International Journal of Science and Healthcare Research
Vol.5; Issue: 2; April-June 2020
Website: ijshr.com
Review Article *ISSN: 2455-7587*

Gold Nanoparticle

Ankita N Gadge[1], Shailesh J Wadher[2], Amol D Landge[3]

[1]Assistant Professor, Department of Pharmacy, SSBT Jalgaon
[2]Professor, Department of Pharmacy, SRTMU Nanded
[3]Principal, SSBT Department of Pharmacy, Jalgaon.

Corresponding Author: Ankita N Gadge

ABSTRACT

Metal nanoparticles are broadly use in a variety of biomedical application because of their microscopic size and stability. Gold nanoparticles (GNPs) are good choice for treatment of various cancerous cells. In this review author described various properties, method of synthesis and application of gold nanoparticles.

Keywords: gold nanoparticle, targeted drug delivery, method, cancer, drug targeting, diagnostics.

INTRODUCTION

A child finds a shiny rock in a creek, thousands of years ago, and the human compete is introduced to gold for the first time. Gold was first exposed as shining, yellow nuggets. It is the first metal known to early on hominids. In many Germanic words gold is identical word. The symbol of gold is Au and this symbol is from the Latin word that is aurum. [1,2]

Alexandria discovers that gold is used for beneficial and medicinal purpose. More than 5,000 years ago, Egyptians and ancients suggested gold in the body exciting the life force for rational, psychological, mental and purification. With the use of gold particle Alexandria developed an elixir. Gold is non-toxic, never corrodes or tarnish, and be shaped easily because of this property of gold; it is such a metal which gives precision. Thus it is ingested into body would treat multiple diseases and gives perfect health. [3,5]

Gold:

- Chemical symbol of gold is Au.
- Gold's atomic number is 79, and its atomic weight is 196.967.
- Gold melts at 1064.43° Centigrade
- The specific gravity of gold is 19.3.

Gold has been one of the valuable material people like most. Because of its intrinsic value, selling the yellow metal is a good way of secure money. Large quantity of people on the market has a preference it in the form of gold bars, whereas minute investors resolve themselves by purchasing fine piece of gold costume jewellery. In these current times, bullion has ceased to be purely a safe investment chance or replace currency. At the same time as a result of widespread research and constant progress, it has been stated that gold is used for technical, scientific, industrial purposes. The special uses of gold refer to; nanogold, colloidal gold and gold nanoparticles which is sub-micrometer-sized particles of gold discrete in a fluid, typically water.

Like gold metal;

- Silver,
- Titanium oxide,
- Iron nanoparticles,

are the metal which also used for study universally. [6-9]

In modern years, make use of nanoparticles, particularly metal nanoparticles has extended in various research. These nanoparticles are utilize in analysis and therapeutics because of their properties of sky-scraping reactivity to the alive cells, tiny size, more surface area to

volume ratio, translocation into the cells , stability shows at high temperatures. These nanoparticles are available in various sizes and shapes because of their capability to react with further nanoparticles in their surroundings. The survival of these gold nanoparticles has well-known to public since ancient times. In 1850s scientists focused their full attention on gold nanoparticles. The chief reasons behind this attention on gold nanoparticles are their optical, electronic and molecular-recognition properties. These properties permit for the gold nanoparticles to have beneficial in various types of fields, counting electron microscopy, electronics, nanotechnology and materials science. Gold nanoparticles have been extensively used in biological electronic microscopy. Gold nanoparticles are coupled with various customary biological probes like glycans, superantigens, antibodies, nucleic acids, receptors and lectins. Because of gold particles have various sizes can be easily marked in electron micrographs. It is potential for many experiments to be conduct at the same time. Gold nanoparticles have various medical applications. For the treatment of some diseases the gold nanoparticles are used.

Gold is the first part of the rheumatoid arthritis therapy thus it has been initiate that gold particles surrounded towards the arthritic hip joints to relieve pain. On the gold nanoparticles some in vitro experiments carried out which have states that gold nanoparticles combined with microwave radiation which completely destroy Alzheimer's disease. Gold nanoparticles are the most important medical purpose for the localization and treatment of cancer. It is already shown that, when gold nanoparticles direct into the nuclei of cancer cells, then they can not only obstruct them from multiplying, but also destroy them. Gold being inert and relatively a smaller amount cytotoxic is widely use for various function together with drug and gene delivery. [10-14]

Definition:

Nanoparticle:

In nanoparticle, 'n' denote nanotechnology, particle size between 1 nanometer (0.001 micrometers) to 100 nanometers (0.1 micrometers), this particle are known as nanoparticle.
[15]

Types of nanoparticles: [16-21]

Nanoparticles are broadly classified into following types:

- Quantum Dots
- Carbon Nanotubes
- Nanorods
- Nanocrystals
- Nanowires
- Nanoribbons

• Quantum Dots

Quantum dot is a nanocrystal made of semiconductor materials that are small enough to exhibit quantum mechanical properties.

• Carbon Nanotubes

Carbon nanotubes are allotropes of carbon with a cylindrical nanostructure. Nanotubes have been constructed with length-to-diameter ratio of up to 132,000,000:1.

• Nanorods

A nanorod is defined as nanometer sized particles that are rod shaped.

• Nanocrystals

A nanocrystal is a nanoparticle with a crystalline structure.

• Nanowires

Nanowires are less than 100 nanometers in diameter and can be as small as 3 nanometers.

• Nanoribbons

A nanoribbons is a nanoparticle with a ribbon structure.

According to Scientific Committee on Emerging and Newly Identified Health Risk [SCENIHR]
Nanoparticle again classified into following types; [22]

1) Category 1: size > 500 nm:

When the size of the material is above 500 nm it understood that the particle size separation at the lower end will be above the selected lower threshold of 100 nm.

2) Category 2: 500 nm> size >100 nm

If the size is <500 nm it is the part of the size allocation will be lower than 100 nm and that material is considered a nanomaterial.

3) Category 3: 100 nm> size >1 nm

The material is said to be a nanomaterial and nano-specific risk assessment is performed.

Size of nanoparticle:

- Fine particles-range between 100 and 2500 nanometers,
- Ultrafine particles and nanoclusters-range between 1 and 100 nanometers,
- Nanoparticle may be shows size related properties or may not be shows any size related any properties.
- Nano particle sized crystals are called as nanocrystals [23].

