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Short Review on Application of Gold Nanoparticles

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Abstract: Nanoparticles have several biomedical and industrial applications in diagnosis of disease, targeted chemotherapy and in drug delivery. Multifunctionality and sub-micronic size is the main characteristics of nanoparticles. Nanoparticles can be integrated with ligands, imaging labels, therapeutic agents and other functionalities for site specific drug delivery and cellular uptake. In the present review we are discussing the application and synthesis of gold nanoparticles which is the most studied among all metallo-nanoparticles. Various anticancer drugs are available but these are cause the necrosis of cancerous cell as well as normal cells. But gold nanoparticles cause the necrosis of only cancer cells. These are targeted drug delivery systems which are smaller than human cells so can easily penetrate the tumour and destroy the cancerous cell. Various anticancer drugs conjugated with gold nanoparticles result in increased efficiency of anticancer drug. Gold nanoparticles are beneficial for chemotherapy and also for diagnosis of cancer due to their photo physical property and optical property. Gold nanoparticles can be functionalized with protein, peptides and nucleic acid. So these have a great application not only in bio sensing drugs but also in drug, gene and protein delivery.

Key word: Gold Nanoparticles · Characteristics · Functionalization · Synthesis · Cancer · Application

INTRODUCTION

Gold nanoparticles have advantages over other metal nanoparticles due to their biocompatibility and non-cytotoxicity. Nanoparticles are nanometres in size. These are 100 to 1000 times smaller than human cells. Gold is used internally in human from last 50 years due to their chemical inertness. The size of gold nanoparticles can be controlled during their synthesis and functionalization with different groups. Gold nanoparticles accumulate in the tumour cells and show optical scattering. So these can act as the probe for the microscopic study of cancer cells. These are also used in chemotherapy and diagnosis of cancer cell [1].

Gold nanoparticles have a great application not only in bio sensing drugs but also in drug, gene and protein delivery [2].

Gold nanoparticles occur in various sizes ranges from 2 to 100 nm. But 20 to 50 nm particles size range show the most efficient cellular uptake. Specific cell toxicity is shown by 40 to 50 nm particles. These 40 to 50 nm particles diffuse in to tumours and easily recover it. But the larger particles i.e. 80 to 100 nm do not diffuse into the tumour and stay near the blood vessels [3]. These have a great extinction coefficient [4]. The surface plasmon band depends upon their size. The surface plasmon resonance shows at 520 nm. The size of conjugated gold nanoparticles depends upon thiol/gold ratio [5]. If the amount of thiol (SH) is high then the particle size will be small. Crystal structure of thiol monolayer protected gold nanoparticles contains 102 gold atoms and 44 p-mercaptobenzoic acid units [6].

Multi-functionalization is the main characteristics of nanoparticles. Nanoparticles can be integrated with ligands, imaging labels, therapeutic agents and other functionalities for specific drug delivery and cellular uptake. Doxorubicin, an anticancer drug can conjugate with gold nanoparticles [7]. By conjugation there is increase in the potency of doxorubicin. So the cytotoxic effect of doxorubicin is increased. Through functionalization gold nanoparticles convert poor active drug to high active drug.

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Thus gold nanoparticles have a great contribution in cancer therapy, diagnosis of cancerous cell and importance in the therapy of HIV [8].

Coumarin, a fluorescent dye when conjugated with polyethylene glycol at one end and with gold nanoparticles on other, then the effect of Coumarin-PGE-thiol is increased as due to PEG the fluorescent quenching effect of gold nanoparticles is decreased [9]. So through PEG spacer the gold nanoparticles can be conjugated with biologically ligands like fluorescent dyes, antibiotics and cause induction of stimulus at the target site.

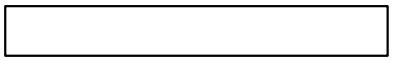
Characteristics of Gold Nanoparticles [3, 5, 10- 12]:

- Gold nanoparticles are chemically inert.
- These have greater biological compatibility.
- Optical properties like plasmon resonance are exhibited by gold nanoparticles.
- These exhibit versatility because of their ready functionalization through thiol linkages.
- Gold nanoparticles provide microscopic probes for the study of the cancer cell.
- Gold nanoparticles accumulate in the cancerous cell and show the cytotoxic effect i.e. apoptosis or necrosis of the specific cell and cell specific receptor.
- These have high stability due to the gold-sulphur bonds.
- Their photo physical properties can be exploited for drug release at remote place.

