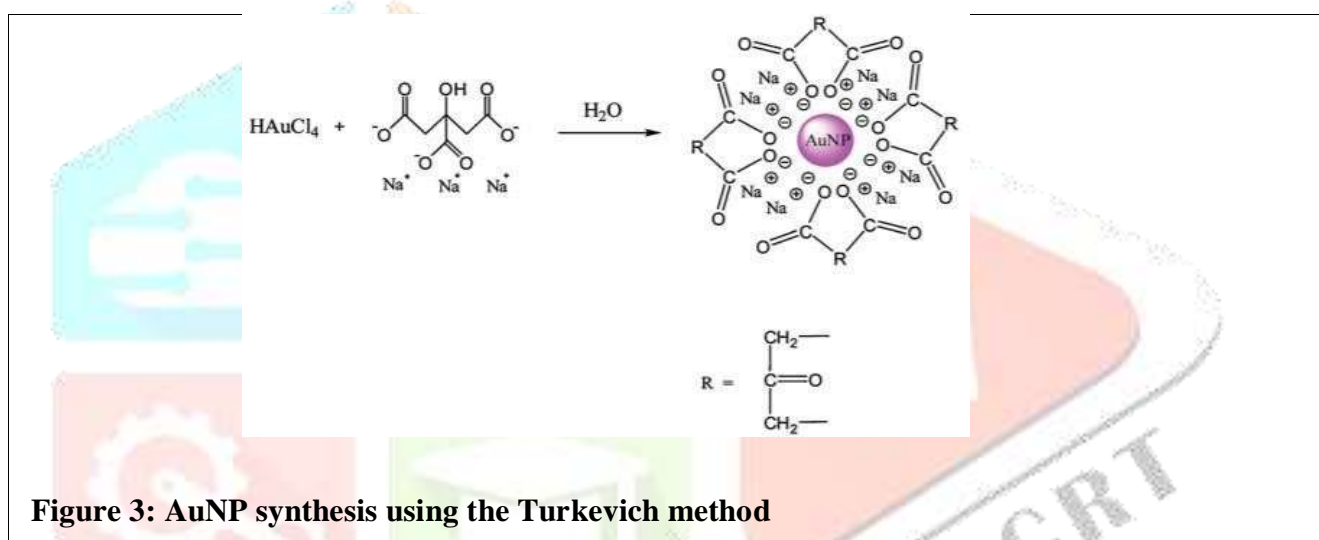


Figure 3: AuNP synthesis using the Turkevich method

In 1973, Frens modified the Turkevich method to obtain AuNPs with diameters ranging from 15 to 150 nm by controlling the reduction agent / stabilizing agent ratio (trisodium citrate / gold). Several research groups have further modified the Turkevich-Frens method.

iv. Electrochemical Method:

In 1994, Reetz et al. studied the electrochemical production of nanoparticles (Reetz and Helbing 1994, Reetz et al. 1995). Their studies have shown that the size-selective nano scale of transition metal particles can be set electrochemically using tetra alkyl ammonium salts as metal cluster stabilizers in a non-aqueous medium. Use the electrochemical synthesis technique to prepare gold nanoparticles on the surface of multi-walled carbon nanotubes with glassy carbon electrodes