Gold Nanoparticle:

Gold is a suspension, containing fluid (generally water) with sub-micrometer-sized gold particles. The nanoparticles containing gold metal are known as gold nanoparticle.
For particles less than 100 nm- liquid is in intense red colour
For larger particle- liquid is in blue or purple in colour. [24]

Types of Gold Nanoparticles: [25]

- Gold Nanorods
- Gold Nanoshells
- Gold Nanocages
- Gold Nanosphere
- SERS Nanoparticles

Gold Nanorods:

Gold Nanorods are synthesized by template method. These can be prepared by electrochemical deposition of gold inside the pores of nonporous polycarbonate template membranes. The diameter of Gold Nanoparticle is according to the diameter of pore of the template membrane.

Gold Nanoshells:

Surface plasmon resonance peaks which ranging from visible to near I.R. region is used for the designing and fabrication of Gold Nanoshells. The core of Gold Nanoshells is made up of silica and outer surface is made up of gold. Gold is responsible for controls the thickness of the shell.

Gold Nanocages:

Through galvanic replacement reaction between truncated silver Nanotubes and aqueous HAuCl gold Nanocages is synthesized.

SERS Nanoparticles:

SERS is an optical technique like fluorescence and chemiluminescence having better sensitivity, high levels of multiplexing, robustness and greater performance in blood and biological.

Gold Nanosphere:

These are synthesized by reduction of an aqueous HAuCl by using citrate as reducing agent. Through citrates or gold ratio the size of Nanosphere can be controlled. By two-phase ratio, the size of Nanosphere can be affected by thiol or gold molar ratios.

Characteristics of Gold Nanoparticle: [26-28]

1. Gold nanoparticles are chemically inert.
2. These have greater biological compatibility.
3. Optical properties like Plasmon resonance are exhibited by gold nanoparticles.
4. These exhibit versatility because of their ready fictionalization through thiol linkages.
5. GNPs supply microscopic probe for the learning of the cancer cell.

6. GNPs gather in the cancerous cell and give an idea about the cytotoxic effect i.e. apoptosis or necrosis of the specific cell and receptor.
7. GNPs have high stability owing to the gold-sulphur bonds.
8. GNPs photo physical properties can be exploited for drug release at remote place.

Measurement of Gold Nanoparticle Size and Concentration by:

1) Ultra Violet Spectrophotometer:

For the measurement of gold nanoparticle size and concentration we use the U. V. visible spectrophotometer. U. V. visible spectrophotometer having fast speed of determination and used for nanoparticle production. The use of cuvettes creates several problems nanoparticles are often produce in high concentrations, and large extinction coefficients, so there is need of dilutions required for the measurement. The concentration may be varying thus requiring measurement of multiple dilutions for a dynamic range. The size of the particle can also be determined by U. V. Spectrophotometer. On the basis of size and shape of particles the wavelength of absorption peak is depend. [29]

The absorption calculated can be calculated by equation:

A= -log (% TRANCEMITANCE / 100%) ——— 1

2) Transmission Electron Microscopy (TEM):

TEM is used for capture images of the gold nanoparticles. In TEM, an electron beam interacts and it is transmitted through a thin sample, and then predictable onto a florescent screen. An image of the sample is produced. The brighter regions of the image stand for areas where more electrons have passed through the sample, whereas the darker regions stand for areas where fewer electrons have been passed through due to higher sample density [30].

3) A Scanning Electron Microscope (SEM):

The SEM is used to study the synthesized gold nanoparticles. In SEM, a set of coils moves the electron beam across a sample in a two dimensional grid. When the electron beam transversely over the sample, different interactions occur. Some of the electrons from the surface material kick of their electrons by the beam thus producing secondary electrons. These secondary electrons can then be detected by the secondary electron detector on a SEM. An image is then produced at the surface of the sample and is projected. Similarly to TEM, SEM images can be magnified up to 100,000 times while maintaining a high resolution.

- ✓ The techniques have a few important differences;
- In TEM an electron beam passes through a thin sample whereas in SEM the electron beam scans the entire surface of the sample,
- In TEM the samples are very thin, and in SEM the sample can be of any thickness, TEM images are shown on fluorescent screens and SEM images are shown on television monitors. [30]

4) X-Ray diffraction (XRD):

XRD is used to examine the synthesized gold nanoparticles. In XRD, x-rays that are produced by the x-ray beam get scattered by the atoms in the sample. Waves are then scattered spherically from the atoms which causes the intensity of the scattered radiation to show minimum and maximums in different directions. XRD allows a better visual of the structure of the observed atoms because it shows axes, shape, size and position of the atoms. [31]

5) Surface-Enhanced Raman Scattering (SERS):

It is a more advanced spectroscopic technique which is a type of Raman spectroscopy. Raman scattering is a type of molecular vibration that can occur between light and molecules. If the energy of light is not enough to excite the molecules from the ground state to the lowest state, the molecule is then instead excited to a virtual state between the two. SERS was

discovered by an accident when a researcher was trying to do Raman scattering and produced a Raman scattering more intense than expected then the strong signal was then coined SERS. Therefore, SERS is a technique that enhancing Raman scattering by molecules adsorbed on a rough surface. Also, if metal nanoparticles are used in SERS, the particle size needs to be from 20-300 nm [32].

6) Surface Plasmon Resonance (SPR):

SPR is used light being directed onto a thin surface which contains gold. Some of the lights electric field can leak onto the surface if the angle of light causes it to be reflected. The electric field excites the surface plasmon waves in the metal. A surface plasmon is an electron wave that travels along the surface of the gold film. The wavelength of this plasmon wave is detected [32].

❖ Techniques of particle size analysis of gold nanoparticles: [33, 36]

Table no. 1: Techniques of particle size analysis of gold nanoparticles;

Technique	Size nm
90º scattering angle	26.5 ± 3.6
Atomic Force Microscopy	24.9 ± 1.1
Differential Mobility Analysis	28.4 ± 1.1
Dynamic Light Scattering 173º scattering angle	28.6 ± 0.9
Scanning Electron Microscopy	26.9 ± 0.1
Small-Angle X-ray Scattering	24.9 ± 1.2
Transmission Electron Microscopy	27.6 ± 2.1

Properties of Gold Nanoparticles: [37-39]

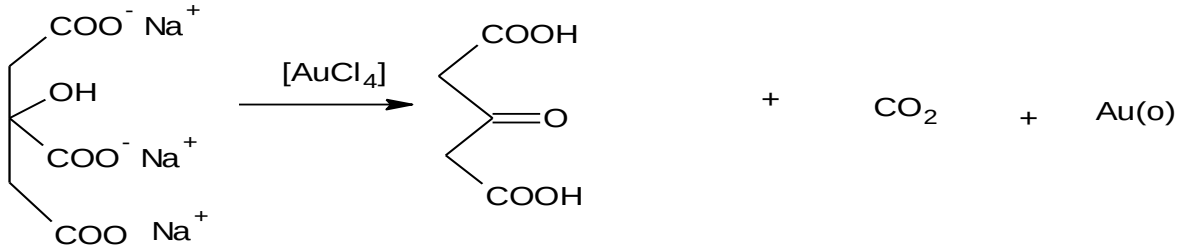
- Chemically inert
- Greater biological compatibility
- Optical properties
- Versatility
- High stability
- The light can be absorbed
- The light can be scattered at the same frequency as the incoming light
- The absorbed light can be re-emitted i.e., fluorescence.
- The optical properties of spherical gold nanoparticles are highly dependent on the nanoparticle diameter.

