World Journal of Pharmaceutical Sciences
ISSN (Print): 2321-3310; ISSN (Online): 2321-3086
Available online at: http://www.wjpsonline.org/
Review Article

A Recent Review on Gold Nanotechnology

[1]Shaina Kujar, [1]Akanksha Choudhary, [1]Manjit Kaur, [1]Prerna Upadhyay and [2]Nitan Bharti Gupta

[1]Student, [2]Assistant professor and HOD, Department of Pharmaceutics, Sri Sai College of Pharmacy, Badhani, Pathankot, Punjab 140001[Affiliations to the I. K. G. Punjab Technical University, Jalander , punjab, India].

Received: 29-06-2019 / Revised Accepted: 27-07-2019 / Published: 01-08-2019

ABSTRACT

This article is mainly aimed on the synthesis and applications of gold nanoparticles in the field of medicine and targeted drug delivery. Nanotechnology has become one of the ubiquitous and advanced areas of research in this field. Among nanoparticles, gold nanoparticles show special advantages in this field due to their unique properties, small size and high surface area-to-volume ratio. Gold nano particles are widely used in various biomedical applications and drug delivery systems due to their inert nature, stability, high dispersity, non-cytotoxicity and biocompatibility. Gold nanoparticles (AuNPs) are important components for biomedical applications. AuNPs have been widely employed for diagnostics, and have seen increasing use in the area of therapeutics. In this mini-review, we present fabrication strategies for AuNPs and highlight a selection of recent applications of these materials in bionanotechnology.

Keywords: Bionanotechnology, Biocompatibility, Gold Nanoparticle, Nanotechnology, Non cytotoxicity, Targeted drug delivery

Address for Correspondence: Shaina Kujar, Sri Sai College of Pharmacy, Badhani, Pathankot;
Email : shainabhatti22@gmail.com

How to Cite this Article: Shaina Kujar, Akanksha Choudhary, Manjit Kaur, Prerna Upadhyay and Nitan Bharti Gupta. A Recent Review on Gold Nanotechnology. World J Pharm Sci 2019; 7(8): 71-81.

INTRODUCTION

Various Nanotechnologies is very immersive manufacturing polymer/gold Nano composite depict high potential technology that allows the wide trends for novel coatings and paintings. GNPs are smaller, faster, cheaper materials and devices. They are used for their versatility and performance of non-volatile Gold nanoparticles (GNPs) are the most compatible memory devices and low efficient temperature printing nonmaterial for preparation of engineered metal inks in electronics . GNPs in Nano platforms can be incorporated as smart sensing devices. Surface developed in novel usages. Gold nanoparticles Plasmon resonance property of GNP makes them most with long diameter from 15-20 nm can be produced by suitable engineered nonmaterial used for bio imaging, reduction of auric chloride with trisodium citrate([1-11]).

The gold nanoparticles in 15-20 nm size range, also named as gold colloids, have gain attention for fabrication of smart sensing increasing performance due to their unique properties in devices in biomedical sciences as diagnostic tools. Regulatory research fields. Although Citrate capped GNPs are negatively charged, which GNPs are defined by tiny size, significant quantities which can be exploited for electrostatic interactions with GNPs are likely required for many commercial and some positively charged bio molecules like antibody. Industrial applications. In novel emerging strategies the compatibility of GNPs is excellent with antibody shows a huge growth of the global demand or antigen and other bio molecules; moreover, GNPs For instance, (a) bio molecule- and/or not affect the functional activity even after immobility-biopolymer-conjugated GNPs are largely used as bio-logical. This in turn can be used for the detection of target markers and bio delivery vehicles in the medicine/ analyte specifically. Therefore, surface functional pharmacy and in cosmetic products. GNPs are employed of gold nanoparticles could produce antibody-antigens ,anti-aging components for skin protection. Reaction, which further amplify the signal in immuno-assay [12].

Gold Nanoparticles

Gold Nanoparticles are small nano particles with a diameter of 1 to 100 nm which, once dispersed in water are also known as colloid gold. [13]

Nanoparticles are nanometres in size. Plasmon band depends upon their size. The surface these are 100 to 1000 times smaller than human cells. Plasmon resonance shows at 520 nm. The size of Gold is used internally in human from last 50 years due to conjugated gold nanoparticles depends upon thiol/gold their chemical inertness. The size of gold nanoparticles ratio. If the amount of thiol (SH) is high then the can be controlled during their synthesis and particle size will be small. Crystal structure of thiol functionalization with different groups.

The size of gold nanoparticles ratio. If the amount of thiol (SH) is high then the could be controlled during their preparation and particle size will be small. Crystal structure of thiol functionalization with different groups. Gold nanopaticles monolayer protected gold nanoparticles contain accumulate in the tumour cells and show optical 102 gold atoms and 44 p-mercaptobenzoic acid units ([13-14]).

Characteristics of Gold Nanoparticles

1. Optical characterstic like Plasmon resonance are depicted by gold nanoparticles.
2. These exhibit versatility because of their high functionalization through thiol linkages.
3. Gold nanoparticles provide microscopic probes for the study required in cancer cell.
4. Gold nanoparticles deposit in the cancerous cell and describe the cytotoxic effect i.e. a necrosis of the specific cell and cell specific receptors.
5. These show high greatest stability because of their gold-sulphur bonds.
6. Their photo physical properties can be exploited because drug release at remote place.([14- 17]).

Types of Gold Nanoparticles: [18]

Gold Nanorods: These are synthesized by template method. They are prepared by electrochemical deposition of gold metal within the pores of nonporous polycarbonate template membranes. Gold nanorods diameter is same as compare to the diameter of pore of the template membrane.