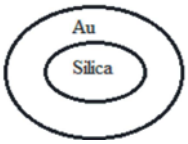
Types of Gold Nanoparticles [13]:

- Gold nanorods
- Gold nanoshells
- Gold nanocages
- Gold nanosphere
- SERS nanoparticles

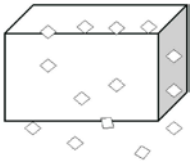
Gold Nanorods: These are synthesized by template method. These are prepared by electrochemical deposition of gold within the pores of nanoporous polycarbonate template membranes. Gold nanorods diameter is according to the diameter of pore of the template membrane [13].



Gold Nanoshells: Surface plasmon resonance peaks (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 controls the thickness of the shell [13].

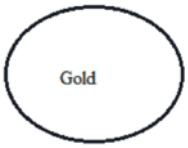


Gold Nanocage: Through galvanic replacement reaction between truncated silver nanocubes and aqueous $HAuCl_4$ gold nanocage is synthesized [13].



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 [13].

Sold Nanospheres: These are synthesized by reduction of an aqueous $HAuCl_4$ by using citrate as reducing agent. Through citrates / gold ratio the size of nanospheres can be controlled. By two-phase ratio, the size of nanospheres can be affected by thiol / gold molar ratios [13].



Synthesis of Gold Nanoparticles [14]: Initially prepared aquaregia solution for washing the glass wares to dissolve the metallic particles which may interfere with the synthesis.

Aquaregia solution-
3 parts of HCl + 1 part of HNO_3
Aquaregia is highly corrosive and oxidising agent.

Then use chloroauric acid ($HAuCl_4$) as a reactant and Sodium borohydride ($NaBH_4$) as reducing agent.

$NaBH_4$ + Deionised water → $NaBH_4$ solution

0.1 M $HAuCl_{4\ (yellow\ colour)}$ + $NaBH_4$ → Gold nanoparticles $_{(ruby\ red\ colour)}$

The change in the colour of gold from yellow to ruby red colour indicates the preparation of gold nanoparticles.

Dialysis tube made up of cellulose membrane and is called Dialysis bag. The dialysis bag is washed with deionised water. Then put this dialysis bag in a beaker and then put this beaker in magnetic stirrer and boil for 5 minutes and then again washed with deionised water. After that cleans it with aquaregia solution. Then pour the AuNPs into bag. After that these are detected by Transmission electron microscopy.

Gold nanoparticles of 1 to 2 nm can be prepared by using diborane as reducing agent with phosphine as stabilising agent to prevent the agglomeration.

Gold nanoparticles of 10 to 150 nm can be prepared by using sodium cirate as reducing agent in water and citrate as a stabilising agent to prevent agglomeration.

Reducing Agents-Sodium borohydride, Sodium citrate
Capping agent / Stabilizing Agents-Phosphine, Citrate

After synthesis the other molecules replace the capping agents by ligands exchange reaction.

Functionalization of Gold Nanoparticles:

- Monolayer protected clusters (MPCs) can be prepared by one-pot protocol [15].

$$HAuCl_4 + NaBH_4 \xrightarrow{HS} AuNPs \xrightarrow{HS} MPCs \xrightarrow{HS} MMPCs$$

(Formation of MPCs by Schiffrin Reaction and MMPCs by Murray's Place Exchange Reaction):

- MMPCs (Mixed monolayer protected cluster) can be prepared directly or by post functionalization of MPCs created by Murray [15, 16] through place exchange reaction of thiol.
- Coumarin, a fluorescent dye when is conjugated with polyethylene glycol at one end and other end with gold nanoparticles. Then the effect of Coumarin-PGE-thiol is increased. So due to PEG the fluorescent quenching effect of gold nanoparticles is decreased.

So through PEG spacer the gold nanoparticles can be conjugated with biologically ligands like fluorescent dyes, antibiotics induce stimulus at the targeted site.