METHODS FOR THE PREPARATION AND ANALYSIS OF GOLD NANOPARTICLE:

There are various methods are available for the preparation of gold nanoparticles:

1) Turkevich method: [40,41]

This method is discovered in 1951 by J. Turkevich and advanced in 1970s by G. Frens. This is the simplest method. Generally, this method is used to produce moderately 10 to 20 nm in diameter monodisperse spherical gold nanoparticles which is suspended in water. Larger particles can also be produced by this method.



5.0×10^{-6} mol of $HAuCl_4$, dissolve in 19 ml of deionized water
(Formation of faintly yellowish solution)
↓
Continue heat until it boils
↓
While stirring vigorously, add 1 ml of 0.5% sodium citrate solution; remain stirring for the next 30 minutes
↓
Colour changes from pale yellowish to wine-red
↓
Make up volume with water till 20 ml
(For evaporation).

Turkevich method is simple and always available and formation of the gold nanoparticles is observed by colour change in the solution.

2) Brust method:

This method was pioneer by Brust in early 1990s. This method used organic liquid for the production of gold nanoparticles, which are normally not miscible with water for ex. toluene. In this method chlorauric acid solution is prepared, and tetraoctylammonium bromide (TOAB) solution in toluene is prepared. When reaction is takes place between them sodium borohydride is add which act as an anti-coagulant agent. The gold nanoparticles size range between 5 to 7 nm is obtained.

$HAuCl_4$ (3 g) in 30 ml of water dissolve
↓
Dissolve tetraoctylammonium bromide (TOAB) (2.187 g) in 80 ml of toluene
↓
Mix both solutions together
↓
Stir vigorously for 10 minutes
Colour of the aqueous phase become clear the organic phase become orange
↓
Add sodium borohydride ($NaBH_4$) 0.38 g
Then colour changes from orange to reddish
↓
Stir the solution for up to 24 h
↓
Separate the organic phase
(wash with dilute H_2SO_4 and then distilled water)
↓
5-6 nm gold nanoparticle generated

• Drawback of burst method: Main Drawbacks
1. Depend on more equipment
2. Complicated procedures
3. Expensive
4. Confined GNP size
5. Distribution [42].

3) Gold nanoparticles generated in ethosome bilayers:

Gold nanoparticles can be prepared by heat phosphatidylcholine (PC) 2 to 6% with 45% ethanol at a temperature 33 to 68^0C. Continuously stir the solution for 30 min to homogenize the sample. After that deionized water is added and colour slowly changes from pale yellow to purple. After 30 min the colour was completely purple this indicates that the gold nanoparticles are formed. [43,45].

Qualitative Analysis:

The gold nanoparticles can be observed by the colour change and the size can be determined from TEM micrographs and by microscope. For the observation of the sample in the microscope small drops of sample is added on the slide of copper grid covered by carbon film and allow evaporating.

4) Martin method: [46]

Martin method is discovered in 2010 by Eah group. They prepared naked gold nanoparticles in water. In this method reduction of $HAuCl_4$ with $NaBH_4$ is occurring. Sizes ranging from 3.2.to 5.2 nm gold nanoparticles are generated. This necked gold nanoparticle are coated with monolayer of 1 dodecanethiol and after that phase transferred to hexane simply by shaking the mixture of water, hexane, and acetone for 30 seconds. This is new synthesis method. This is simple, greener, and cheap. This technique is important for many practical applications.

5) Chemometric technique: [47]

Gold nanoparticle generated by chemometric technique. Approach based on multivariate analysis. Three parameters such as stirrer speed, ionic strength of the medium, and concentration of sodium citrate solution analyses. Here the addition of 5 ml of 5 mM of gold, chloride hydrate 2 mg/mL is added to 85ml of deionized water which is filtered. Then reflux in 250 ml flask over a hot plate and heated to boiling point, 5 ml sodium citrate solution is quickly added to this boiling solution and stirred for half hour until colour change to wine red.

6) Perrault Method:

This method is discovered by Perrault in 2009. In this method hydroquinone is used. Hydroquinone is act as reducing agent by reducing chloroauric acid in an aqueous solution which contain gold nanoparticle. Citrate is used for control particle growth. [48].

7) Sonolysis

Sonolysis is the method which used for the experimental generation of gold particles. This development based on ultrasound. In case of production of gold nanoparticle by Sonolysis, the reaction between chloroauric solutions with glucose is occurring. Nanoribbons are formed. 30 to 50 nm width of nanoribbons will produce which are flexible in nature and can be blend with angles larger than 90̊. The glucose shows the morphology towards nanoribbons. [49]

8) Block Copolymer-mediated Method

In this method block copolymer used. This method is fast synthesis method for gold nanoparticles using block copolymer. In this synthesis method, block copolymer act as reducing agent and stabilizing agent.

Drawback:

Concentration of gold nanoparticle is in limited yield. [50]

9) Laser Ablation Synthesis:

In this method the Au and Ag metal foils are use. The vial containing 10 mL of deionized water and the Au and Ag metal foils are placed in a vial and heat media. In this synthesis; Laser pulse required 1064 nm. The laser will operated in single-shot mode 5 ns, 10 Hz and focusing lens is used which gives 86.4 cm focal length. The laser power will require 0.980 mW, and the energy will be 106 mJ. This process is carried out for time interval of 5 min, 10 min, 15 min, and 20 of near IR laser pulse irradiation. [51]

Analysis:

UV-Vis spectrophotometer is used for the analysis of gold nanoparticle and spectra are recorded in the range of 300 to 900 nm.

