IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

A Comprehensive Overview Of Recent Improvements In Gold Nanoparticles (Aunps): Properties, Shapes, Methods, And Characterization

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ABSTRACT

Currently, nanotechnology is the most promising leading potential area and scientific in modern key skill growth the humanity. Current years have shown great progress and significant roles in the study and proposal of nonmaterial in the development of nanotechnology, biomedical, nanoscience, and biological applications. The Nano word is originated from word of Greek "Nano'' which intended for small and uses a prefix for one billion parts. Nanoparticles are those which have in size range is 1-100nm and two and more than two dimensions. They have various shapes and sizes that can be simply synthesized by adjusting the concentration and components such as cage-like, rod-like, and other various types of shapes. Various studies of gold nanoparticles have studied fictionalization among various bimolecular, like as targeting ligands, genes, peptides, and other drugs. They conjugate among antibiotics or drugs and show enhanced antiviral or antibacterial activity as compared to alone antibiotics or drugs. electronic and optical properties it is widely used in the color-indicating probes in the growth of analytical techniques whichever is applicable for the sensing of different analytes. Thus, this article aims to spotlight the gold nanoparticles, various methods of preparation, characterization techniques, and also focus on the properties. The methods that will be used to prepare gold nanoparticles are Physical Chemical and Biological. Evaluation parameters will include U.V, DSC, DLS, FTIR, TEM, SEM, Zetasizer, and Invivo &Invitro respectively.

Keywords: Gold Nanoparticles, Synthesis, Nanomaterial, Analysis, Target, Plants, Plants, Physical, Bacteria.

1. INTRODUCTION

In recent years, there has been tremendous progress and significance in the research and proposal of nonmaterial in the development of nanotechnology, biomedical, nanoscience, and biological applications [1]. The term "Nano" is derived from the Greek word "Nano," which means "little," and is used as a prefix for one billion components. Nanoparticles are defined as having a size range of 1-100nm with two or more dimensions. Because of their adaptability, gold nanostructures are unquestionably the most widely generated in the field of nanomedicine and nanotechnology [2]. In the year 1857, Faraday and others initially discovered colloidal gold, which is any suspension or solution of gold nanoparticles in liquid, mostly water, descending gold chloride amid phosphorous and eliciting a concentrated red, blue, and purple tint of colloidal gold. The objective of a pharmacological dose is to strengthen the dynamic capacity of management and is limited by written and retained rights. Nanotechnologies in pharmacy, engineering, computer science, material science, biotechnology, and medicine, among other fields [1]. Nanoparticles are often encountered in amorphous and crystalline forms, with various applications and usage across the world. Because of their distinctive physiochemical qualities, they are employed in a variety of sectors, including optical devices, food, healthcare, synthetic biology, and cellular transportation [3]. Gold nanoparticles are distinguished by their stable nature, regulated geometry, and surface shape. Numerous of these are relevant in light harvesting assemblies, molecular switches, electronics, sensing, and data packing, as well as in the treatment of many illnesses, diagnosis, and detection. Quantization of electronic states and a greater surface-to-volume ratio are two physical factors responsible for the different features of nanomaterials in terms of chemical, mechanical, and thermal properties. A nanoscale structure has distinct physiochemical characteristics than microscopic molecules or bulk material. Gold nanoparticles are inorganic particles that have an inner core of gold atoms and a surface on a negative group. The surface is easily operationalized for active biomedical purposes, and the technique of synthesis is synthesized with a gold metal stabilizer, reductant, and other ingredients. The surface is effectively operationalized for active biomedical purposes, and using synthesized the method of preparation with a gold metal stabilizer, reductant, and precursor. This technology enables the perfect organization of electrical and optical characteristics that effectively depend on the size range of 1-100nm and various forms such as nanorods, nanospheres, nanocages, and the Nano shell of the generated gold nanoparticles [4]. All of the optical, electrical, catalytic, and magnetic characteristics of nanostructures are affected by their size and form, hence increasing emphasis is being placed on regulating size and shape. It was employed as a coloring's ingredient in ancient times because of its brilliant color, size, and concentration of different hues such as maroon, orange, ruby red, and yellow. A prominent example of glass ornamentation in churches is creature. Because nanoparticles have unique inherent reactivity, such as increased surface area, a suitable material for the creation of nanoparticle therapies would be developed. The contact will occur with biological systems and nonmaterial in different ways depending on the cell type, utilizing distinct targeting organelles or channels. Their specific features include: different electronic properties [5] tunable optical is unique unbreakable binding likeness to amines, disulfide, and thiol 2, synthetic manipulation is simple, and X-ray absorption coefficient is high, while different investigations have