Gold Nanoshell: Surface Plasmon resonance peaks (ranging from visible to near I.R. region). It is used for the designing and fabrication of gold nanoshells. The inert core of gold nanoshell is the development of silica and outer surface is manufactured by gold. It controls the thickness of the shell.

Gold Nanocages: Through galvanic replacement reaction between truncated silver Nanocages and aqueous HAuCl gold nanocages are manufactured.

Gold Nanospheres: These are synthesized by the reduction **of** an aqueous HAuCl by 4 using citrate as reducing agent. Through citrates / gold ratio are the sizes of nanospheres can be controlled. By two-

phase ratio, the size of nanospheres can be affected by thiol / gold molar ratios

SERS Nanoparticles: SERS is an optical technique like Optical properties, plasmon resonances are fluorescence and chemiluminescence which exhibited by gold nanoparticles. Sensitivity, high levels of multiplexing, robustness and greater performance in biological membrane.

Methods of Preparation of Gold Nanoparticle

Chemical Methods

In chemical methods AuNPs are produced by reduction of Hydrochloroauric acid (HAuCl4), using some sort of stabilizing agent. After dissolving HAuCl4, the solution is continuously stirred while a reducing agent is added. These causes Au3+ ions will become neutral gold ions.

i) Turkevich method: Generally, it is used for producing monodispersed spherical AuNPs suspended in water with 10–20 nm in diameter. Larger particles can also prepared but this comes at the cost of monodispersed. It consist of the reaction of small amounts of hot HAuCl4 in the presence of reducing agents like citrate, amino acids, ascorbic acid or UV light. The colloidal gold will be formed because the citrate ions act as both as reducing agent, and a capping agent. For produceing larger particles, sodium citrate amount should be less, possibly down to 0.05%, after which ,so they not able to reduce all the gold. The reduction in the concentration of sodium citrate will reduce the concentration of the citrate ions in solution, which will stabilizing the particles, therefore it will cause the small particles to aggregate into larger ones, until the total surface area of all particles produces small enough to be covered by the existing citrate ions .([19-21])

ii) Burst and Schiffrin Method: Discovered by Brust and Schiffrin in early 1990s, and gold nano particle dissolved in organic liquids that is not miscible with water (like toluene). It reduces HAuCl4 solution with tetra octylammonium bromide (TOAB) solution in toluene and sodium borohydride (NaBH4) as an anti-coagulant and areducing agent, respectively. The AuNPs will be 2 to 6 nm in diameter. NaBH4 is the reducing agent, and TOAB they are both the phase transfer catalyst and the stabilizing agent. TheBrust method which is two-phase synthesis and stabilization with thiol, published. After then gold is reduced using NaBH4 in presence of analkanethiol. The alkanethiols stabilize the AuNPs, resulting in a color change from orange to brown. Purification of AuNPs should be stabilized with dodecanethiol from TOAB was reported by Schriffin. [22, 23, 26]

iii) Seeded Growth Method: The Turkevich and Brust methods develop spherical AuNPs, but in Seeded growth method AuNPs can also exist in various of nanostructures such as rods cubes, tubes. The most widely used technique to obtain AuNPs is better obtained by seeded mediated growth.The basic principle of this technique is to first produce seed particles by reducing gold salts with a strong reducing agent such NaBH4. The seed particles added to a solution of metal salt in presence of a weak reducing agent (ascorbic acid) and structure directing subdtances usually added to prevent further nucleation and accelerate the anisotropic growth of AuNPs. Geometry of AuNPs can be changed by reducing agents, structure directing agents and varying the concentration of seeds. ([23-27]).

Physical Methods

γ- Irradiation method was proved the best method for the synthesis of AuNPs with controllable size and high purity. The γ-irradiation method is accepted to synthesize AuNPs with size 2- 40 nm. In this method natural polysaccharide alginate solution was used as stabilizer. Some scientist gave the single γ-irradiation method to synthesized AuNPs of size 2 - 7 nm by using bovine serum albumin protein as stabilizer various physical technique such as ultrasonic waves microwaves, laser ablation, solvothermal method, electrochemical and photochemical reduction is available in literature for AuNPs synthesis. ([27-33])

Biological Methods

The development of eco-friendly technologies in AuNPs synthesis is of contumacious importance to expand their biological applications. AuNPs with well-known size, shape, chemical composition and organoliptic properties have been synthesized by using various microorganisms, and their properties in many medical and technological areas have been searched The biosynthesis of gold nanoparticles by microbes is thought to be safe, clean, nontoxic, and environmentally acceptable eco friendly procedures.The use of microbes for AuNPs synthesis consisting of bacteria, fungi, yeast, and actinomycetes can be classified as intracellular and extracellular synthesis according to the location where AuNPs are formed. ([34])

Biosynthesis of Gold Nanoparticles Using Microorganisms

Biosynthesis is based on the biological species and inorganic molecules interact with each other.

(i) Biosynthesis of Gold NPs using Fungus: Fungi can secrete various secondary metabolites and enzymes that are used in the laboratory. Fungi can secrete large amount of enzymes and they have

high metal tolerance capability . Fungi also take up the metals intra-cellularly. The most commonly used group of fungi for the biosynthesis of gold NP- Actinomycetes (because they are an intermediate to both the prokaryotes and fungi).