10) Synthesis of Au Nanoparticles by Ethylene Glycol:

For the synthesis, add 50 μL of $HAuCl_4$ and 100 μL of PVP in the flask lots of times after every 60s interval until 6 mL of $HAuCl_4$ will thoroughly used. In general, the reduction of $AuCl_4$ by ethylene glycol and $NaBH_4$ is occurring for a small time of 10 to 30 min. This mixture is then heated and refluxed at a temperature 200–220°C. The colour of mixture changes from yellow to violet or deep purple colour. This product is then washes and centrifuge using the Kubota 3740 centrifuge for 15 min for separating the supernatant. By adding triple volume of acetone the product is wash and purify. Then, it is centrifuged for 30 min, with the use of ethanol to remove impurities. Finally, the pure Au nanoparticles of about 100–250 nm will place onto a copper substrate. Au nanoparticle is then evaporated at room temperature for 5-7 h and we get pure gold nanoparticles. [52,53]

11) Self-Assembly of Au Nanoparticles:

In this method, here is importance of control evaporation of ethanol solvent. Solvents such as ethanol are use for the dispersion of Au nanoparticles. Ethanol containing the pure Au nanoparticles 1 mL

is prepared. This prepared sample is added on the copper substrate. This can be evaporating, after complete evaporation of ethanol, again second stop given on the flat copper substrate and so on till getting thin layer of Au nanoparticle. We use all 1mL of prepared ethanol sample and evaporate at room temperature, after overnight evaporation we get self assembly of gold nanoparticle on the copper substrate. [54]

Analysis:

For the analysis of gold nanoparticle which is prepared by the method 10 and 11 can be analyze by U. V. Spectroscopy, take 1 to 2 mL of sample and observe the absorbance at a wavelength 200 to 1100 nm, during synthesis reducing agent use.

12) Synthesis of gold nanoparticles by grapes:

For the synthesis of gold nanoparticles by grapes, 50 mL of 0.01 M of HAuCl4 was added into 25 mL of aqueous extract of grapes and shake the reaction mixture and allowed to settle at room temperature. The color change in the mixture indicates that there is formation of gold nanoparticles. [55].

Qualitative Analysis:

This method can be analyze by U. V. Spectroscopy, and FTIR spectral analysis, as the grapes extract was mixed with the aqueous solution of the chloroauric acid, slowly it started to change the colour due to the reduction of gold ion to gold which indicates the formation of stable gold nanoparticles.

13) Physical methods:

The method is based on the solvated metal. So called solvated metal atom dispersion technique (SMAD). A familiar reactor is used to generate atoms from a piece of bulk gold. The Au atoms will frozen at 77 K in acetone vapour and will then warmed up to give gold colloids, this stabilize by acetone molecules. The effect of the narrowing of the gold particles is obtained by digestive ripening of the gold-toluene dispersion at 120℃. Particles size will be narrowed down to 4-4.5 nm. [56]

14) Synthesis of Gold Nanoparticles by Reducing Potential:

The chemical reduction of aqueous solution of chloroauric acid is one of the most widely used methods for the synthesis of gold colloids. In this study, the reducing properties of different medicinal plant extracts are independently investigated using an oxidation-reduction titrimetric assay involving $KMnO_4$. The appearance of a purple color in the reaction vessels suggested that there is formation of gold nanoparticles with size < 20 nm. [57,58]

Analysis:

These reaction mixtures were further characterized by UV/Vis spectroscopy. A strong, broad absorption band is formed.

Application of Gold Nanoparticles:

Gold nanoparticle has various applications which are discuss below:

1) Diagnosis Purpose:

Gold nanoparticles are useful in diagnosis purpose:

a) AuNPs in clinical immunoassays:

By Tanaka the development of a novel enhancement for immune chromatographic test strips occurs, where both the primary and the secondary antibodies are conjugated with AuNPs. Gold nanoparticles have found promising applications in signal enhancement of the standard enzyme-linked immunosorbent assays (ELISAs) where they can be conjugated with the antibodies or coupled with silver-enhancement. The immunosensors obtained showed excellent reproducibility and stability. Application of AuNPs in this field is a promising area under development [59,60].

b) AuNPs-based DNA-detection clinical assays:

By Mirkin, a recent development of usual Au-nanoprobe cross-linking method is

discovered. It is the biobarcode system, used for protein detection. The method involves the capture of the analyte with a magnetic particle featuring recognition elements, in this case binding of a functionalized AuNPs with a second recognition agent and "barcode" DNA strands. After magnetic separation of the sandwich complex, the DNA barcodes are released and the DNA strands detected and quantified using the Au-nanoprobe sandwich assay followed by silver enhancement. This method is used for measuring the concentration of amyloid-β-derived diffusible ligands, a potential Alzheimer's disease marker present at extremely low concentrations in the cerebrospinal fluid of affected individuals. [61,62]

c) Detection of Mycobacterium Tuberculosis:

This method is the rapid and sensitive detection of Mycobacterium tuberculosis, the etiologic agent of human tuberculosis in clinical samples. This has important promise for cancer diagnosis [63,64].

2) Non-Analytical Applications of Nanoparticles:

For non analytical application nanoparticles based materials have been developed for drug and gene delivery, tissue engineering, tumor destruction, separation and purification of biological molecules and cell, and also Phagokinetic studies.

a) Tissue engineering:

The osteoblasts are the cells are responsible for the bone matrix growth. Osteoblasts are found on the advance surface of the rising bone. When the surface of an artificial bone implant is left smooth then body will try to reject it. Thus the production of a fibrous tissue covering on the surface of the implant get smooth surface on artificial bone. Natural bone surface contains features about 100 nm across. This thin layer will responsible for reducing bone implant contact due to which further inflammation occur. Nano-sized features can help to get smooth surface. [65]

b) Cancer therapy

In the cancer therapy, the destruction of the cancer cell is occurs. The destruction of cancerous cell is done by the laser generated singlet oxygen, which is cytotoxic. For the generation of singlet oxygen, a greater quantity of a special dye used and dye is then goes into the cancer cells when it is compared with a healthy tissue. Dye stayed trapped inside the nanoparticles. This dye will not spread to other cells and other parts of body. [66]

c) Manipulation of cells and biomolecules:

Cell separation and probing are the different application of gold nanoparticle. Cylindrically shaped nanoparticles can be produced by employing metal electro deposition into nonoporous alumina template. The various magnetic particles on which study is carried out are spherical in shape, which fairly limit the possibilities to make these nanoparticles multifunctional. [67]

3) Analytical applications of nanoparticles:

The physical and chemical properties of nano-materials provide excellent forecast for designing a new generation with novel functions of bioelectronics devices. Au nanoparticles (AuNPs) represent excellent biocompatibility and display unique structural, electronic, magnetic, optical and catalytic properties which have made them a very attractive material for biosensor, chemisensor and electro catalyst [68].