been performed on the involves in anisotropic gold nanoparticles since the beginning of the twentieth century. The catalytic, structural, electrical, and magnetic properties of anisotropic gold nanoparticles differ from, and are typically larger than, those of globular gold nanoparticles [6]. Dimensions based on gold nanoparticles are classified into three types: I single-dimensional gold nanoparticles such as nanobelts, nanorods, nanowires, and nanotubes (ii) truncated triangles, stars, dimpled nanoplates, pentagons, hexagons, squares, and rectangles. (iii) Three-dimensional gold nanoparticles, such as gold nano dumbbells and gold nanotapoles, as well as branching gold nanoparticles, such as gold nano dendrites, Nanostars, and nanorods. Gold nanoparticles have been shown to be capable of multi-functionality since they may be used for medicinal and imaging purposes. These kinds of displays are made from various inorganic, organic, or hybrid inorganic and organic materials, although the inorganic are the most significant for simultaneous therapy and diagnosis. Because of their stability, drug loading capacity is large, and modification is simple [7].

1.1. Gold nanoparticles:

Gold nanoparticles come in a variety of sizes and forms, including octahedral, sub-octahedral, spherical, decahedral, multiple twined, icosahedral multiple, tetrahedral, irregular morphologies, nano prism, nanotriangle, nanorods, and hexagonal platelets. They transport a spectrum of big particles to tiny nanoparticles with diameters ranging from 1-100nm and are capable of crossing the cell membrane and cooperating with DNA [3]. They have a variety of forms and sizes that can be easily synthesized by altering the concentration and components such as cage-like, rod-like, and other shapes. Many research on gold nanoparticles have been conducted to investigate fictionalization among diverse bimolecular, such as targeting ligands, genes, peptides, and other medicines. They demonstrate improved antiviral or antibacterial activity when conjugated among antibiotics of medications when compared to antibiotics of drugs alone. Conjugation of gold nanoparticles amid bimolecular reduces bacterial cell development. It focuses on the electrical and optical characteristics, which are heavily influenced by their size and form [1]. Size, color, activity, and condition of matter are all physical qualities. Furthermore, gold nanoparticles differ from one another in form and clustering to offer a collection of various shapes, and morphologies impact optical characteristics. As a result, triangular nanoparticles have optical features that distinguish them from other forms in order to establish the medicinal application and purify the gold nanoparticles using plant extract. Therapeutically appropriate medications for anticancer target tumor cells to eliminate them by bimolecular ultrasensitive detection, as well as employed for hyperthermia therapy [5]. Gold nanoparticles' wide surface area and biological safety are other significant qualities employed in biological safety. Appropriate attachment to various organic molecules and safety gold nanoparticles usable as primarily epidermal DNA vaccine release through gene gun gold nanoparticles and vaccine carrier It is employed as a medication carrier among temperature-sensitive polymers by coating nanoparticles. The unique gold nanoparticles were created chemically by combining several ligands such as magnesium oleate molecules, citrate, didecylsulfides, and others. The average diameter of gold nanoparticles investigated using high resolution transmission electron microscopy (HRTEM) photomicrographs is 5.3 0.8 and 15.0 1.7 nm, respectively [4]. The utilization of gold nanoparticles in four broad areas, including thermal sensing, labelling, and delivery [8]. and its use in medicinal science,

