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A Review on Gold Nanoparticles: Properties, Synthesis and Biomedical Application in Drug Delivery and Cancer Therapy

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Abstract: Gold nanoparticles (AuNPs) are very small particles and are made up of gold. These particles are too much small and can't see with eyes. These gold nanoparticles (AuNPs) are used in the delivery of the drug and in the treatment of cancer. This helps the drug to reach the target site of the body that's why the effectiveness of the drugs are increased. In this review paper the Properties of the Gold nanoparticles (AuNPs) including its Prepration, Synthesis method and the application of gold nanoparticles are discussed. The gold nanoparticles particles also have some unique properties such as Surface Plasmon resonance and Biocompatibility. The review paper discussed about the potential of the Gold nanoparticles in drug delivery, to enhance the therapeutic effect of AuNPs and to minimize the Adverse effect. Also the application of AuNPs in cancer therapy are Photothermal therapy, radiation therapy and the targeted chemotherapy. This review paper aims to provide the In-depth understanding of the Gold nanoparticles (AuNPs) and the gold nanoparticles play an important role in delivery of the drugs and in the treatment of cancer.

Keywords: *Gold Nanoparticles, Synthesis Method, Physiochemical Properties, Biomedical Application, Drug Delivery, Cancer Therapy.*

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I. INTRODUCTION

Nanoparticles are defined as the tiny particles and have the size range between the 1 - 100 nm (nanometers) and these particles are very small can't see with eyes, to see these particles and study about their structure and properties the special equipment are required such as Transmission Electron Microscopy (TEM), Scanning Electron Microscopy (SEM), Atomic Force Microscopy (AFM).

Gold nanoparticles are biocompatible, stable, versatile and also have low toxic effects that's make them suitable for the biomedical application. The gold doesn't react with any other substances easily, they are tiny particles and wine-red solution that are helpful in the prevention of damage from the free radicals. Gold nanoparticles deliver the drugs to the targeted site which reduce the side effects. The AuNPs target the cancer cells and it's delivered the heat or radiation to the specific site and it's also helpful for the doctors to see inside the body by using techniques such as MRI & CT.

AuNPs shows the unique optical properties such as Surface Plasmon resonance (SPR) which absorb the light and scatter the light. In recent years, various synthesis techniques have been developed to produce AuNPs with specific shapes and sizes, allowing for better control over their interaction with biological systems. Their ability to conjugate with drugs, targeting ligands, and imaging agents has made them powerful tools in targeted drug delivery, enhancing therapeutic outcomes while minimizing side effects.

This review provides a comprehensive overview of the properties of gold nanoparticles, common synthesis methods, and their expanding role in drug delivery and cancer therapy.

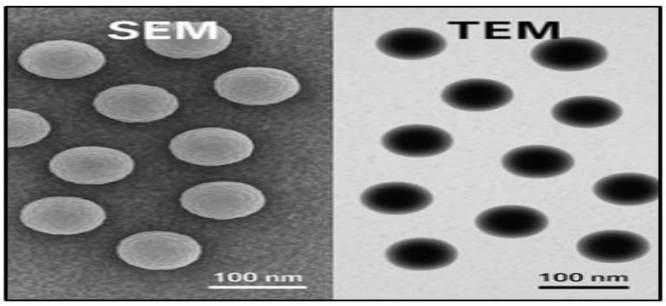

Fig 1 SEM and TEM Image of gold Nanoparticles "Image generated by Chat GPT, Open AI."

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II. TYPES OF GOLD NANOPARTICLES

According to their shape the different types of gold nanoparticles are discussed below:

A. Nano sphere
B. Nanoshell
C. Nanorod
D. Nanocluster
E. Nanocage
F. Nanostar

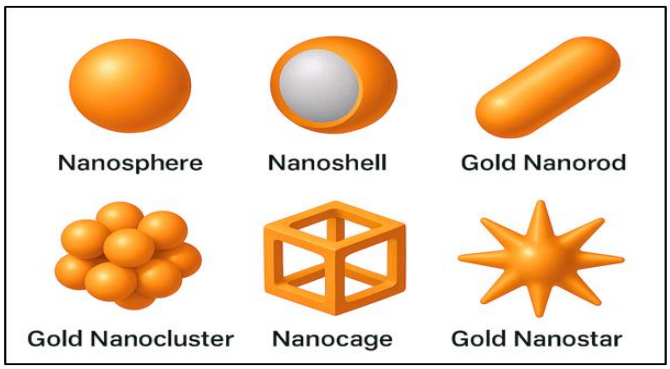

Fig 2 Different types of gold nanoparticles according to their shape "Image generated by Chat GPT, Open AI."