Gold nanoparticles have following analytical application;

a) Enzymatic biosensor based on gold nanoparticles:

From redox-protein to the electrode surface the direct electron transfer (DET) is a very important subject in bioelectrochemistry. To understand this mechanism, construct the

biochemical sensors. Polymer such as chitosan possesses electrical, optical and magnetic properties. These properties are superior to those of a parent polymer and nanoparticle. The gold nanocomposite is formed by this polymer, for completing the DET of some redox-protein and fabricating novel biosensor. [69-72]

b) Application of gold nanoparticles for genosensors:

In 2001 Wang's group reported on the use of colloidal gold tags for electronic detection of DNA hybridization. DNA sensing applications need sky-scraping sensitivity through amplified transduction of the oligonucleotide interaction. AuNPs-based schemes reported have led to enhanced sensitivity of bioelectronics assays by several orders of importance. Thus, AuNPs-based electrochemical device will provide novel prospect for gene diagnostics in the future. [73-74]

c) Application of gold nanoparticles for immunosensors:

For the detection of binding event between antibody and antigen immunosensors plays an important role. Development in the immunoassay technique is carried out. This decreases the working time, increasing assay sensitivity, low volume analysis. They attain brilliant detection limits with small analyte volumes. They are easy and economical to mass production. [75-77]

d) Application of gold nanoparticles for electro-catalytic chemo sensors:

Gold nanoparticle shows a good catalytic activity and the interest in the gold nanoparticles catalytic activity greater than before. This activity has attention because of their relative high surface area to volume ratio, and their interface dominated properties, which shows developing nanosized electro catalyst. [78-81]

e) Multicolor optical coding for biological assays:

The combination of different size and different colours quantum dots, will gives more advantages. The selection of nanoparticles used in this method if shows that 6 different colours as well as 10 intensities then it is sufficient to decide over 1 million combinations. A precise control of quantum dot ratios will achieve. [82,83]

f) Application of nanoparticles for signal amplification:

i. Silver nanoparticles enhance Local Plasmon Resonance signals:

Localize surface plasmon resonance (LSPR) spectrum is sensitive to the nanoparticle size and shape and external dielectric nanoenvironment. This sensitivity of nanoenvironment by LSPR λmax allows for the development of nanoscale affinity biosensors. [84]

ii. Gold nanoparticles enhance the signal of Quatz Crystal Microbalance:

The novel approach for high sensitivity detection of target biomolecules is discovered by Amanda. A quartz crystal microbalance (QCM) device using gold nanoparticle as signal enhancement probes. [85,86]

iii. Nanoparticles enhance the Florescence:

When interaction between glucose and dextran occur with boronic acid capped silver nanoparticles in solution, and then nanoparticle enhances the fluorescence and decreases the absorbance. [87,88]

CONCLUSION

Gold nanoparticles exhibit unique and tunable optical property due to the fact of surface plasmon resonance. SERS have been used in new way for the detection of cancer. Gold nanoparticles are produced by reduction of chlorauric acid. These gold nanoparticles are very simple and inexpensive to use.

ACKNOWLEDGEMENT

I would like to express my special thanks of gratitude to my guide Professor Dr. S.

J. Wadher as well as Professor Dr. S. G. Gattani who gave me the golden opportunity to do this review on the topic Gold Nanoparticle, which also helped me in preparing review and I came to know about so many new things I am really thank full to them. Secondly I would also like to thank my Brother in law and my sister who helped me a lot in finalizing this review within the limited time frame. A special thanks to my family for all the sacrifices that you have made on my behalf. I would also like to thank all my friends who incented me to strive towards my goal.

Abbreviations:

Au – Gold
XRD - X-Ray diffraction
$HAuCl_4$- Chlorauric Acid
GNPs – Gold Nanoparticles
U. V. - Ultra violet spectroscopy
SPM - Surface Plasmon Resonance
SEM - Scanning Electron Microscope
TEM - Transmission Electron Microscopy
SERS - Surface enhance Raman scattering
ns- Nanosiemens
nm- Nanometer

REFERENCE

1. El-Ansary, Al-Daihan, on the toxicity of therapeutically used nanoparticles: An overview, J. Toxicol. 754810:1–754810:9 (2009).
2. E. E. Connor, J. Mwamuka, A. Gole, C. J. Murphy, M. D. Wyatt, Gold nanoparticles are take up by human cells but do not cause acute cytotoxicity, J. Small, volume 1, 1, 325–327 (2005).
3. P. Ghosh, G. Han, M. De, C. K. Kim, V. M. Rotello, Gold nanoparticles in delivery applications, J. Advance Drug Delivery Review. 60, 1307–1315 (2008).
4. D. Pissuwan, T. Niidome, M. B. Cortie, The forthcoming applications of gold nanoparticles in drug and gene delivery systems, J. Contr. Release. 149, 65–71 (2009).
5. J. B. Delehanty, K. Boeneman, C. E. Bradburne, K. Robertson, J. E. Bongard, I. L. Medintz, Peptides for specific intracellular delivery and targeting of nanoparticles: Implications for developing nanoparticles-mediated drug delivery, J. Ther. Deliv. 1, 411–433 (2010).
6. D. A Giljohann, D. S. Seferos, W. L. Daniel, M. D. Massich, P. C. Patel, C. A. Mirkin, Gold nanoparticles for biology and medicine, J. Angew. Chem. Int. 49, 3280–3294 (2010).
7. R. A. Petros, J. M. Desimone, Strategies in the design of nanoparticles for therapeutic applications, J. Nat. Rev. Drug Discovery. 9, 615–627 (2010).
8. J. Shi, A. R. Votruba, O. C. Farokhzad, R. Langer, Nanotechnology in drug delivery and tissue engineering: From discovery to applications, J. Nano Lett. 10, 3223–3230 (2010).
9. J. Turkevitch, P. C. Stevenson, J. Hillier, A study of the nucleation and growth process in the synthesis of colloidal gold, J. Faraday Soc. 11, 55–75 (1951).
10. M. Brust, M. Walker, D. Bethell, D. J. Schiffrin, R. J. Whyman, Synthesis of thiol derivatized gold nanoparticles in a two phase liquid-liquid system, J. Chem. Soc. Chem. Commun. 7, 801–802 (1994).
11. S. Mandal, P. R. Selvakannan, S. Phadtare, R. Pasricha, M. Sastry, Synthesis of a stable goldhydrosol by the reduction of chloroaurate ions by the amino acid, aspartic acid, J. Proc. Indian Acad. Sci. Chem. Sci. 114, 513–520 (2002).
12. G. A. Ozin, K. Hou, B. V. Lotsch e "Nanofabrication by self-assembly," J. materials Today, vol. 12, no. 5, pp. 12–23, (2009).
13. P. K. Jain, I. H. ElSayed, M. A. El-Sayed, "Au nanoparticles target cancer," J. Nano Today, vol. 2, no. 1, pp. 18–29, (2007).
14. D. Vanmaekelbergh, "Self-assembly of colloidal nanocrystals as route to novel classes of nanostructured materials," J. Nano Today, vol. 6, no. 4, pp. 419–437, (2011).
15. P. Christian, F. Von der Kammer, M. Baalousha, Th. Hofmann, Nanoparticles: structure, properties, preparation and behavior in environmental media, J. Ecotoxicology, 17:326–343 (2008).
16. Amir H. Faraji, Peter Wipf, Nanoparticles in cellular drug delivery, J. Bioorganic & Medicinal Chemistry, 17 2950–2962 (2009).
17. C. B. Murray, C. R. Kagan, M. G. Bawendi, Synthesis and Characterization of Monodisperse Nanocrystals and Close-Packed Nanocrystal Assemblies. J. Annual Review of Materials Research, 29 (1), 545–610 (2000).
18. X. Wang, L. Qunqing, X. Jing, J. Zhong, W. Jinyong;, L. Yan, J. Kaili, F. Shoushan,