Thermomonospora are the species of fungi to produce gold NP with the Actinomycetes cells. Another Actinomycete, Rhodococcus when exposed to AuCl4-, reduces the gold ions to produce monodispersed. Using Rhodococcus species are an example of actinomycetes fungi shows an optimum growth at 27℃ and pH=7. They GNPs intracellularly i.e within the actinomycetes cells, on the cytoplasmic membrane. ([35])

(ii)Biosynthesis of Gold NPS using Algae: Using Sargassum wightii Greville, a marine alga: Sargassum wightii is the first ever algae have to produce very stable gold NP. The stability of the NP produced makes these algae an agile candidate for the NP production. Isolate the Sargassum wightii greville from the habitat clean then and shade them in dry for 3-5 days, powder the products using pestle mortar, take 1 g sea weed powder in a 5oo ml flask with 1ooml 10^{-3} M eq HuACl solution and bioreduction process is completed in 12 hours. Now coat the AuNP with carbon coated copper .its analysis is done with TEM and SEM.

(iii) Biosynthesis of Gold Nanoparticle Using Yeast: Using C. albicans: HAuCl4 (Chloroauric acid), horseradish peroxidase-conjugated antirabbit IgG, 3,3′- diaminobenzidine tetrahydrochloride, Tween 20 and diethyl nitrosamine are used as chemicals. The cytosolic extract was isolated from C. albicans [culture the cells on YEDP agar plates harvest and homogenize the cell culture after 24 h in a protease inhibitor cocktail sonicator , then vortex the homogenate with subsequent cooling pellet . product is carried out and collect the supernatant]. Take different volumes of the cytosolic extract and add into 5 ml of solution with 10−3 M aqueous HAuCl4. Make the volume up to 10ml and incubate the solution for 24 h until the reaction is completed. The gold NP thus formed was identified by ultraviolet-visible spectroscopy; transmission electron microscopy, atomic force microscopy, and Fourier transform infrared analyses.

(iv) Biosynthesis of Gold NPs using bacteria

a) Pseudomonas Aeruginosa: Two strains of Pseudomonas aeruginosa were taken and cultured in nutrient broths and agar plates. Strain-1 will produces pyoverdin, a soluble fluorescent pigment and the other strain-2 will produces pyocyanin, a blue pigment after being cultured on agar media. Standard strain of P. aeruginosa ATCC 90271 was used too. Grow the bacteria in a 50 mL nutrient broth under standard aerobic conditions and incubate at 37℃ and agitate at 150 rpm for 24 h. Now obtain the supernatant by centrifuge at 5000 rpm for 5 min. Mix HuACl with 50 ml of cell free supernatant so that final concentrate of AuNP is 1mp. Incubate the solution as well as control at 37 degree Celsius, now obtain the gold nanoparticles. ([37-38])

A) Synthesis of Gold Nanoparticles using plant extracts

Nanoparticles synthesise can be produced by various chemical and physical methods, but use of such methods are harmful in one or the other way. The photosynthesis of nanoparticles can be carried out by using as the intersection of nanotechnology and biotechnology. In developing country resources demands are increases fastly so we have to protect the environment and environmentally benign technologies in material synthesis, it has received increased attention. This has motivated the researchers to synthesis the nanoparticles using this route that allow better control of shape and size for various applications.

Synthesis of gold nanoparticles using plant extract is important not only because of its reduced environmental, but also because, it can be used to produce large quantities of gold nanoparticles. Plant extracts may act as duall in nature as well as reducing agents and stabilizing agents in the synthesis of nanoparticles.

The use of plant extract for reducing metal salts to nanoparticles has considerable seek attention within the last few decades. The properties of gold nanoparticle are different from that of bulk; the gold nanoparticles are wine red solution while the bulk gold is yellow solid. The gold nanoparticles are produced into a variety of shapes including nanorods, nanospheres, nanocages, nanostars, nanobelts and nanoprisms. The size and shape of gold nanoparticles shows their chemical and physical properties. The triangular shaped nanoparticles show elegant optical properties in comparison to spherical one. Due to their wide spread applications in targeted drug delivery, imaging, diagnosis and therapeutics due to very small size, high surface area, stability, non-cytotoxicity and tunable optical, physical and chemical properties, gold nanoparticles have revolutionised the field of medicine [39- 44].

Gold nanoparticles of size 5-100 nm were produced using buds of Syzygium aromaticum and the particles has the to be of crystalline nature. The flavonoids present in buds that is used for reduction of gold nanoparticles. Banana peels are a

extensively available example as a natural material. The peels of banana are usually removed. Some researchers used this waste material for the synthesis of nanoparticles.

The gold nanoparticles with average particle size of 300 nm were synthesised using banana peel extract and confirmed by different method. Mentha piperita extract was used to prepare spherical shaped gold nanoparticles with size around 150 nm and showed antimicrobial activities against Staphylococcus aureus and Escherichia coli. The extract of Madhuca longifolia for the reduction of the gold nanoparticles.

The synthesis of crystalline nature gold nanoparticles is a simple, inexpensive and ecofriendly biomethodologies using biomass of Suaeda monoica leaves was reported with particle size ranged from 3.89 to 25.83 nm with average particle size 16.805 nm. The plant leaves were used as a medicine for hepatitis and injury and show antiviral activity. The leaves were extract of Stevia rebaudiana for the reduction of gold ions to nanoparticles have produced and spherical shaped nanoparticles with size is from 5 to 20 nm have been synthesised .

The use of plant extracts for making metallic nanoparticles is inexpensive, easily measured and environmentally benign. The biological synthesis of gold nanoparticles can be extracted out by using the leaf of Coleus amboinicus and size of gold nanoparticles ranged from 4.6 to 55.1 nm. The spherical nanoparticles produced in the beginning of the reaction were stable due to they are protected by sufficient biomolecules. The gold nanoparticles with a particle size ranging from 5 to 15 nm were synthesised using Zingiber officinale extract they act as both as reducing and stabilizing agent. The extract of Pistacia integerrima that act both as reducing and stabilizing agent for the production of gold nanoparticles with particle size in range of 200nm. ([45])

Evaluation of Gold Nanoparticle [45-52]

a) Absorbance Spectroscopy: Spectroscopy is useful to characterize metal nano Absorbance Spectroscopy: Spectroscopy is useful to characterize metal nanoparticles, because they possess bright colour which is visible by naked eye. By this technique, qualitative information about the nanoparticle can be obtained.