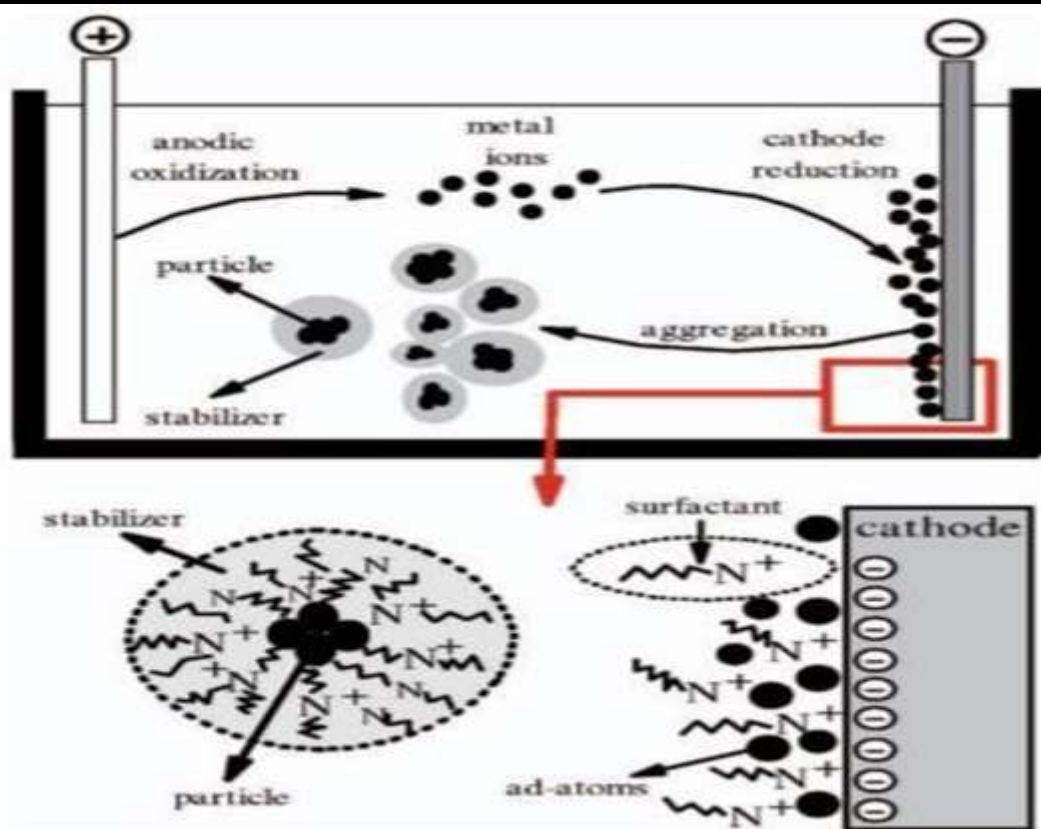


Figure 4. The electrochemical system for synthesizing gold Nanoparticle

i. Seeding growth method:

Seeding growth method: Another method also reported for the synthesis of gold nanoparticles is the method of seed growth. Gold nanoparticles of 5-40 nm diameter and a narrow size distribution have been synthesized according to the seed growth process. The particle size can be controlled by the variable ratio of seed to metal salt and can therefore be prepared in any size of 5-40 nm²⁰. Advantage of this method of being a simple, fast and low-cost process; while trisodium citrate was used in the seeding stage as a source of OH⁻ ions, sodium borohydrate (NaBH₄) was used as a reduction agent which is shown in Figure.

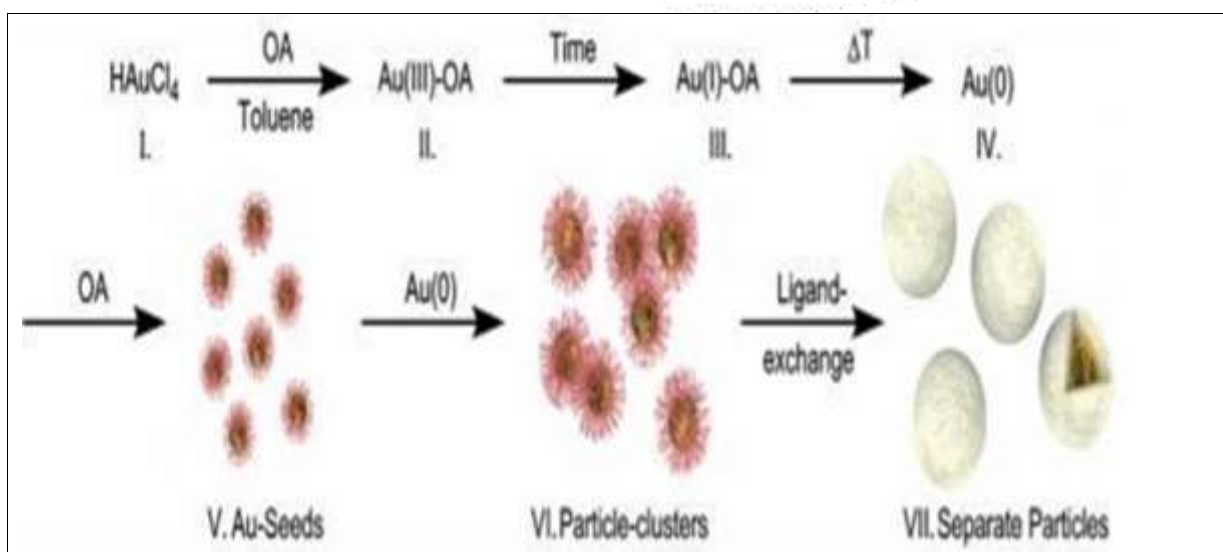


Figure 5. Seeding Growth Approach to Gold Nanoparticle

ii. Biological Method:

Because of their availability, low cost, eco-friendliness and non-toxic nature, the use of plants for the synthesis of nanoparticles has recently gained importance. The biosynthesis of AuNPs using plants like *Azadirachta indica*, *Medicago sativa*, *Aloe vera*, *Cinnamomum camphor*, *Pelargonium graveolens* (Shankar et al. 2004), *Coriandrum sativum*, *Terminalia catappa*, and lemongrass has been reported in recent years.

While chemical methods are the most common approach to metallic nanoparticles synthesis, their applications are limited using expensive and toxic reagents as reducing and stabilizing agents. These nanoparticles can also have harmful effects in biomedical applications²⁴. Therefore, eco-friendly, and cost-effective procedures for the synthesis of nanoparticles that do not use any toxic chemicals are becoming increasingly necessary. Biological nanoparticles synthesis has been at the center of attention in recent years as a green and environmentally friendly method. In biological methods, microorganisms, enzymes and plant or plant extracts synthesize nanoparticles.

iii. Green Method:

A new method of green chemistry for the preparation of gold nanoparticles was reported in which gold nanoparticles were formed by natural chitosan in aqueous NaCl solution from the bulk gold substratum without using any external stabilizer and reducing agent.

By adopting a method of sunlight irradiation, gold nanoparticles were successfully synthesized and modified with folic acid and capped with 6-mercaptopurine. Solar energy has been used in this method to reduce gold salt. A further green synthetic route also synthesizes gold nanoparticles of the size 15-80 nm. In this method, the use of citrus fruit juice extracts reduced HAuCl_4 .



Fig 6 Green method to gold nanoparticles

iv. Brust method: This method used to produce gold nanoparticles in organic liquids that are normally not miscible with water (like toluene) It involves the reaction of a chloroauric acid solution with tetraethylammonium bromide (TOAB) solution in toluene and sodium borohydride as an anti-coagulant and a reducing agent, respectively.