Fabrication of Ultralong and Electrically Uniform Single-Walled Carbon Nanotubes on Clean Substrates. J. Nano Letters 9 (9): 3137–3141 (2009).
19. M. Fujita, K. Wakabayashi, K. Nakada, K. Kusakabe, Peculiar Localized State at Zigzag Graphite Edge. Journal of the Physics Society Japan 65 (7): 1920 (1996).
20. K. Nakada, M. Fujita, G. Dresselhaus, M. S. Dresselhaus, Edge state in graphene ribbons: Nanometer size effect and edge shape dependence. J. Physical Review B 54 (24): 17954 (1996).
21. K. Wakabayashi, M. Fujita, H. Ajiki, M. Sigrist, Electronic and magnetic properties of nanographite ribbons. J. Physical Review B 59 (12): 8271 (1999).
22. Burgess, Particle Size Analysis: AAPS Workshop Report, Cosponsored by the Food and Drug Administration and the United States Pharmaceopeia, J. The AAPS 6, (2004).
23. May, W.; Parris, R.; Beck, C.; Fassett, J.; Greenberg, R.; Guenther, F.; Kramer, G.; Wise, S.; Gills, T.; Colbert, J.; Gettings, R.; MacDonald, B.; Definitions of Terms and Modes Used at NIST for Value-Assignment of Reference Materials for Chemical Measurements; J. NIST Special Publication 260-136, (2000).
24. W. Cai, X. Chen, Nanoplatforms for targeted molecular imaging in living subjects. J. Small, 3: 1840-54 (2007).
25. W. Cai, T. Gao, H. Hong, J. Sun, Application of gold nanoparticles in cancer and Nanotechnology, J. Nanotechnology, Science and Applications, 1: 17-32. (2008)
26. I. X. El-Sayed, A. M. Huangand, Selective laser photo-thermal therapy of epithelial carcinoma using anti-EGFR antibody conjugated gold nanoparticles. J. Cancer Letter, 2: 129-135 (2006).
27. M. M. Alvarez, J. T. Khoury, T. G. Schaaff, M. N. Shafigullin, I. Vezmar, R. L. Whetten, Optical absorption spectra of Nanocrystal gold molecules, J. Phys. Chem., 101: 3706-3712 (1997)
28. S. Bhattacharya, A. Srivastava, Synthesis of gold nanoparticles stabilised by metal-chelator and the controlled formation of close-packed aggregates by them, J. Proc. Indian acad. Sci. (Chem. Sci.), 115: 613-619 (2003).
29. C. Burda, X. Chen, R. Narayanan, M. A. El-Sayed, "Chemistry and Properties of Nanocrystals of Different Shapes" J. Chem. Rev. 105, 1025- 1102 (2005).
30. M. Horisberger, J. Rosset, "Colloidal gold, a useful marker for transmission and scanning electron microscopy", Journal of Histochemistry and Cytochemistry Volume 25, Issue 4, pp. 295–305, (1977).
31. P. K. Jain, K. S. Lee, I. H. El-Sayed, M. A. El-Sayed, Calculated Absorption and Scattering Properties of Gold Nanoparticles of Different Size, Shape, and Composition: Applications in Biological Imaging and Biomedicine. The Journal of Physical Chemistry B 110 (14), 7238-7248 (2006).
32. K. Kwon, K. Y. Lee, Y. W. Lee, M. Kim, J. Heo, S. J. Ahn, S. W. Han, Controlled Synthesis of Icosahedral Gold Nanoparticles and Their Surface-Enhanced Raman Scattering Property. The Journal of Physical Chemistry C 111 (3), 1161-1165 (2006).
33. D. Andreescu, Stabilizer-free nanosized gold sols, Journal of Colloid and Interface Science 298, 742–751 (2006).
34. W. Patungwasa, J. Hodak, pH tunable morphology of the gold nanoparticles produced by citrate reduction, J. Materials Chemistry and Physics 108, 45–54 (2008).
35. D. Andreescu, Stabilizer-free nanosized gold sols, Journal of Colloid and Interface Science 298, 742–751 (2006).
36. D. Huang, F. Liao, S. Molesa, D. Redinger, V. Subramanian, Particle size analysis of gold nanoparticles, Journal of the Electrochemical Society, 150, G412-417 (2003).
37. G. Peng, U. Tisch, O. Adams, M. Hakim, N. Shehada, Y. Y. Broza, S. Bilan, R. Abdah-Bortnyak, A. Kuten, H. Haick, Properties, J. Nature Nanotech., 4, 669-673 (2009).
38. T. Stuchinskaya, M. Moreno, M. J. Cook, D. R. Edw ards, D. A. Russell, Gold nanoparticle, J. Photochem. Photobiol. Sci., 10, 822-831 (2011).
39. S. D. Perrault, W. C. Chan, Gold nanoparticle-properties and application, J. Proc. Nat. Acad. Sci. USA, 107, 11194-11199 (2010).
40. J. Turkevich, P. C. Stevenson, J. Hillier, "A study of the nucleation and growth processes in the synthesis of colloidal gold", J. Faraday. Soc. 11, 55–75 (1951).
41. J. Kimling, M. Maier, B. Okenve, V. Kotaidis, H. Ballot, A. Plech, "Turkevich Method for Gold Nanoparticle Synthesis