By applying Beer's law absorbance can be measured:

1. Depending on path length.
2. Gold nanoparticle conc.
3. Extinction coefficient (A) can be measured.

b) Infrared Spectroscopy: This method can provide information on organic layers surrounding metallic nanoparticles such as gold nanoparticles and It also gives valuable information to understand surface structure of nanoparticle.

c) TEM: (Transmission electron microscope) is also widely used to characterize nonmaterial's to collect information about particle size, shape, crystallinity and interparticle interaction. TEM is a high spatial resolution structural and chemical characterization machine. It has the capability to directly image atoms in crystalline structure at resolutions close to 0.1nm, smaller than interatomic distance. An electron beam can also be focused to a diameter smaller than ~0.3nm, allowing.

d) SEM: (Scanning Electron Microscopy) It is a powerful technique for imaging any material surface with a low resolution of 1nm. The interaction of an incident electron beam with the substances produces secondary electrons, with energies smaller than 50ev.it can give the information about the purity of gold nanoparticles sample.

e) AFM: (Atomic force microscopy) It is a better option for nonconductive gold nanoparticle. Typically, it has vertical resolution of less than 0.1nm and lateral resolution of around 1nm.It gives detailed information on the atomic scale, which is important for understanding electronic structure and chemical bonding of atoms and molecules.

f) XRD: X-rays Diffraction, It is useful and widely used toll for determining the crystal structures of crystalline materials. Diffraction line widths are closely related to the size and their portion, strain in nanocrystal. The line width is broadened, as the size of the nanocrystal decreases, due to loss of long range order relative to the bulk. XRD line can be used to determine the particle size by Debye-Scherrer method.

$D = 0.9\lambda / b\cos\Theta$ Where, D= nanocrystal diameter

λ=light wavelength

b=full width half at max. Of the peak (radians)

Θ=Bragg angle

g) FTIR: (Fourier–transformer infrared spectroscopy) it is widely acceptable techniques compared to IR spectroscopy. Functional groups attached to the gold nanoparticle show variant FTIR pattern than those of different free group.

h) EXAFS: (Extended X-ray Absorption Fine Structure) It is one of the most reliable and powerful characterization toll to evaluate the structure of gold nanoparticles; especially it is useful to determine bimetallic nanoparticles. To collect appropriate information about the structure, the sample of metallic nanoparticles should be homogeneous. This method provides the no. Of

atoms surrounded by the x-ray absorbing .and their interatomic distance in the shell.

i) XPS: (X-ray Photoelectron Spectroscopy) it is used to give information on metal state. For eg. the oxidation state of metal on the surface. It is often oxidized by air. So, by using this technique 0 valence of surface of gold metal is confirmed.

APPLICATION OF GOLD NANOPARTICLE

Application in Bionanotechnology

a) Sensing: AuNPs are readily conjugated with specific moieties such as antibodies or oligonucleotides for the identification of target biomolecules, allowing in vitro identification and diagnostics applications for cancerous diseases.

As an example, AuNPs play a critical role in the "bio-barcode assay", an ultrasensitive technique for detecting target proteins and nucleic acids. The principle of the "bio-barcode assay" utilizes alternative AuNPs with both barcode oligonucleotides and target-specific antibodies, and magnetic microparticles (MMPs) effective with monoclonal antibodies for the target moiety. These complexes produce a mixed complex upon detection of the target molecule that releases a large amount of barcode oligonucleotides, providing both identification and quantification of the target. As an example of the specificity of this method, have demonstrated the detection of prostate specific antigen (PSA) using this methodology with a limit of detection of 330 fg/ml. ([53-54]).

b) Therapeutics: The transport of therapeutic agents to the cells by AuNPs is a sensitive process in biomedical treatment. Several research groups have used functionalized AuNPs to interrogate the interactions with cell membrane to improve delivery efficiency. For example, Stellacci et al. have demonstrated that surface ligand arrangement on AuNPs can enhance cell membrane penetration. AuNPs effective with an ordered arrangement of amphiphilic molecules will penetrate into the cell membrane while AuNPs coated with a random arrangement of these same molecules were trapped in vesicular bodies.

AuNP therapeutics can be administered into cells by various mechanisms either by passive or active targeting mechanisms. Passive targeting is based on the enhanced permeability and retention (EPR) effect where the AuNPs will accumulate on the tumor via its discontinuous vasculature, allowing larger particles to pass through the endothelium. Active-targeting act on a surface functional ligand arranged designed for the target analyte to provide specificity and selectivity. Effective targeting and delivery strategies required AuNPs have been developed for therapeutic applications including photothermal therapy, genetic regulation, and drug treatment. ([55-59])

c) **Imaging:** The various optical and electronic properties of AuNPs have been used for cell imaging using various techniques, including computed tomography (CT), dark-field light scattering, optical coherence tomography (OCT), photothermal heterodyne imaging technique and Raman spectroscopy. For example, AuNPs serve as a specific agents for CT imaging based on the higher atomic number and electron density of gold (79 and 19.32 g/cm3) as compared to the recently used iodine (53 and 4.9 g/cm3). Hainfeld et al. have demonstrated the feasibility of AuNPs to enhance the in vivo vascular important in CT imaging, and Kopelman et al. further designed immuno-targeted AuNPs to selectively target tumor specific antigens.([59-60])