including as drug administration, immunochromatographic imaging, tumor and tissue imaging, and pathogen research using surface Plasmon resonance (SPR) 52 Properties differ from those of its bulk form since bulk gold is yellow and solid in nature, whereas wine red solution is said to be anti-oxidant. Their physicochemical properties are distinct, including shape, surface area, amphilicity, surface carrier capabilities, and biocompatibilities, which combine to make them suitable for gene delivery, whereas the purpose of conjugate gold nanoparticles expresses various factors such as conjugate strategy, protein structure, and particle morphology [9]. It has a variety of morphologies ranging from bulk gold nanospheres to a polymeric nucleus surrounded by a gold coating or capping. They can also build small or large chains of spherical nanoparticles, with preferred optical characteristics depending on chain size [6]. Gold nanoparticles interact among a wide variety of organic chemicals because they have less harmful and balanced physicochemical features, making them useful as therapeutic agents or vaccine carriers into specific cells, where they can boost medicinal efficacy and destroy pathogens [3].It has a high affinity for alkynes in comparison to other transition metal catalysts, however homogeneous systems are neither ecologically or economically friendly due to the rapid reduction of gold complexes in metallic gold between C-H alkynes activation. Appropriate distinctive electrical and optical features are commonly exploited in the development of analytical procedures whichever appropriate for the sensing of various analytes [10]. Despite the fact that our understanding of cancer biology has vastly improved in the previous two decades, cancer remains the world's most serious health problem and the second leading cause of death. Every year, the illness causes 10 million new cases and more than 5 million deaths. Cancer diagnosis was traditionally deadly, however if diagnosed early, the diagnosis is excellent [9]. A huge number of cancer patients remain asymptomatic because they are in the late stages of their disease. Chemotherapy, surgery, and radiation are currently insufficient therapies. In light of the scarcity of medicines and clinical trials for multidrug-resistant cancer management, it is critical that new technologies emerge for the precise detection and treatment of this disease [8]. The fundamental objective of cancer treatment should result in better therapeutic effectiveness with little or no adverse effects. One intriguing option is to use nanotechnology to deliver tailored drugs. This review will focus on the use of gold nanoparticles as diagnostic and cancer treatment techniques.

1.2. Properties of Gold Nanoparticles

There are several types of physical-chemical properties of gold nanoparticles such as:

1.2.1. Ideal Physical Properties of Gold Nanoparticles

When used, a gold nanoparticle does not promote tissue infection and has no effect on the immune system. It may be utilised as a synthetic or natural polymer; it is inexpensive, toxic-free, decomposes quickly, and does not clot readily. The diameter is under 100 nanometers. Hydrodynamic diameters more than 10 nm are more likely to be expressed by the liver, whereas diameters less than 6 nm are frequently removed via renal clearance [11]. The size of gold nanoparticles used in radiodensities affects both the biological system and radiation. Because of its interaction with the negatively charged lipid membrane, the positive surface charge of gold nanoparticles is thought to promote absorption into cells. The Localized Surface Plasmon Resonance underneath the encouragement of light, conductance electrons on a noble metal vibrate jointly, which is termed Plasmon the Plasmon resonance absorption

group occurs when the incoming photon frequency is resonant among the conduction electrons' simultaneous oscillations. Surface enhanced fluorescence has two completely opposite impacts on the signal power of fluorescent molecules: fluorescence augmentation and fluorescence quenching. These effects are dependent on the distance between the gold nanoparticles and the fluorescence molecules. Gold nanoparticles capture photons and convert them into kinetic energy via photo thermal conversion. The circulating electrons propagate across the lattice/photon, and the kinetic energy component is converted into lattice vibration energy. The vibration energy obtained through the lattice is finally represented in the form of heat. This is referred to as the Photo thermal effect. Gold nanoparticle photosensitization occurs when photon energy is stimulated and transferred to neighboring molecules, such as molecular oxygen or organic photosensitization. This will result in the production of cytotoxic oxygen-group-based compounds, which will play an important role in the PDT therapy of cancer. Colorimetric responses are excessive molar absorption coefficients, and the sensitivity of gold nanoparticles discovered by colorimetric analysis approaches nanogold levels that are less than typical colorimetric methods. The color change of the gold nanoparticles-induced Plasmon as of purple or grey, red to blue, once it curled to aggregate the analytes is used in biosensing assays. Cytokines, nucleic acids, and tumor-related proteins are among the analytes examined. One of the metals with radioactivity is gold, which is a radionuclide with nuclear characteristics. Nuclear properties 198Au (t1/2 = 2.7 d) and 199Au (t1/2 = 3.2 d) are excreted in urine [12] liver and are normally applicable for biomedicine. 198Au discharge particles with a maximum energy of 0.96 MeV and a ray with a maximum energy of 412 keV Because 198AuNPs have a high concentration of these radioactive atoms, it is necessary to employ fewer nanoparticles to achieve the desired level of radioactivity for imaging and therapy. When the atomic number is more than 53, the absorbed dosage of the X-ray increases [13] Gold has an atomic number of 79, which significantly increases the X-ray absorption coefficient. Reduce X-ray damage to general tissues and activate a radiation sensitizer designated for oncology. Gold improves the depiction of a tissue response or cancer cell to X-rays by producing photoelectrons, Compton electrons, Auger electrons, and additional secondary electrons. Secondary electrons immediately ionize DNA molecules, causing them to disrupt the DNA strand, base, and sugar cross-linking. These secondary electrons react with water in tissues to produce free radicals, which bind to DNA, resulting in electron transport of oxidation and target molecule DNA, which is the physical basis for the radiation sensitization process of gold nanoparticles [14].