Revisited", J. Phys. Chem. B 110, 15700–15707 (2006).
42. M. Brust, M. Walker, D. Bethell, D. J. Schiffrin, R. Whyman, "Synthesis of Thiol-derivatised Gold Nanoparticles in a Two-phase Liquid-Liquid System", J. Chem. Commun. (7): 801–802 (1994).
43. R. A. Sperling, P. Rivera Gil, F. Zhang, M. Zanella, W. J. Parak, Biological applications of gold nanoparticles, J. Chem. Soc. Rev. 37, 1896-1908 (2008).
44. Ranajay Saha, Surajit Rakshit, Dipanwita Majumdar, Achintya Singha, Rajib Kumar Mitra, Samir Kumar Pal, Nanostructure, solvation dynamics, and nanotemplating of plasmonically active SERS substrate in reverse vesicles, J. Nanopart Res, 15:1576 (2013).
45. Patricia de la Presa, Tatiana Rueda, Mari#a del Puerto Morales, F. Javier, Gold Nanoparticles Generated in Ethosome Bilayers, As Revealed by Cryo-Electron-Tomography, J. Phys. Chem. B , 113 (10), 3051-3057 (2009).
46. M. N. Martin, J. I. Basham, P. Chando, S. K. Eah, Charged Gold Nanoparticles in Non-Polar Solvents: 10-min Synthesis and 2D Self-Assembly. J. Langmuir 26:7410 (2010).
47. H. Soheila, E. Pouneh, G. Maedeh, Preparation of Gold Nanoparticles for Biomedical Applications Using Chemometric Technique. J. Tropical Journal of Pharmaceutical Research June, 12 (3): 295-298 (2013).
48. S.D. Perrault, W.C.W. Chan, "Synthesis and Surface Modification of Highly Monodispersed, Spherical Gold Nanoparticles of 50-200 nm". J. Am. Chem. Soc. 131 (47): 17042–17043 (2009).
49. G. Frens, "Particle size and sol stability in metal colloids", J. Colloid & Polymer Science, 250, 736–741 (1972).
50. G. Frens, "Controlled nucleation for the regulation of the particle size in monodisperse gold suspensions", J. Nature (London), Phys. Sci. 241, 20–22 (1973).
51. Gloria M. Herrera, Amira C. Padilla, Samuel P. Hernandez-Rivera, Surface Enhanced Raman Scattering (SERS) Studies of Gold and Silver Nanoparticles Prepared by Laser Ablation, J. Nanomaterials 3, 158-172, (2013).
52. F. Li, D. P. Josephson, A. Stein, "Colloidal assembly: the road from particles to colloidal molecules and crystals," Angewandte Chemie International Edition, vol. 50, no. 2, pp. 360–388, (2011).
53. N. V. Long, C. M. Thi, M. Nogami, M. Ohtaki, "Novel issues of morphology, size, and structure of Pt nanoparticles in chemical engineering: aggregation, agglomerate, assembly, and structural changes," New Journal of Chemistry, vol. 36, pp. 1320–1334, (2012).
54. Nguyen Viet Lon, Michitaka Ohtaki, Masayoshi Yuasa, Satoshi Yoshida, Taiga Kuragaki, Cao Minh Thi, Masayuki Nogami, Synthesis and Self-Assembly of Gold Nanoparticles by Chemically Modified Polyol Methods under Experimental Control Journal of Nanomaterials Volume 2013, Article ID 793125, 8 pages, (2013).
55. S. Lokina, V. Narayanan, Antimicrobial and Anticancer Activity of Gold Nanoparticles Synthesized from Grapes Fruit Extract, J. Chem Sci Trans. 2(S1), S105-S110 (2013).
56. Günter Schmid, Benedetto Corain, Nanoparticulated Gold: Syntheses, Structures, Electronics, and Reactivities, Eur. J. Inorg. Chem. 3081_3098 (2003).
57. S. Ponarulselvam, C. Panneerselvam, K. Murugan, N. Aarthi, K. Kalimuthu, S. Thangamani, Synthesis of silver nanoparticles using leaves of Catharanthus roseus Linn. G. Don and their antiplasmodial activities, Asian Pac J Trop Biomed. 2(7): 574–580 (2012).
58. H. Rostami1, A. Haghnazari, G. Kavei, B. Ghareyazie, F. Hesari, Phytobiosynthesis of gold nano-particles and comparison of two plant species, Indian Journal of Biotechnology, Vol 10, pp 245-247 (2011).
59. Pedro Baptista, Eulalia Pereira, Peter Eaton, Gonçalo Doria, Adelaide Miranda, Inês Gomes, Pedro Quaresma, Ricardo Franco, Gold nanoparticles for the development of clinical diagnosis methods, J. Anal Bioanal Chem, 20-27, (2007).
60. C. P. Chan, Y. C. Cheung, R. Renneberg, M. Seydack, New trends in immunoassays, J. Adv Biochem Eng Biotechnol. Springer, 120-125, (2007).
61. Minjia Hao, Zhanfang Ma, An Ultrasensitive Chemiluminescence Biosensor for Carcinoembryonic Antigen Based on Autocatalytic Enlargement of Immunogold Nanoprobes, J. MDPI, Sensors (Basel). 12(12): 17320–17329 (2012).