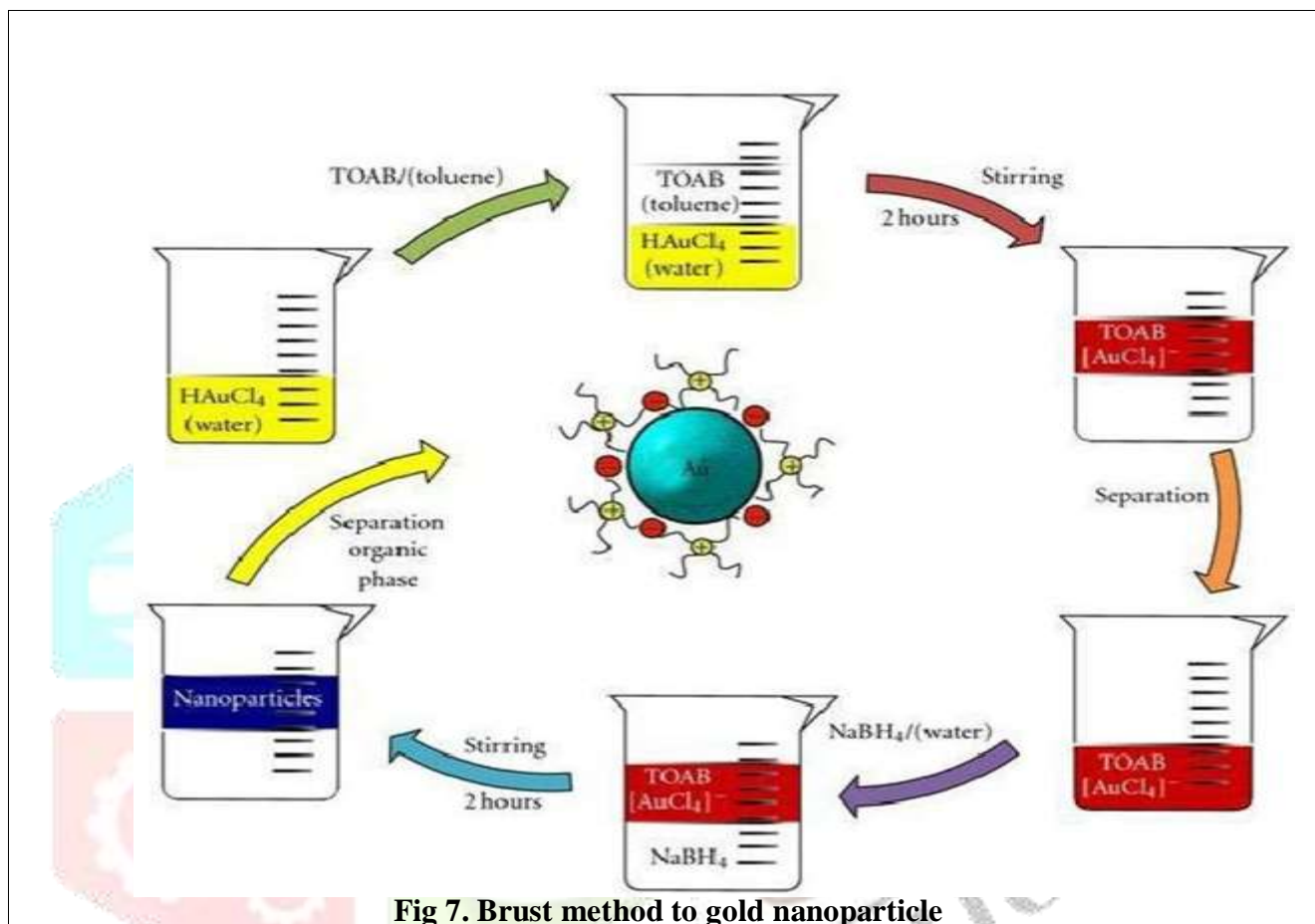


Fig 7. Brust method to gold nanoparticle

10. FACTORS AFFECTING GOLD NANOPARTICLES SYNTHESIS:

The synthesis of gold nanoparticles is greatly influenced by various physiochemical factors such as Ph, temperature, concentration of $\text{H[AuCl}_4\text{]}$ and incubation time.

i. Effect of ph on gold nanoparticles synthesis

pH is an important factor that influences the biological synthesis of nanoparticles. pH influences the size and shape of the nanoparticles. Therefore, nanoparticles size and shape can be controlled by altering the pH of the media (Patra and Baek, 2014). For example, in *Streptomyces hygroscopicus* well separated spherical gold nanoparticles were synthesized in the range of 2 ± 10 nm at neutral pH. When the pH was decreased, a number of hexagonal and pentagonal nanoplates were produced (Sadhasivam et al., 2012). Similarly, polyhedral gold nanoparticles with smooth edges were produced at pH 9 having an average size of 20 ± 10 nm, while at other pH large irregular shape gold nanoparticles were produced. The variety in the size and shapes of particles formed at the different pH levels indicates that, changes in this parameter would play an important role during optimization of a process controlling particle morphology.

ii. Effect of temperature on gold nanoparticles synthesis

nanoparticles. Synthesis of nanoparticles increases with increasing the reaction temperature up to a certain extent; above that temperature gold nanoparticles were not synthesized. Each microbe has an optimum temperature for gold nanoparticles synthesis, for example *Streptomyces* sp. NK52 has an optimum temperature for gold nanoparticles synthesis at 40 °C while *Streptomyces* sp. ERI-3 optimum synthesis temperature was at 30 °C . Temperature played an important role in the synthesis of gold nanoparticles in *Acinetobacter* sp. SW30. Higher the temperature did not synthesize nanoparticles may due to inactivation of the cells, leading to their death.

iii. Effect of HAuCl_4 concentration on gold nanoparticles synthesis

Concentration of HAuCl_4 also plays an important role in the gold nanoparticles synthesis. A quantitative increase in gold nanoparticles synthesis with increase in metal ion concentration has been reported earlier. This is due to availability of more and more substrate ions to reducing and stabilizing agents present in the reaction mixture. Further, if the concentration of metal ion is more or less than a critical level, hence no synthesis occurs (Vineet and Sudesh, 2013).

iv. Effect of incubation time on gold nanoparticles synthesis

Incubation time plays a crucial role in nanoparticles synthesis. The quality and type of nanoparticles synthesized using green technology are greatly influenced by length of time for which the reaction medium is incubated. Similarly, the characteristics of the synthesized nanoparticles were also altered with time and greatly influenced by the synthesis process.