After the preparation of gold nanoparticles, in the aqueous dispersion of gold nanoparticles coumarin-PEG-thiol is added for conjugation. There is a covalent interaction.

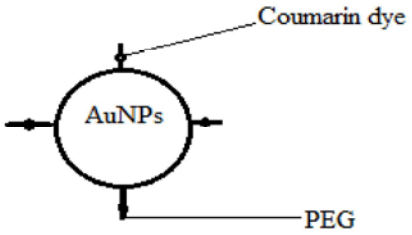


Fig. 1: Gold nanoparticle with coumarin-PEG

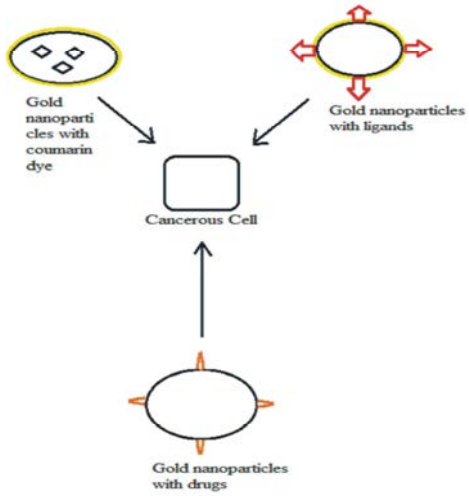


Fig. 2: Application of gold nanoparticles in delivery of drug for cancerous cell

Application

Gold Nanoparticles for the Delivery of Protein, Peptides and Nucleic Acid: These can be employed as a carrier for delivery of peptides, proteins and nucleic acid like DNA due to their tunable size [17].

Gold nanoparticles are functionalized with cationic 4° ammonium group, can bind DNA plasmid through electrostatic interactions and protect DNA from enzymatic digestion.

Gold nanoparticles can work as a carrier for peptides and proteins, have reported that the cationic tetra alkyl ammonium functionalized GNP's recognise the cell surface receptor [18].

Gold nanoparticles act as a carrier of insulin. Chitosan coated gold nanoparticles easily adsorb insulin on their surface and the transmucosal delivery of insulin is enhanced [19].

Photo Physical Property of GNPs for Delivery of Drug:

- GNPs cause local heating when irradiated with light in 800 to 1200 nm. They cause the photo thermal destruction of tumours.

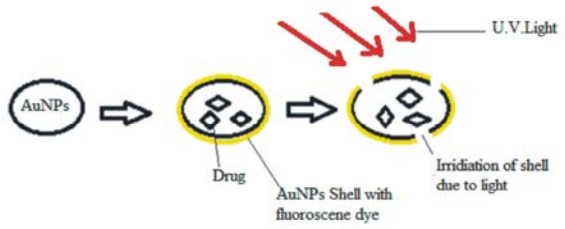


Fig. 3: Drug release after irradiation of light

- GNPs are doped into the shells of capsules containing the drug. When the light irradiated on it then the shells rupture and the drug release (Figure 3) [20].

***In vivo* Targeting Using Gold Nanoparticles:** It can be done by using two approaches [21].

- Active Targeting
- Passive Targeting

Active Targeting: It depends on the recognition of ligands on the gold nanoparticles surface by cell surface receptors [22].

Passive Targeting: It depends on the extravasations of vectors through leaky blood vessels in unhealthy tissue [23].

- Gold nanoparticles are used to identify the protein interaction under the study of immunohistochemistry.
- These are used as a lab tracer to detect the presence of DNA in sample. So these are used in fingerprinting.
- These are used for the detection of aminoglycosides antibiotics like streptomycin, gentamycin and neomycin.
- Gold Nanorods can be used to detect the cancer stem cells.
- Gold nanoparticles are used for identifying the different classes of bacteria. At present time identification of bacteria is done by expensive machine. So GNPs are used for identification of different bacterial classes that will be beneficial for cancer diagnosis [24].

CONCLUSION

Gold nanoparticles emerge as promising carriers of bio molecules like protein, peptides, nucleic acid and insulin. Their low inherent toxicity, multifunctionality, high surface area, photo physical and optical properties impart unique attributes that have a great importance in chemotherapy, cancer diagnosis and drug delivery.

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