1.2.2. Ideal Chemical Properties of Gold Nanoparticles

Gold nanoparticles that are easy to couple can form strong chemical bonds along the S and N hold groups. These identify gold nanoparticles to interact with a wide range of polymers, chemical ligands, or a specific group. This surface modification provides gold nanoparticles with exceptional drug targeting, drug transport capabilities, and biocompatibility. Gold nanoparticles' biocompatibility is determined by their in vivo biological rate, which may be determined using pharmacokinetics, toxicity, clearance, and tissue distribution. It is a necessary prerequisite for the complete Invivo use of gold nanoparticles. This is enhanced by surface variation, the majority of which is determined by the arrangement of gold S-bonds. To improve the pharmacokinetics of gold nanoparticles, either increase the circulatory half-life

by decreasing clearance through the mononuclear phagocyte system or increase the physical size. Polyethylene glycol has been widely used to inhibit gold nanoparticle phagocytosis via the mononuclear phagocyte system of gold nanoparticles and to improve the half-life of circulation as the length of the Polyethylene glycol chains rises [15]. A gold nanoparticle contrast of 100 nm can pass for a longer period of time. While gold nanoparticles as small as 6 nm are swiftly filtered out and eliminated by the kidney [16]. Because of the tumor's rapid growth, the blood vessels internal are imperfect and the lymphatic vessels are underdeveloped, so the gold nanoparticles target on two features: active targeting (stimuli response and tumor cell) and passive targeting (retention effect, MPS escape, and enhanced permeability). These identify gold nanoparticles of a certain size to readily travel through tumor arteries and concentrate in tumor areas, which has been used for tumor imaging and treatment [17]. Delivery of gold nanoparticles can be mutual among nucleic acid, proteins and chemotherapeutic medicines during electrostatic covalent interactions or adsorption. These advantages, together with its excellent targeting and biocompatibility, make it the most competent release for tumor targeting. Gold nanoparticles can capture photosensitized [18] doxorubicin [19], phthalocyanine4 [20], and mitoxantrone [21] to boost therapeutic effects and create tumor targeting in chemotherapy. Gold nanoparticles' catalytic activity can catalyze the oxidation of carbon monoxide while also lowering ambient temperature and increasing efficiency. Gold nanoparticles' biological function includes inherent antineoplastic biological action. This asset is typically related with gold nanoparticle size. Small gold nanoparticles can cause cellular oxidative stress, DNA interaction, and cell death, as well as damage to the mitochondria. At the same concentration, massive gold nanoparticles do not exhibit the same detrimental impact.

1.3. Advantages of nanoparticles

Gold Nano Particles (GNP) are easily synthesized in different shape and sizes by various methods enabling wide range of optical, physical, and chemical properties listed below.

i) Due to High Surface area the drug loading capacity of GNPs is also enhanced

ii) Their size enables them to be biocompatible with bimolecular such as proteins, enzymes, carboxylic acid and DNA and amino acids, an enablement of biofunctionalization [22].

iii) GNP’s controlled dispersity and nanosized help GNPs to reach the targeted site when administered to blood flow.

iv) They are non-cytotoxic to the normal cells Also, used as also cancer antigen and in tumor therapies [23].