11. APPLICATION OF GOLD NANOPARTICLES:

Figure 6 illustrates the various pharmaceutical applications of nanoparticles. The wide applicability of gold nanoparticles is due to the Nanoparticles novel properties, which contribute to excellent catalytic applications, good biocompatibility, large surface area, and conductivity. Bio-sensing applications are

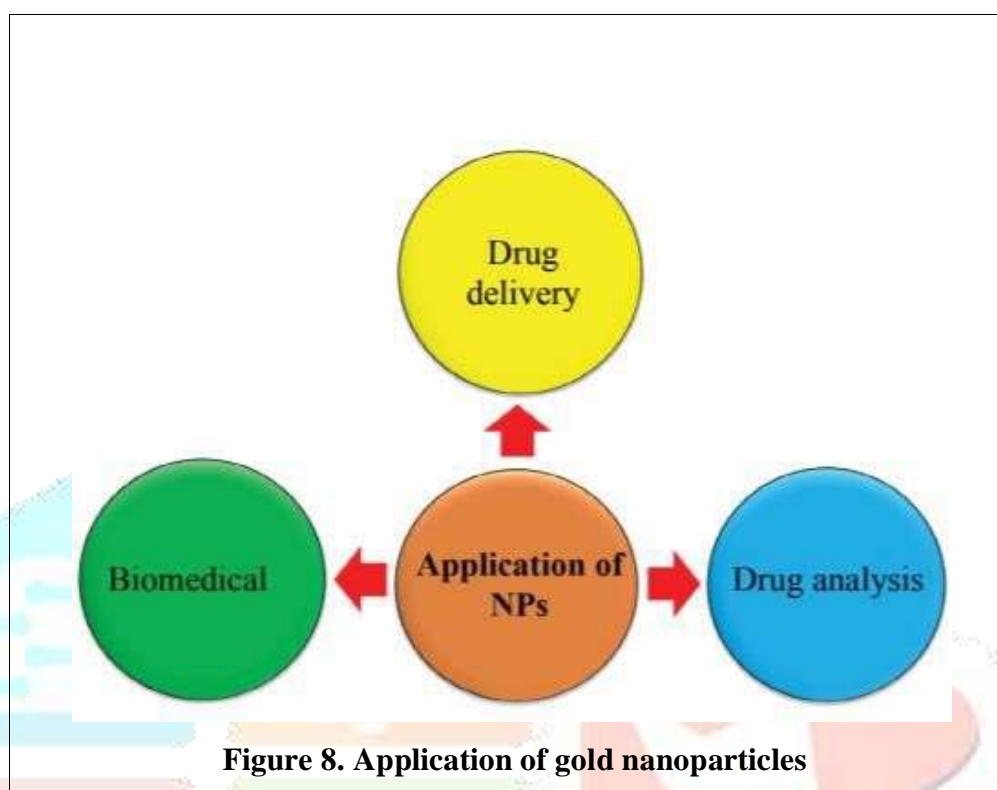


Figure 8. Application of gold nanoparticles

widely used when the nanoparticles combined with biomolecules and used in combination with Au / NPs and AuNPs / MPA (mercaptopropionic acid) used in the manufacture of biosensors showing a wide linear range between 0.25 mM and 0.025 mM glucose concentration.

i. Application in biomedical:

Nanoparticles are used as bio labels in biomedical applications. Specific recognition, covalent coupling, physical adsorption, and electrostatic binding have been reported using various methods to provide hybrid molecules. For example, gold nanoparticles are used in vivo gene therapy, proteins, nucleic acid delivery and targeting. Fig.7 shows the application of gold nanoparticles in biomedical.