A. Gold Nanosphere

A gold nanosphere is tiny and spherical shape particles made up of gold and they have high surface area and due to the gold-sulphur bonds the gold Nanosphere are stable and these are helpful in the delivery of the drug at the targeted site and in the treatment of the cancer. These Nanosphere are made of Gold ions(HAucl) and citrate both are the liquid when these are mixed the citrate reduce the gold ions(Reduction).

B. Gold Nanoshell

A gold nanoshell made up of silica core and the gold shell that is thin layer surrounded the silica core and both are the biocompatible materials. These nanoshell are designed to absorb the specific wavelength of the light.

C. Gold Nanorod

A nanorod is rod-shaped particle with the length range from 10-100 nanometers(nm) and the diameter around 1-10. These nanorod are made through by using the template, using chemical reactions and by using the deposition of materials on the surface.

D. Gold Nanocluster

A Nanocluster is bunch of the atoms or molecule that are clustered together. These are made up of chemical synthesis and the techniques such as laser ablation or sputtering.

E. Gold Nanocage

A Nanocage is cage-like structure and the network of the atoms or molecules formed the three dimensional structure. These are made by using the sol-gel process and through the templated directed synthesis.

F. Gold Nanostar

The gold Nanostar has star-shaped structure and typically with central core and multiple branches and also the optical properties are enhanced due to this branched structure. These Nanostar have surface area-to-volume ratio. The Nanostar are made through the wet chemical synthesis to formed the Nanostar in liquid solution and also through the template direct synthesis & the laser ablation.

III. CHARACTERISTICS OF GOLD NANOPARTICLES

- The gold nanoparticles are biocompatible, stable, versatile and also have low toxic effects which helps to reduce the side effects.
- The AuNPs have high surface area-to-volume ratio that are suitable in the catalysis and sensing.
- They have shown unique properties such as Surface Plasmon resonance (SPR) which absorb the light and scatter the light.
- The AuNPs have conductivity of electricity that makes the AuNPs useful in the application of electronics and sensing.
- The AuNPs have higher reactivity because of its higher surface area. In the oxidation and reduction chemical reactions & the various chemical reactions the AuNPs acts as a catalyst.

IV. SYNTHESIS METHODS

A. Chemical Reduction Method

The chemical reduction method is most commonly used technique for the synthesis of gold nanoparticles. This method involves the reduction of gold ions to the gold nanoparticles by using a reducing agent.

B. Procedure

- Firstly, prepared the gold salt solution by dissolving the chloride trihydrate (HAuCl4.3H2O) in deionized water.
- After that add the reducing agent to the gold salt solution that we prepared already and stir until it get dissolved.
- Then heat the solution to 10 - 15 minutes at 100°C and after that the reduction reaction occurs.
- Then cooled the solution at room temperature and centrifuge the solution to separate out the gold nanoparticles.

C. Advantages

- It is simple and cost-effective technique for synthesizing gold nanoparticles.
- It can produce controlled shape and size of gold nanoparticles.

D. Turkevich Method

This method is a modification of the chemical reduction method. It involved the reduction of gold ions to gold nanoparticles by using the sodium citrate as the reducing agent.

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E. Procedure

- Firstly, prepared the gold salt solution by dissolving the chloride trihydrate (HAuCl4.3H2O) in deionized water.
- After that add the sodium citrate as reducing agent to the gold salt solution that we prepared already and stir until it get dissolved.
- Then heat the solution for 10 - 15 minutes at 100℃ and the reduction reaction occurs.
- After that cooled the solution at room temperature and centrifuge the solution to separate out gold nanoparticles.

F. Advantages

- Through this method the spherical and controlled size of gold nanoparticles are produced.
- It is simple technique and cost effective.

G. Brust-Schiffrin Method

It is a technique in which the gold nanoparticles are synthesized using a two phase system. It involved the reduction of gold nanoparticles by using the sodium borohydride as reducing agent.

H. Procedure

- Firstly, prepared the gold salt solution by dissolving the chloride trihydrate (HAuCl4 . 3H2O) in toulene.
- Then added the alkanethiol to the above solution and stir until it gets dissolved.
- After that added the NaBH4 to the above solution until it turns into dark brown and then the reduction reaction occurs.
- At last, stir the solution for 2-3 hours and then centrifuge the solution to separate out the gold nanoparticles.

I. Advantages

- Through this method the gold nanoparticles are produced small and monodisperse.
- It can produce the controlled shape of gold nanoparticles.