In vitro diagnostic assay:

Oligonucleotides-capped AuNPs used with polynucleotide or protein such as p53, which is a tumor suppressor gene replacing using various checked /characterization methods such as atomic force microscopy, gel electrophoresis, chronocoulometry, amplified voltammetric detection, SPR imaging, scanometric assay, and Raman spectroscop. In some reports, very small quantity like picomolar or femtomolar concentrations of DNA targets has been targeted. DNA-based adsorbate molecules had been tested, which is based on the SERS signals that vary independently in intensity as a function of the distance from the gold nanoshell surface. (61-69)

Gold nanoparticles as Biomolecule and drug delivery vehicles

AuNPs have been used in exploratory drug delivery applications due to the following properties:

(i) The high surface area of nanoparticles provides sites specific drug loading and enhances solubility and stability of loaded drugs.
(ii) The biological function of nanoparticles with targeting ligands to enhance therapeutic potency, decrease side effects and improve solubility.
(iii) They have advantage of multivalent interactions with cell surface receptors or other biomolecules.
(iv) Enhanced ADME and tumor tissue deposition as compared to free drugs, and
(v) Biological selectivity which allows nanoscale drugs to preferentially accumulate at tumor sites due to their ''leaky'' blood vessels and it is called enhanced permeability and retention (EPR) effect. ([70])

Delivery of Pharamceutical Agent via Direct conjugation with AuNPs

Curcumin having number of therapeutic characterstic treating neurodegenerative disease like Parkinsonism and Alzheimer disease, anticancer agent, and their antioxidant properties play pivotal role for modifying therapeutic efficiency. Poddar P. et. al. produced functionalized AuNPs with curcumin and test the antioxidant characteristic of curcumin by the simple reduction of Au3+ ions required curcumin in an aqueous phase. This type of conjugation states that enhance the solubility and availability of curcumin with potential antioxidant activity. Theoretical outcomes of the study also propose that due to loosing of intermolecular H-bonding that increased availability of curcumin in the presence of Au ions and water molecules. ([71])

Delivery of Pharamceutical Anticancer agent via Surface modification

Several studies have reported the use of AuNPs as drug delivery vehicles. In addition to produce surface modification and their large surface-to-volume ratio, AuNPs also contain a number of different properties that can be used in drug delivery applications. AuNPs have been altered with many to a variety of antitumor drugs, including paclitaxel, cisplatin, camptothecin, doxorubicin, curcumin and others. The antitumor substances added with AuNPs, together with the method of functionalization or surface modification is reported by which stated that universal effort and open challenges in the research to defeat cancer.

Functionalization and surface modifications of AuNPs for biomedical resarch start work initially conducted by Nuzzo and White sides on the production of self assembled monolayer (SAMs) of molecules on planar.

Gold and later by Murray in searching the alternative and conformations of such concepts by electrochemical, scanning probe, and mass spectrometric methods. A rich variety of functional molecular linkers are currently employed in addition of AuNPs used in biomedical applications; however, these groups used for attachment of these molecules to the gold surface generally include: thiolate. AuNPs are interacting strongly with lipid membrane. AuNPs -loaded liposomes application in liposomal drug delivery systems having more advantage as compared to conventional liposomal drug administration.

Table: Common functionalization methods of AuNPs and their applications:

Ligands/Carrier Molecule functional group	**Key Feature**	**Application**	**References**
Polyvinyl pyrolidone (PVP)	PVP binds strongly to the AuNP surface	Improve Bioavailability of lipophilic drugs	71
Polyethylene Glycol (PEG) attached through thiol group	Adherence to the cell membrane	Cellular and intracellular targeting, biodistribution studies	**72**
Amine Group	siRNA Carrier	Useful in RNAi technology	**73**
PEG Proteins, Carboxyl group as functional group	Glutamic acid as a reducing agent	Cellular and intracellular targeting, Bioaimaging of cancer cells	**71-75**
Peptide Cell surface receptors	Cytoplasmic and nuclear translocation	Cellular and intracellular targeting, Bioaimaging of cancer cells	**76**
Antibodies	Smaller size, label fidelit	Immunoassays and diagnosis e.g.- antibodies	**77-78**

Delivery of gene

As we have shown, drug delivery systems based on AuNPs they provide various opportunities to improve the solubility, optimal bio-distribution, in vivo stability, and ADME or pharmacokinetics of drugs. On the other hand AuNP can also be used to carry nucleic acids. Nucleic acids are used to treat and control diseases are termed ‘gene therapy’. This type of therapy can be carried out by using viral and non-viral vectors to transport foreign genes into somatic cells to treat defective genes or provide additional biological functions and also its repairing. The use of viruses as a vehicle for gene therapy is now well known, however, viral vectors have disadvantages such as the stimulate of an immune response, irregular cytotoxicity, limitations in targeting specific cell types, low DNA carrying capacity, lack of ability to infect

non-dividing cells, and diffculites in process and packaging. AuNPs have long been studies as alternative nonviral vectors and attracted a great interest as non-viral gene delivery because of their unique properties. [79]

Delivery of proteins and peptides

The several of protein-nanoparticle conjugates are the bioactivity of the protein. The protein activity of the AuNP preparation can thus be increased, which is of great influence in the study on the interface of protein utilized for enzyme immobilization, drug delivery, and biocatalysis.. AuNPs can be used as nanocarriers for peptides and proteins. Delivery of functional proteins inside living cells has been limited approach due to their poor permeability through the cell membrane. Stability of the protein against digestion by enzymes having another challenge for delivery. Potentially, AuNPs with engineered monolayer are able to overcome these errors. Whereas non covalent addition with AuNP can retain the structure and activity of the protein, but covalent approaches have also been applied without altering the protein's activity.