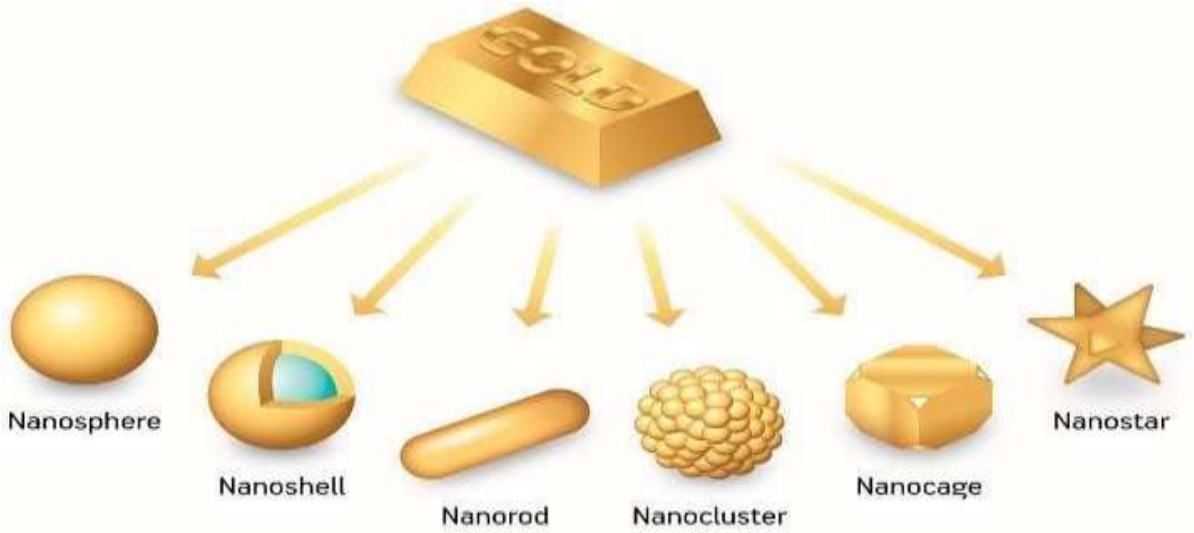
1.4. Disadvantages of gold nanoparticles

The size of gold nanoparticles acts as two faces of a coin, as what is advantageous to cure illness, might be potentially dangerous to Human health [24]. Being synthesized artificially gold nanoparticles might constitute a potential new class of non-biodegradable pollutants posing a threat to environment [25].

1.5. Various shapes of gold nanoparticles

Gold nanoparticles can be classed based on their size, shape, and physical qualities. It displays numerous sizes ranging from 1 nm to 8 m, as well as diverse forms such as Nanospheres, Nanorods, Nano shell, Nanocluster, Nanostars, and so on. (Fig. 1) [26]

Figure1: Types of gold nanoparticles.



1.5.1. Au nano spheres or au nano colloids, size – (2 nm to100 nm)

The Au Nano-sphere is primarily created by reducing an aqueous HAuCl4 solution with a reducing agent, mostly citrate. We manufacture the desired size of Au nanospheres by adjusting synthesis factors such as reactant concentrations, HAuCl4, and blocked co-polymers, and similarly by managing the citrate/Au ratio. There are several techniques for producing nanospheres, including air and thermally stable Au nanoparticles with decreased dispersity utilizing a two-phase approach using tetraethyl ammonium bromide as a phase transfer reagent [27]. Again, reactants added to the cooled solution at high speeds result in monodispersed Au nanospheres [28].

1.5.2. Au nano rods

Gold nanoparticles are simple to make and have a huge surface area per unit volume for light interaction. The pores of the membrane play a deciding element of the diameter and length in the template technique of synthesis of Au nanorods, i.e. electrochemical deposition of Au within the pores of nonporous polycarbonate or alumina template membranes [29]. However, because to the lower yields of nanorods utilizing the template approach, we frequently adopt "Seed-mediated synthesis," which results in greater aspect ratios than other yield methods. Au Chloride is reduced using a strong reducing agent, i.e. NaBH4, which serves as the seed solution, acts as a nucleation site for nanorods. Furthermore, if AgNO3 is added to the solution, the yield of nanorods increases substantially. Other techniques of production of Au nanorods documented include synthesis of nanorods on Mica surfaces, photochemical approaches, bio reduction, and others [30].

1.5.3. Au nano shells

Nano-shells have a dielectric core that is coated with a metallic shell (Au) and display Plasmon resonance, which is caused by a quasi-particle called Plasmon, which is formed when electrons oscillate with respect to all ions in collective excitation or quantum plasma oscillation. Similarly, the SERS effect is seen, which is controlled by the shell thickness and core radius. The therapeutic uses of nano shells include biomedical optical imaging, fluorescence augmentation of weak molecular emitters, and surface enhanced infrared absorption spectroscopy. Because of their strong reflecting optical qualities, nano

shells are also utilised in optical imaging. To limit the inference from deflections, infrared areas between 700-900nm are favored since absorbance levels of all bimolecular approach a minimum. By choosing the composition and dimensions of the layers, the desired Au nano-shell may be created or manufactured.