J. Sol-Gel Method

In this Sol-Gel Method by using the sol-gel precursor the gold nanoparticles are synthesized. It involved the reduction of gold ions to gold nanoparticles by using a reducing agent.

K. Procedure

- Firstly, prepared the gold salt solution by dissolving the chloride trihydrate (HAuCl4 .3H2O) in deionized water.
- Then added the sol-gel precursor to the above solution until it gets dissolved.
- After that the solution undergo hydrolysis and condensation reaction to formed a colloidal solution.
- Then add the reducing agent in the colloidal solution and the reduction reaction occurs.
- After that placed the solution for a few hours and the centrifuge to separate out the gold nanoparticles.

L. Advantages

- This method controls the shape and size of gold nanoparticles.
- It's produced the high-purity of gold nanoparticles.

Table 1 Summary of Gold Nanoparticle Synthesis Methods

Synthesis Method	Reagents Used	Description
Chemical Reduction	$HAuCl_4$ + Reducing agent (e.g., $NaBH_4$)	Gold ions reduced to nanoparticles by a chemical agent
Turkevich Method	$HAuCl_4$ + Sodium citrate	Uses citrate as both reducing and stabilizing agent to form spherical AuNPs
Brust-Schiffrin Method	$HAuCl_4$ + $NaBH_4$ + Thiol compounds	Two-phase (water-organic) method for small, monodisperse AuNPs
Sol-Gel Method	$HAuCl_4$ + Sol-gel precursors + Reducing agent	Uses hydrolysis and condensation in sol-gel network formation

V. PROPERTIES OF GOLD NANOPARTICLES

A. Physical Properties

- *Size and shape:*

Gold nanoparticles are of the various shapes (spherical rod-shaped triangular and other shapes) and sizes (1-100nm) Their shape and size affect their optical, electrical and chemical properties.

- *Surface Area:*

Gold nanoparticles have high surface area-to-volume ratio that are useful for the application such as catalysis, sensing and biomedical application. The high surface area also improved the biocompatibility.

- *Density:*

Gold are very dense metal and the gold nanoparticles are made up of gold. It means they aren't easily deformed or broken.

- *Thermal conductivity:*

Gold nanoparticles have high thermal conductivity because of the small size and high surface area which helps them to absorb and transfer heat energy more efficiently and these properties are helpful for the photothermal therapy.

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B. Chemical Properties

➢ *Reactivity:*

Gold nanoparticles have high surface area-to-volume ratio and have unsaturated surface bonds that makes the gold nanoparticles more reactive. In simply the due to their physical and chemical properties the gold nanoparticles are highly reactive that means they are easily interact with other molecules.

➢ *Catalytic Activity:*

Gold nanoparticles acts as catalyst. It is used as catalyst in fuel cells, in chemical synthesis reactions, environmental application and in the biomedical application.

➢ *Stability:*

Gold nanoparticles are known for their stability and resist various environmental factors such as temperature and pH changes. The stable gold nanoparticles make them suitable for the application of catalysis, sensing and detection and in the biomedical application.

➢ *Biocompatibility:*

The gold nanoparticles are biocompatible that means they are non-toxic, non-reactive, do not harm cells and doesn't react with the biological molecules. That makes them suitable for the application of imaging and diagnostics, drug delivery, therapy and biosensing.

➢ *Optical Properties*

Gold nanoparticles show unique optical propertie that is surface plasmon resonance and the gold nanoparticles absorb and scatter the light. The gold nanoparticles also show fluorescence that they can emit the light after absorbing it and also have optical sensitivity that detect the small changes in their environment. This all properties of gold nanoparticles are useful in the application of imaging, biosensing, photothermal therapy and in the biomedical application.

C. Biomedical Application of Gold Nanoparticles in Drug Delivery and Cancer Therapy

Gold nanoparticles (AuNPs) play an important role in the biomedical field due to their unique properties such as the gold nanoparticles are small size, high surface area-to-volume ratio, biocompatible and they have strong interaction with light. These all characteristics of gold nanoparticles are useful in drug delivery and cancer therapy.

➢ Gold Nanoparticles in Drug Delivery

The gold nanoparticles delivered the drug to their specific site. Gold nanoparticles are the highly efficient drug carrier because of the high surface area-to-volume ratio and they have the ability to conjugate with various biomolecules that is drugs, peptides, antibodies and nucleic acid.