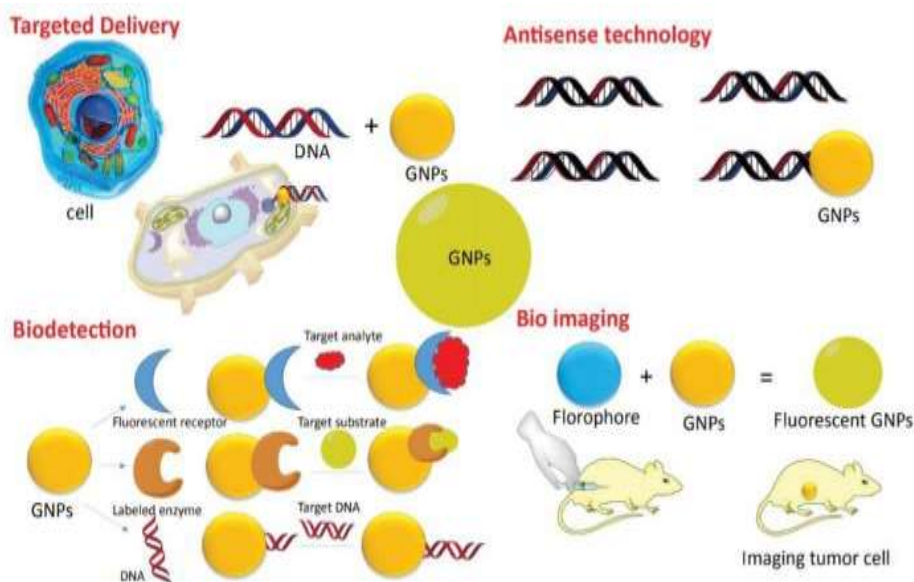


Figure 9. The potential application of Gold nanoparticles in the biomedical field.

ii. Application of Gold nanoparticles in Chemotherapy:

The use of colloidal gold in therapeutic treatments, often for cancer or arthritis, is gold nanoparticles in chemotherapy and radiotherapy. The technology of gold nanoparticles shows promise to advance cancer treatments. Some of the properties of gold nanoparticles, such as small size, non-toxicity, and non-immunogenicity, make these molecules useful for the targeted delivery of drugs. With tumor - targeting delivery vectors becoming smaller, it becomes more likely to be able to bypass the body's natural barriers and obstacles. IN order to increase the specificity and likelihood of drug delivery, tumor - specific ligands can be grafted onto the particles together with the chemotherapeutic drug molecules to allow these molecules to circulate throughout the tumor without redistribution into the body

TREATMENT

- Photothermal cancer therapy
- Radiofrequency therapy
- Drug vectorization
- Anti-bacterial therapy
- Drug vectorization

i. Photothermal cancer therapy: A direct method of accessing and destroying tumor cells can be accomplished by photothermal cancer therapy or photodynamic therapy (PDT). This procedure is known to treat small tumors that are difficult to access and prevent the inconvenience (adverse effects) of conventional methods, including unnecessary destruction of healthy tissues. By exposure to light, the cells are destroyed, rupturing membranes causing digestive enzyme release. AuNPs have high cross-sections of absorption that require only minimal energy input from irradiation. It has been shown that human breast carcinoma cells infused with in vitro metal nanoparticles have increased morbidity with near-infrared exposure (NIR).

ii. Radiofrequency therapy:

Treatment with radiofrequency therapy involves the destruction of tumor tissue cells by radiofrequency diathermy through the differential heating of cancer tissue. This differential heating results from the supply of blood in the body that carries the heat and cools the heated tissue. Due to its high atomic number of ^{197}Au , gold nanoparticles are excellent-ray absorbers. This allows the element to have a higher mass, providing a greater area of absorption of x-rays. By acting as a contrast agent and injecting it into cancerous tumor cells, the cancerous tissue would be exposed to a higher dose during radiotherapy treatment.

iii. Angiogenesis therapy:

Angiogenesis is a process in which new blood vessels are formed from pre-existing vessels. It involves the degradation, activation, migration, proliferation, and differentiation of endothelial cells into vessels of the extracellular matrix. It is said to play a major role in cancer cell growth and spread. As a result of oxygen and nutrients, tumor progression occurs as a result of the transition from a tumor at the dormant proliferation stage to the active stage. This active stage leads to a cellular hypoxia state, resulting in increased regulation of proteins such as VEGF pro-angiogenesis. This results in the spreading alongside the newly created blood vessels of inflammatory proteins and cancer cells.

iv. Drug vectorization:

Another way to use AuNPs in cancer therapy is as targeted drug delivery agents. Research shows that AuNPs can be easily operated and combined with a variety of molecules, including chemotherapy drugs such as doxorubicin²⁰.