62. R. Tanaka, T. Yuhi , N. Nagatani, T. Endo, K. Kerman, Y. Takamura, E. Tamiya, A novel enhancement assay for immunochromatographic test strips using gold nanoparticles, J. Anal Bioanal Chem 385:1414–1420, (2006).
63. Qiang Zhang, Chenyang Xue, Yanling Yuan, Junyang Lee, Dong Sun, Jijun Xiong Fiber, Surface Modification Technology for Fiber-Optic Localized Surface Plasmon Resonance Biosensors, J. Sensors (Basel). 12(3): 2729–2741 (2012).
64. Wulf-Dieter Moll, Peixuan Guo, Grouping of Ferritin and Gold Nanoparticles Conjugated, to pRNA of the Phage phi29DNA-P ackaging Motor, Journal of, Nanoscience and Nanotechnology, Vol.7, 1–11, (2007).
65. O. Adamopoulos, T. Papadopoulos, Nanostructured bioceramics for maxillofacial applications, Journal of Materials Science: Materials in Medicine, 18 (8), 1587-1597 (2007).
66. I. Roy, T. Y. Ohulchanskyy, H. E. Pudavar, E. J. Bergey, A. R. Oseroff, J. Morgan, T. J. Dougherty, P. N. Prasad, Ceramic-Based Nanoparticles Entrapping Water-Insoluble Photosensitizing Anticancer Drugs: A Novel Drug-Carrier System for Photodynamic Therapy. J. Am. Chem. Soc. 125 (26), 7860-7865 (2003).
67. D. H. Reich, M. Tanase, A. Hultgren, L. A. Bauer, C. S. Chen, G. J. Meyer, Biological applications of multifunctional magnetic nanowires (invited). Journal of Applied Physics, 93 (10), 7275-7280 (2003).
68. L. G. Andrey, Enzyme-catalyzed direct electron transfer: Fundamentals and analytical applications, J. Electroanalysis, 9 (9), 661-674 (1997).
69. M. L. Mena, P. Yanez-Sedeno, J. M. Pingarron, A comparison of different strategies for the construction of amperometric enzyme biosensors using gold nanoparticle-modified electrodes, J. Analytical Biochemistry, 336 (1), 20-27 (2005).
70. L. G. Andrey, Enzyme-catalyzed direct electron transfer: Fundamentals and analytical applications, J. Electroanalysis, 9 (9), 661-674 (1997).
71. K. R. Brown, A. P. Fox, M. J. Natan, Morphology-Dependent Electrochemistry of Cytochrome c at Au Colloid-Modified SnO2 Electrodes, J. Am. Chem. Soc. 118 (5), 1154-1157 (1996).
72. J. Jia, B. Wang, A. Wu, G. Cheng, Z. Li, S. A. Dong, Method to Construct a Third-Generation Horseradish Peroxidase Biosensor: Self-Assembling Gold Nanoparticles to Three-Dimensional Sol-Gel Network, J. Anal. Chem. 74 (9), 2217-2223 (2002).
73. J. Zhang, M. Oyama, Gold nanoparticle-attached ITO as a biocompatible matrix for myoglobin immobilization: direct electrochemistry and catalysis to hydrogen peroxide, Journal of Electroanalytical Chemistry, 577 (2), 273-279 (2005).
74. V. V. Shumyantseva, S. Carrara, V. Bavastrello, D. Jason Riley, T. V. Bulko, K. G. Skryabin, A. I. Archakov, C. Nicolini, Direct electron transfer between cytochrome P450scc and gold nanoparticles on screen-printed rhodium-graphite electrodes, J. Biosensors and Bioelectronics, 21 (1), 217-222 (2005).
75. R. Liang, J. Qiu, P. A. Cai, Novel amperometric immunosensor based on three-dimensional sol-gel network and nanoparticle self-assemble technique, J. Analytica Chimica Acta, 534 (2), 223-229 (2005).
76. D. P. Tang, R. Yuan, Y. Q. Chai, X. Zhong, Y. Liu, J. Y. Dai, L. Y. Zhang, Novel potentiometric immunosensor for hepatitis B surface antigen using a gold nanoparticle-based biomolecular immobilization method, J. Analytical Biochemistry, 333 (2), 345-350 (2004).
77. M. Dequaire, C. Degrand, B. Limoges, An Electrochemical Metalloimmunoassay Based on a Colloidal Gold Label, J. Anal. Chem. 72 (22), 5521-5528 (2000).
78. R. M. Penner, C. R. Martin, Preparation and electrochemical characterization of ultramicroelectrode ensembles, J. Anal. Chem. 59 (21), 2625- 2630 (1987).
79. A. Escorcia, A. A. Dhirani, Electrochemical properties of ferrocenylalkane dithiol-gold nanoparticle films prepared by layer-by-layer self-assembly, Journal of Electroanalytical Chemistry, 601 (1-2), 260-268 (2007).
80. R. H. Tian, J. F. Zhi, Fabrication and electrochemical properties of borondoped diamond film-gold nanoparticle array hybrid electrode, J. Electrochemistry Communications, 9 (5), 1120-1126 (2007).

81. L. Ding, C. Hao, Y. Xue, H. Ju, A Bio-Inspired Support of Gold Nanoparticles-Chitosan Nanocomposites Gel for Immobilization and Electrochemical Study of K562 Leukemia Cells, J. Biomacromolecules, 8 (4), 1341-1346 (2007).
82. B. K. Jena, C. R. Raj, Ultrasensitive Nanostructured Platform for the Electrochemical Sensing of Hydrazine, J. Phys. Chem. C, 111 (17), 6228-6232 (2007).
83. W. J. Parak, D. Gerion, T. Pellegrino, D. Zanchet, C. Micheel, S. C. Williams, R. Boudreau, M. A. Gros, C. A. Larabell, A. P. Alivisatos, Biological applications of colloidal nanocrystals, J. Nanotechnology, 14 (7), R15-R27, (2003).
84. W. J. Haes, R. P. Van Duyne, A Nanoscale Optical Biosensor: Sensitivity and Selectivity of an Approach Based on the Localized Surface Plasmon Resonance Spectroscopy of Triangular Silver Nanoparticles, J. Am. Chem. Soc. 124 (35), 10596-10604 (2002).
85. N. H. KIM, T. J. BAEK, H. G. PARK, G. H. SEONG, Highly Sensitive Biomolecule Detection on a Quartz Crystal Microbalance Using Gold Nanoparticles as Signal Amplification Probes, J. Analytical Sciences, 23 (2), 177-181 (2007).
86. K. Aslan, J. Zhang, J. R. Lakowicz, C. D. Geddes, Saccharide Sensing Using Gold and Silver Nanoparticles-A Review, Journal of Fluorescence, 14 (4), 391-400 (2004).
87. J. Hu, Z. Wang, J. Li, Gold Nanoparticles with Special Shapes: Controlled Synthesis, Surface-enhanced Raman Scattering, and The Application in Biodetection. J. Sensors, 7, 3299-3311 (2007).
88. K. Aslan, J. R. Lakowicz, C. D. Geddes, Rapid deposition of triangular silver nanoplates on planar surfaces: Application to metal-enhanced fluorescence, J. Phys. Chem. B, 109 (13), 6247-6251 (2005).

How to cite this article: Gadge AN, Wadher SJ, Landge AD. Gold nanoparticle. International Journal of Science & Healthcare Research. 2020; 5(2): 21-35.

******