➢ Passive Targeting Via Enhanced Permeability and Retention (EPR) Effect

Tumours have abnormal structures like a messy, irregular sponge that traps the nanoparticles and have leaky blood vessels that the AuNPs are leaking in. The gold nanoparticles deliver the drugs directly to the tumor where gold nanoparticles accumulate and stay there and also the kidneys don't filter out the nanoparticles quickly so that's why they remain in the tumor. This makes the treatment more effective and less harmful to the healthy tissues and these also reduce the side effects.

➢ Active Targeting Through Ligand Functionalization

In this we add targeting ligands to the nanoparticles and the targeting ligands help the nanoparticles to attach to the specific cancer cells after that they allow the nanoparticles to deliver the drugs directly to the specific site. The various ligands that are used such as antibodies, peptides, aptamers and folic acid. This method helps to be more accurate to deliver the drugs directly to the cancer cells and also isn't harmful for the healthy cells. The targeted nanoparticles improved the treatment and also reduced the side effects.

D. Controlled Drug Release Mechanism

Gold nanoparticles delivered the drugs at the target site. Some common mechanism include:

➢ *pH-Responsive Release:*

Tumors are more acidic than the normal tissues and the gold nanoparticles detects acidity. When the gold nanoparticles detects acidity it released the drugs.

➢ *Enzyme-Responsive Release:*

Some specific enzymes are produced by tumor cells and the gold nanoparticles detects these enzymes. When it detects the enzyme it released the drugs.

➢ *Light-Triggered Release:*

Near infrared (NIR) laser heats the gold nanoparticles, weakening chemical bonds and allow the drugs to release at the right spot.

➢ *Gene Delivery Applications*

Gold nanoparticles also helps to fix the faulty genes in the cancer cells by delivering the small interfering RNA (siRNA), plasmids or antisense oligonucleotides. The gold nanoparticles surface modified with cationic polymer or lipids that helps to attach these siRNA, plasmids or antisense oligonucleotides and enter into the cancer cells and then delivered these to cancer cells.

E. Gold Nanoparticles in Cancer Therapy

Gold nanoparticles enhancing the existing cancer treatment by photothermal therapy (PTT) that is heat based cancer treatment, Photodynamic therapy(PDD), Radiation therapy and chemotherapy.

➢ *Photothermal Therapy (PTT)*

The photothermal therapy is a heat based treatment in which the gold nanoparticles absorb the light and convert the light energy into the heat (when the gold nanoparticles absorb the light then the electron are excited and these excited electrons release their energy as heat). These heat destroyed the cancer cells without harming the healthy tissues.

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➢ *Mechanism of Action*

The gold nanoparticles accumulate in the tumor via passive or active targeting. Then the laser light (NIR) excited the gold nanoparticles and the excited gold nanoparticles produce heat. Then the temperature rises around (42°c - 45°c) induced apoptosis or necrosis in cancer cells.

➢ *Photodynamic Therapy (PDT)*

Photodynamic therapy is a light-activated cancer treatment that involves the use of photosensitizers, the photosensitizers produce the reactive oxygen species when exposed to the light, which damage the cancer cells. The ROS cause oxidative damage and cancer cells death.

➢ *Role of Gold Nanoparticles(Aunps) in PDT*

- AuNPs acts as a carrier for the photosensitizers improving their solubility and stability.
- The gold nanoparticles increase the Reactive oxygen species (ROS) production when exposed to the light, the treatment are more effective.
- The gold nanoparticles treating the deep-seated tumors by combining the PDT with the AuNPs. The combination of PDT-AuNPs target the cancer cells and minimize the harm to healthy cells.

➢ *Radiation Therapy Enhancement*

Gold nanoparticles have a high atomic number (Z = 79) which absorbing the X-rays and when they absorb X-rays they released the secondary electrons.

➢ *Mechanism of Action*

Gold nanoparticles accumulate in the tumor tissues. When X-rays exposure the AuNPs absorb the energy and emit the photoelectrons and Auger electrons. These electrons cause DNA damage in cancer cells and increased the cancer cells death.

➢ *Chemotherapy Enhancement*

Gold nanoparticles act as nanocarriers that deliver the chemotherapy drugs directly to the cancer cells such as doxorubicin, paclitaxel and cisplatin. They improved the drug solubility, drug stability and target cancer cells.

VI. CONCLUSION

Gold nanoparticles have great potential in medicine, especially for drug delivery and cancer treatment. Their small size and unique properties allow them to target specific cells, improve treatment accuracy, and reduce side effects. They can also be used for early disease detection and imaging. Although there are still challenges like safety and large-scale production, ongoing research continues to improve their design and application. In the future, gold nanoparticles could play a key role in developing safer, more effective, and personalized medical treatments.

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