Nanoscale phenomenon mediated by AuNPs was developed, in that co-administration with AuNPs with percutaneous delivery of protein drugs. The AuNPs with a mean size of 5 nm revealed to be penetrate into the skin permeability due to the bio-interaction with skin lipids and the consequent overlapping openings into the skin layer i.e. stratum corneum, when simultaneously applied with AuNPs, the protein drugs also granted the ability to penetrate the barrier and dissolve deep into the layers of skin. This indicated that co-administration of skin-permeable AuNPs could mediate proteins across the barrier of skin. ([80-85])

Future prospective

Gold nanoparticles are one of the most elegant nanomaterials for various applications like antimicrobial, electronic, catalytic, and various biomedical applications. The present review theory literature for understanding of synthesis of gold nanoparticles using plant extracts. Synthesis of gold nanoparticles using plant extract is useful not only because of its reduced environmental, but also because it can be used to synthesize large quantities of nanoparticles. Plant extracts used as reducing agents and stabilizing agents in the synthesis of nanoparticles.

Synthesis of gold nanoparticles using plant extracts over the other physical methods as it is safe, eco-friendly and simple to use. Plants have large potential for the assembly of gold nanoparticles of wide potential of applications with desired shape and size. A detailed study is needed to give a brief mechanism of biosynthesis of gold nanoparticles using biomacromolecules present in different plant extracts which will be valuable to improve the properties of gold nanoparticles. ([86-92])

Conclusion

AuNPs have multiple contributions that make them potent tools for the use in bionanotechnology. There are various types of gold nano particle like gold nanoshell, nano tubes and nanorods which can be used in imaging, conjugation, therapeutic and in gene drug delivery and protein for transferring in gene and gene therapy. They can be produced by multiple methods like physical methods chemical, microbiological and by plant extract also. The wide range of surface functionality and bioconjugates coupled with the outstanding physical properties of AuNPs make these system smore potentional for imaging applications. Moreover, the creation of highly sensitive and selective diagnostic system for target impurities can be achieved by engineering their surface monolayer. AuNP-based delivery vectors have effective function in therapeutics with their high surface loading of drug and gene as well as the controllable release of the payloads. Taken together, AuNPs are incredibly versatile materials, auxiliary for next - generation in bio medical applications.

REFERENCES

1. Jain PK et al. M.A tration by the citrate reduction method. The optimal (2006) Calculated absorption and scattering properties of gold nanoparticles of different size, shape, and composition: gold salt concentration, trisodium citrate concen-application in biological imaging and biomedicine. J Phys Chem 2006; 110: 7238-7248.
2. Daniel MC and Astruc D. Gold nanoparticles: and shape of synthesized gold nanoparticles were Assembly, supramolecular chemistry, quantum-size-related characterized using transmission electron microscopy, properties and applications toward biology, catalysis, and nanotechnology. Chem Rev 2004 ; 104: 293-346.
3. Sardar R et al. gold nanoparticle of 15-20 nm (18 nm) size were Gold Nanoparticles: Past, Present, and Future. obtained. Narrow size distribution and small monosize Langmuir 2009; 25: 13840-13851.
4. Freudenberg's et al. Reduction : The third role of citrate. Recent development , in the preparation of goldnano composite coatings. J Am Chem. Socand 2010; 129:13939-13948.