The advantages of gold Nano particles in drug vectorization. To effectively treat different types of cancers, they can pack several different sizes and types of dendrimers and several different types of ligands. Research shows, for example, that 80-90% of tumor cells in breast cancer have estrogen receptors and 60-70% of tumor cells in prostate cancer have androgen receptors.

v. Other Applications:

Indirectly therapeutically, gold nanoparticles can be used. The angiogenesis issue describes the formation of new blood vessels that may not only increase the spread of cancer cells, but may also proliferate the spread of rheumatoid arthritis-responsible proteins. As AuNPs decrease angiogenesis, the result is reduced rheumatoid arthritis.

- vi. HIV:** Several AuNP valences have been found to inhibit HIV fusion. 2-nm AuNP- mercaptobenzoic acid has been combined with a derivative of a known CCR5 antagonist, a small molecule that antagonizes the CCR5 receptor, and CCR5 is commonly used to enter the cell by HIV. The antagonist of the CCR5 would bind to CCR5, leaving no binding spots for HIV. Ultimately, this will result in an effect that will limit HIV infection.
- vii. HEPATITIS B:** DNA gene samples prepared for AuNPs-Hepatitis B virus (HBV) could be used directly to detect HBV DNA. The detection-visualized fluorescence-based method is highly sensitive, simple, low cost, potentially applicable to multi-gene detection chips. The sample used here is essentially a biosensor to detect specific material.
- viii. TUBERCULOSIS:** Sensitive detection in clinical samples of Mycobacterium tuberculosis, the cause of human tuberculosis, was a successful application of the AuNP-nanoprobe colorimetric method to clinical diagnosis.

12. CONCLUSION

Gold nanoparticles have revolutionized the medicine sector in some ways due to its wide-ranging applications in targeted drug delivery, imaging, diagnosis and therapy due to its extremely small size, high surface area, stability, non-cytotoxicity and adjustable optical used in cancer therapy with various biomolecules such as proteins, DNA, amino acids, and carboxylic acids and provide an excellent drug delivery system. Targeted delivery and scheduled release of therapeutic drugs to the specific site is achieved by using gold nanoparticles because they can carry a high drug load and release it to the specific site through different routes of administration and can interact with cancer cells. Conjugation with gold nanoparticles has minimized side effects of conventional drugs and increases patient's quality of life.

As we have seen, the synthesis AuNPs is an important area of research in nanotechnology. Generally, there are two approaches for the synthesis of AuNPs: the "bottom-up" approach and the "top down" approach (Eustis and El-Sayed 2006). The bottom-up approach consists of nano sphere lithography, templating, chemical, photochemical, electrochemical, so nonchemical and thermal reduction techniques.

Au-NPs could be prepared and conjugated with many functionalizing agents, such as polymers, surfactants, ligands, dendrimers, drugs, DNA, RNA, proteins peptides and oligonucleotides. Au-NPs showed excellent optical properties due to its surface Plasmon absorption, which were utilized for labelling, imaging, and sensing. SERS, as a recent spectroscopic technique, could provide large Raman signals. SERS combined elastically scattered visible light from Au-NPs, which could be imaged using a dark-field optical microscope. Inelastic SERS effect from adsorbed molecules could result a Raman spectrum, leading to the identification of biomolecules. Hence, Au-NPs, as a biosensor, could help to diagnose cancer, Alzheimer, HIV, and Tuberculosis. Therefore, Au-NPs would be a general vector for the drug treatments. Toxicity of Au-NPs occurred from the presence of CTAB, which required in stabilizing Au-NPs during synthesis process., could help to diagnose cancer, Alzheimer, HIV, and Tuberculosis. Therefore, Au-NPs would be a general vector or the drug treatments.

Today the nanotechnology carries have a major role in the pharmaceutical research for detecting various diseases. The new system gold nanoparticles are play a major role in controlled drug delivery system externally and theoretically could deliver up to three or four drugs. With a lot of diseases, especially cancer and AIDS, it is possible to get a synergistic effect with more than one drug, so the gold nanoparticles drug delivery system could provide multiple drugs in the treatment of cancer or aids.