1.5.4. Au nano cage

Au gold cages contain hollow chambers that can hold Nano items for a variety of uses. These are possible drug carriers, and we may adjust the surface Plasmon resonance peaks by determining the porosity and thickness of the walls. The nano cages with controlled porosity are created using a galvanic replacement reaction between silver Nano-cubes as templates and aqueous HAuCL4. Nano cages have a wide range of uses, depending on their size, including hyperthermia-generating devices for cancer ablation, colorimetric sensors, and optical contrast agents for diagnostics in optical coherence tomography (OCT). Surface changes on nanocages might be conducted and used in a variety of biomedical applications.

1.5.5. Gold Nanostars

Nanostars are a sort of nanoparticle that has a spherical center and several types of branches, similar to a ‘star,' and is made entirely of platinum, palladium, Rhodium, and gold, silver, and other metals. Gold Nanostars is typically synthesized using a one-pot technique and seed-mediated methods. As a result, several capping molecules, such as sodium dodecyl sulphate (SDS), gelatin, ethane-sulfonic acid, polydiallyldimethyl ammonium chloride (PDADMAC), polyvinylpyrrolidone (PVP), cetyltrimethylammonium bromide (CTAB) or chloride (CTAC), have been utilised [31].

1.5.6. Nanocluster

The Nanocluster is known as colloidal gold because the solution of water is commonly disseminated and its size ranges between 1 and 100 nm. Fluorescent gold nanoclusters with diameters smaller than 3nm are a specific type of nanogold particle. In recent years, a variety of gold Nanoclusters have been organized, and their potential applications in areas such as environmental science, medicine, biology, and analytical chemistry have been established [32].

2. METHODS OF PREPARATION FOR GOLD NANOPARTICLES:

2.1. The Chemical Reduction Method

The gold nanoparticles are prepared through two methods

(i) oxalic acids, citric acid, formaldehyde, hydrogen, hydroxylamine, acetylene, sugars, carbon monoxide, sulphites, and hydrogen peroxide, among others. Gold nanoparticles are synthesized from an unsolvable thiolate chitosan derivative via reduction of theHAuCl4 during thiolate chitosan (QTDT) while reducing as well as coupling agent intended for gold nanoparticles, and the synthesized QT/Aunano is applicable when a superior catalyst for the reduction of methylene blue [33]. The Citrate thermal reduction process was appropriate for the manufacture of gold nanoparticles capable of SERS (surface enhanced Raman spectroscopy). In a short period of time, the reaction is carried out with a less expensive reagent, inositol hex phosphate (IP6), while the reduction agent is HAuCl4.Additional method for the synthesis of thermo-sensitive gold nanoparticles. gold nanoparticles in this method were decrease through the trisodium citrate whichever was shared among hydrogen tetrachlorocuprate (III)

tetrahydrate (chloroauric acid) as well as modified through 11-mercaptoundecanoic acid (MUA) through the self-build monolayers (SAM). In seeding growth method, the syntheses of gold nanoparticles in this method enclose in PEG Joined through dendrimers as well as contain high near infra-red absorption through with formaldehyde as a reducing agent. The consists of size range 1.8 - 3.7 nm have been synthesized through with peptide-biphenyl hybrids (PBHs) whichever are superior stabilizer for gold as capping agents through single-phase system. The type of capping agent and structure being used for synthesis depend upon Size of gold nanoparticles. The method of reduction intended for preparations of Au nanoparticles and dendrimers. These are synthesized though HAuCl4 that is an aqueous solution as well as dendrimers dilute solution through sodium borohydride [34]. The water-soluble gold nanoparticles having size < 10 nm through two dissimilar thiols with 1-mercaptoundec-11-yl-hexa (ethylene glycol) (EG6) and dodecanethiol (C12) that is the one-step synthesis method. the non-seed mediated temperature synthesis method of gold nanoparticles having mean diameter of 75 + 10 nm were developed through the reduction of gold ions in ethylene glycol as well as NaOH as reducing agent [35].