5. Jans H et al. Growth by citrate reduction of HAuCl. Poly (acrylic acid)-stabilized colloidal gold Technol. Adv Powder 4Q 2010; 21: 111-118.
6. Li DX et al. Monodispersity and shape of gold nanoparticles formed by Hierarchicalgold /copolymernano-structures as the Turkevich method. New J Chem 2010; 20.7782.
7. Buche V et al. Printed gold for electronic applications. Gold Bull 2010; 43: 181.
8. Wallace WT et al. Fabrication of Macroscopic and Oon selected gold clusters: Evidence for efficient room-Freestanding Films of Metallic Nano-particle Monolayer's temperature CO generation. J Am Chem Soc 2002; 124: 7499.
9. Zhou XC et al. The particle size in monodisperse gold suspensions. Nat. Size-Dependent Catalytic Activity and Dynamics of Phys Sci 2014; 241: 20-22.
10. Turkevich J et al. A study nanoparticles at room temperature: The case of pH values of the nucleation and growth processes in the synthesis of Colloid Surf. A- Physicochem Eng Asp 1951; 301: 174.
11. Richars GD. Preparation of colloidal gold particles Correlation between the composition of multivalent of various sizes using sodium borohydride and sodium antibody conjugates with colloidal gold nanoparticles and cyanoborohydride. Anal Bio chem 1996; 23: 168-170.
12. Bhattacharya S, Srivastava A. Synthesis of gold nanoparticles stabilized by metal-chelator and the controlled formation of close-packed aggregates by them. Proc Indian acad Sci (Chem. Sci.) 2003; 115: 613-619.
13. Sayed E et al. Selective laser photo-thermal therapy of epithelial carcinoma using anti-EGFR antibody conjugated gold nanoparticles. Cancer Letter 2006; 2: 129-135.
14. Alvarez MM et al. Optical absorption spectra of Nanocrystal gold molecules Phys Chem 1997; 101: 3706-3712.
15. Connor EE et al. Gold nanoparticles are taken up by human cells but do not cause acute cytotoxicity. Small 2005;1: 325-327.
16. Chah S et al. Gold nanoparticles as a colorimetric sensor for V.M. Rotello, Chem Biol 2004; 12: 323-328.
17. Cai w et al. Application of gold nano particles in cancer nanotechnology ,science and application 2008;1:17-32.
18. Jadzinsky PD et al. Structure of a Thiol Monolayer-Protected Gold Nanoparticle at 1.1 Å Resolution. Science 2007; 318: 430-433.
19. Turkevich J et al. A study of the nucleation and growth processes in the synthesis of colloidal gold. Discussions of the Faraday Society 1951;11: 55-75.
20. Ji X et al. Sizem Control of Gold Nanocrystals in Citrate Reduction: The Third Role of Citrate. J American Chem Soc 2007;129: 13939-13948.
21. Kumar S et al. Modeling of Formation of Gold Nanoparticles by Citrate Method, Industrial & Engineering Chemistry Research 2007;46:3128-3136.
22. Gangwar R K et al. Conjugation of curcumin with PVP capped gold nanoparticles for improving bioavailability. Materials Science and Engineering: C 2012; 32: 2659-2663.
23. Giersig M , Mulvaney P, Preparation of ordered colloid monolayers by electrophoretic deposition, Langmuir : the ACS journal of surfaces and colloids 1993;9: 3408- 3413.
24. Faraday M , The Bakerian Lecture: Experimental Relations of Gold (and Other Metals) to Light, Philosophical Transactions of the Royal Society of London 1857;147:145-181.
25. Waters C A et al. Purification of dodecanethiol derivatised gold nanoparticles. Chemical Communications 2003; 540- 541.
26. Shao L et al. Plasmonic Properties of Single Multispiked Gold Nanostars: Correlating Modeling with Experiments, Langmuir : the ACS journal of surfaces and colloids 2012;28: 8979-8984.
27. Sau TK , Murphy CJ. Room Temperature, High-Yield Synthesis of Multiple Shapes of Gold Nanoparticles in Aqueous Solution, Journal of the American Chemical Society 2004;126: 8648-8649.
28. Gole A, Murphy CJ, Seed-Mediated Synthesis of Gold Nanorods: Role of the Size and Nature of the Seed, Chemistry of Materials 2004; 16: 3633-3640.
29. Tue Anh N et al. Synthesis of alginate stabilized gold nanoparticles by γ-irradiation with controllable size using different Au3+ concentration and seed particles enlargement, Radiation Physics and Chemistry 2010;79: 405-408.
30. Akhavan A et al. Radiation synthesis and characterization of protein stabilized gold nanoparticles, Chemical Engineering Journal 2010; 159:230-235.
31. Radziuk D et al. Ultrasound-Assisted Fusion of Preformed Gold Nanoparticles, The Journal of Physical Chemistry C 2010;114:1835-1843.
32. Liu YC et al. Size-Controlled Synthesis of Gold Nanoparticles from Bulk Gold Substrates by Sonoelectrochemical Methods. J Phy Chem B 2004; 108: 19237-19240.
33. Lee JH et al. Production of aqueous spherical gold nanoparticles using conventional ultrasonic bath. Nanoscale Res Lett 2012;7: 420.

34. Gutierrez W et al. Microwaveassisted synthesis of gold nanoparticles self-assembled into self-supported superstructures, Nanoscale 2012; 4: 2281-2287.
35. Fleming DA, Williams ME. Size-Controlled Synthesis of Gold Nanoparticles via High-Temperature Reduction, Langmuir. ACS J surfaces and colloids 2004; 20: 3021-3023.
36. Sheikhloo Z et al. Biological Synthesis of Gold Nanoparticles by Fungus Epicoccum Nigrum. J Cluster Sci 2011; 22: 661.
37. Sunkar S, Nahciyar V. Facile route to the synthesis of silver nanoparticles by the endophytic fungus Alternaria sp. Asian J Microbiol Biotechnol Environ Sci 2013; 15: 495.
38. Sunkar S ,Nahciyar V. Endophytic fungi mediated extracellular silver nanoparticles as effective antibacterial agents. Int J Pharma Pharmaceutical Sci 2013; 5: 95.
39. Buchanan RE, Gibbons NE . Bergey's Manual of Systemic Bacteriology, 9th ed., Williams and Wilkins Co1984: 141–1991.
40. Sabella S et al. Aunps are toxic in vitro and in vivo: a review. J Nanosci Lett 2011; 1: 145-165.
41. Jayaseelan *C* et al. *Green* synthesis of gold nanoparticles using seed aqueous extract of Abelmoschus esculentus and its antifungal activity. Ind Crop Prod 2013; 45: 423-429.
42. Shankar SS et al. Bioreduction of chloroaurate ions by geranium leaves and its endophytic fungus yields gold nanoparticles of different shapes. J Mater Chem 2003;13: 1822.
43. Raghunandan D et al. Rapid biosynthesis of irregular shaped gold nanoparticles from macerated aqueous extracellular dried clove buds (Syzygium aromaticum) solution. Colloids Surfaces B Biointerfaces 2010; 79: 235-240.
44. Bankar A et al. Banana peel extract mediated synthesis of gold nanoparticles. Colloids Surfaces B Biointerfaces 2014; 80: 45-50.
45. MubarakAli D et al. Plant extract mediated synthesis of silver and gold nanoparticles and its antibacterial activity against clinically isolated pathogens. Colloids Surfaces B Biointerfaces 2014; 85: 360-365.
46. Mohammed FA et al. Biosynthesis of anisotropic gold nanoparticles using Maduca longifolia extract and their potential in infrared absorption. Colloids Surfaces B Biointerfaces 2011; 88: 287-291.
47. Daniel MC, Astruc D. Gold nanoparticles: assembly, supramolecular chemistry, quantum-size-related properties, and applications toward biology, catalysis, and nanotechnology. Chemical reviews 2014; 104(1): 293346.
48. Sekar RP. Formulation and evaluation of azathioprine loaded silver nanopartilces for the treatment of rheumatoid arthritis. Asian J Biomedical and Pharmaceutical Sciences 2013; 3: 28.
49. Li X et al. Three-dimensional orientation unlimited polarization encryption by a single optically configured vectorial beam. Nature communications 2013; 3: 998-4.
50. Weindling P .Epidemics and genocide in Eastern Europe, 18901945. Oxford University Press, USA.
51. Apostolou P et al. Anvirzel™ in combination with cisplatin in breast, colon, lung, prostate, melanoma and pancreatic cancer cell lines. BMC Pharmacology and Toxicology 2013; 14: 18.
52. Akbar Vet al. Gold nanoparticles for biomedical applications. Young Researcher Club. Islamic Azad University, Ardabil, Iran. Science and Researcher Branch 2014.
53. Li C et al. High-Yield Synthesis of Single-Crystalline Gold Nano-octahedral. 2007.
54. Huo Q al et. J Nanobiotech 2011; 9:20.
55. Bogdanovic J et al. Biochem 2010; 405:96–102.
56. Fang S-B et al. J Microbial Meth 2009; 77:225–228.
57. Laderman EI et al.Vaccine Immunol 2008; 15:159–163.
58. Nam JM et al. J Am Chem Soc 2002; 124:3820–3821.
59. Nam JM et al. Science, 2003; 301:1884–1886.
60. Zhang J et al. Small 2010; 6:201–204.
61. Medley CD et al . Anal Chem 2008; 80:1067–1072.
62. Liu G et al . Anal Chem 2009; 81:10013–10018.
63. Bunz UHF, Rotello VM. Angew Chem Int Edit 2010; 49:3268–3279.
64. Miranda OR et al. Curr Opin Chem Bio 2010; 14:728–736.
65. De M et al. Nat Chem 2009; 1:461–465.
66. Qian W et al. J Biomed Opt 2010; 15:058002.
67. Kim CS et al . J Biomed 2009; 14:034008.
68. Zagaynova EV et al. Phys Med Biol 2008; 53:4995–5009.
69. Leduc C et al . ACS Nano 2011; 5:2587–2592.
70. Berciaud S et al. Phys Rev Lett 2004; 93:257402.
71. Zavaleta CL et al. Proc Natl Acad Sci 2009; 106:13511–13516.
72. Keren S et al .Proc Natl Acad Sci 2008; 105:5844–5849.
73. Alric C et al. J Am Chem Soc 2008; 130:5908–5915.