13. REFERENCES

1. F.K. Alazani, A.A. Radwan, and I.A. Alsarra. Biopharmaceutical applications of nanogold. Saudi Pharm J .2010;18:179-193
2. Di Guglielmo C, Lopez DR, De Lapuente J, Mallafre JM, Suarez MB. Embryotoxicity of cobalt ferrite and gold nanoparticles: a first in vitro approach. Reproduce Toxicol.2010;30:271-276.
3. Khlebtsov NG, Dykman LA. Optical properties and biomedical applications of plasmonic nanoparticles. J Quantitat Spectroscop Radiat Transf. 2010;111:1-35
4. Mendoza KC, McLane VD, Kim S, Griffin JD. Invitro application of gold nanoprobe in live neurons for phenotypical classification, connectivity assessment, and electrophysiological recording, Brain Res.2010;1325: 19-27.
5. Lukianova-Hleb EY, Wagner DS, Brenner MK, Lapotko DO. Cell-specific transmembrane injection of molecular cargo with gold nanoparticle-generated transient plasmonic nanobubbles. Biometer.2010;33:5441-5450
6. L. Dykman, N. Khlebtsov. Gold in biomedical applications: recent advances and perspectives, Chem. Soc, Rev.2012; 41:2256–2282.
7. J. Jiang, G. Oberdörster, P. Biswas. Characterization of size, surface charge, and agglomeration state of nanoparticle dispersions for toxicological studies, J. Res. 2009;11:77– 89.
8. H. Chunbai, Y. Hu, L. Yin, C. Tang, C. Yin. Effects of particle size and surface charge on cellular uptake and bio distribution of polymeric nanoparticles, Biol. Mater.2010; 13:3657–3666.
9. Tedesco S, Doyle H, Blasco J, Redmond G, Sheehan D. Oxidative stress and toxicity of gold nanoparticles in *Mytilus edulis*. Aquatic Toxicol 2010.
10. Etame AB, Smith CA, Chan WC, Rutka JT. Design and potential application of PEGylated gold nanoparticles with size-dependent permeation through brain microvasculature. Nanomed: Nanotechnol Biol Med.2010 ; 7: 992-1000
11. Zhao P, Li N, Astruc D. State of the art in gold nanoparticle synthesis. Coord Chem Rev.2013 ;257: 638 – 665.
12. Pissuwan D, Niidome T, Cortie MB, 2011 The forthcoming applications of gold nanoparticles in drug and gene delivery systems. J Control Release; 149: 6571 Patil et. al., Am. J. PharmTech Res. 2019;9(02) ISSN: 2249-3387 www.ajptr.com 354
13. Guo W, Pi Yunqing, Song H, Tang W, Sun J 2012 Layer-by-layer assembled gold nanoparticles modified anode and its application in microbial fuel cells. Colloid Surface A: Physicochemist Engineer Aspects 415: 105-111.

14. Chen K-S, Hung T-S, Wu H-M, Wu J-Y, Lin M-T, Feng CK ,2010 Preparation of thermosensitive gold nanoparticles by plasma pretreatment and UV grafted polymerization. Thin Solid Films 518: 7557-7562.
15. Huang J, L i Q , S un D , L u Y , S u Y , Y ang X ,2007 e t a l. 18. Biosynthesis of silver and gold nanoparticles by novel sundried Cinnamomum camphor leaf. Nanotechnology. 1 8: 1 05104
16. Rezende TS, Andrade GRS, Barreto LS, Costa Jr NB, Gimenez IF, Almeida LE (2010) Facile preparation of catalytically active gold nanoparticles on a thiolated chitosan. Mater Lett 64: 882-884.
17. Tarnawski R, Ulbricht M. Amphiphilic,2011 gold nanoparticles: Synthesis, characterization, and adsorption to PEGylated polymer surfaces. Colloid Surface A: Physicochem Engineer Aspects; 374: 13-2118.
18. Mendoza KC, McLane VD, Kim S, Griffin JD,2010 Invitro application of gold nanoprobe in live neurons for phenotypical classification, connectivity assessment, and electrophysiological recording. Brain Res; 1325: 19-27.
19. 19.Guo W, Pi Y, Song H, Tang W, Sun J,2012 Layer-by-layer assembled gold nanoparticles modified anode and its application in microbial fuel cells. Colloid Surface A: Physicochem Engineer Aspects; 415: 105-111.