74. Cao YC et al, Nanoparticles with Raman spectroscopic fingerprints for DNA and RNA detection . Science 2002; 297: 1536-1540.
75. Qin WJ, Yung LY. Nanoparticle-based detection and quantification of DNA with single nucleotide polymorphism (SNP) discrimination selectivity, Nucleic acids research 2007; 35.
76. Zhang J et al . A gold nanoparticle-based chronocoulometric DNA sensor for amplified detection of DNA. Nature protocols 2007; 2888-2895.
77. Chen J et al. Immuno gold nanocages with tailored optical properties for targeted photothermal destruction of cancer cells. Nano letters 2007; 7: 1318-1322.
78. Li ZB et al. Semiconductor quantum dots for in vivo imaging. J nanoscience and nanotechnology 2007; 7: 2567-2581.
79. Lal S et al. Profiling the Near Field of a Plasmonic Nanoparticle with Raman-Based Molecular Rulers. Nano letters 2006; 6: 2338-2343.
80. Iyer et al. Exploiting the enhanced permeability and retention effect for tumor targeting. Drug discovery today 2006; 11: 812-818.
81. Singh DK et al. In situ synthesis and surface functionalization of gold nanoparticles with curcumin and their antioxidant properties: an experimental and density functional theory investigation. Nanoscale 2013; 5: 1882-1893.
82. Gangwar RK et al. Conjugation of curcumin with PVP capped gold nanoparticles for improving bioavailability. Materials Science and Engineering: C 2012;32: 2659-2663.
83. Cho WS et al. Sizedependent tissue kinetics of PEG-coated gold nanoparticles. Toxicology and applied pharmacology 2010;245: 116-123.
84. Sun L et al. Functional gold nanoparticlepeptide complexes as cell-targeting agents, Langmuir. The ACS J surfaces and colloids 2008; 24: 10293-10297.
85. Tkachenko AG et al. Cellular trajectories of peptide-modified gold particle complexes: comparison of nuclear localization signals and peptide transduction domains. Bioconjugate chemistry 2004; 15:482-490.
86. Sharma A et al. Antibody immobilized cysteamine functionalized-gold nanoparticles for aflatoxin detection. Thin Solid Films 2010;159: 1213-1218.
87. Liu Yet al. Single chain fragment variable recombinant antibody functionalized gold nanoparticles for a highly sensitive colorimetric immunoassay. Biosensors & bioelectronics 2009; 24: 2853-2857.
88. Kim JH et al. A functionalized gold nanoparticles assisted universal carrier for antisense DNA, Chemical communications (Cambridge, England) 2010; 46: 41514153.
89. Pissuwan D et al. The forthcoming applications of gold nanoparticles in drug and gene delivery systems. J Controlled Release 201;149: 65-71.
90. Ghosh P et al. Gold nanoparticles in delivery applications, Advanced drug delivery reviews, 2008; 60: 1307-1315.
91. Rana S et al Monolayer coated gold nanoparticles for delivery applications, Advanced drug delivery reviews 2012; 64: 200-216.
92. Liu F et al . Modulating the activity of protein conjugated to gold nanoparticles by site-directed orientation and surface density of bound protein. ACS applied materials & interfaces 2015; 7: 3717-3724.