(ii) Surfactants, polymers, phosphorus ligands, and Sulphur ligands are used in the stabilization process to minimize the buildup of gold nanoparticles. Gold nanoparticles with a size range of 7.8 + 1.7 nm were manufactured by reducing HAuCl4 using sodium borohydride as a reducing agent. As a capping agent, bovine serum albumin proved suitable. for the creation of gold nanoparticles using reduction procedure organ gels that were utilised as template Surfactant aided synthesis has been applied for the manufacture of gold nanoparticles by using a bifunctional ligand hexadecyl trimethyl ammonium bromide (CTAB) as a linker between solid substrate and gold nanoparticles. In Hot injection method synthesized in gold nanoparticles through using dissimilar surfactants like as poly (N-vinylpyrrolidone), 1, 5-pentanediol, AgNO3, 1- octa decanethiol, oleyl amine, to stabilize the colloidal solution.

The gold nanoparticles were synthesized through the chemical reduction of gold salt in organic solvent in the presence of stabilizing agent [36].

2.1.1. The Green methods

Green methods are eco-friendly synthesis methods and do not produce any toxicity. We can synthesize gold nanoparticles of various sizes by using different green methods as depicted below:

i) In sun light irradiation method, we use solar energy to reduce the gold salt, where controlled synthesis of AuNPs is carried using folic acid and capping by 6-mercaptopurine.

ii) Synthesizing of AuNPs (15 - 80 nm), when HAuCl4 is reduced using citrus fruits juice extracts. i.e. Citrus reticulate Citrus Limon and Citrus sinensis [37].

iii) Synthesis of AuNPs from gold substrate using chitosan in aqueous NaCl solution. (no external reducing agent is used) [38].

iv) Synthesis of AuNPs (2-7 nm) using egg shell membrane i.e. a biomaterial, here egg shell membrane (ESM) is immersed in aqueous HAuCl4 [39]. Similarly, AuNPs (5-17 nm) are synthesized using high-power ultrasounds and sodium dehydrates.

2.1.2. The Citrate reduction (Turkevich method)

i) In 1951, Turkevich's reductive approach was found. It is a popular and commonly utilised strategy. Using a modified approach, Frens' group created AuNPs (20nm) by reducing citrate with gold particles. Later in 2007, Peng's group investigated the mechanics of this process by varying the ratios of gold ester components; AuNPs with diameters ranging from 16 to 147 nm may be generated. The nucleation process utilised in synthesis may be built by measuring pH value or decreasing citrate, which is accomplished as

ii) smoothing nanowires to dots

iii) Attachment to polycrystalline nanowires and naming nucleation (pH value may help in determining nucleation pathway) Size stabilization is accomplished by employing a number of capping/stabilizing agents. The primary limitation of this approach was the limited range of AuNPs that could be produced. Several advances in the unique technology, however, have allowed researchers to broaden the size range of particles that may be manufactured using this method. In 1973, it was discovered that by varying the ratio of falling to stabilizing agents, gold nanoparticles with specific sizes ranging from 16 to 147 nm could be obtained. Subsequently, the roles of sodium citrate, temperature, pH, and concentration were well understood, paving the way for the development of a particle growth model [40].

2.1.3. The Brust-Schiffrin method

The approach, named for physicist Brust Schiffirin, was discovered in 1994. Air and thermally stable AuNPs (1.5-2.5 nm) with a low dispersion value were used. Two reaction pathways play critical roles in the genesis and proliferation of AuNPs, namely the transformation of AuCl-4 from aqueous solution to organic solvent needed for staining using a phase transfer reagent, followed by a reductive route using sodium borohydride and dodecanethiol [30]. Brust-Schiffirin approach creates hydrophobic mineral groups that dissolute without changing characteristics, resulting in more stability than other methods, and the method is often utilised when employing percaptopheno. The alkanethiol ligands (RS) were utilised in Replacement processes, and positive results were obtained when Murray's group modified the approach, which included protecting gold particles with monolayer protected gold clusters (MPCs) as a multifunctional chemical reactor [41].

2.2. Physical method

2.2.1. The Electrochemical method

The GNPs were synthesized electrochemically in a two-electrode cell with cathode reduction and anode oxidation. Reetz proposed the electrochemical synthesis of nanoparticles in 1994. This technology has been deemed better to other nanoparticle creation procedures because to its lower processing temperature, low cost, good quality, minimal equipment, and simplicity of process management [30]. The AuNRs were separated from the cathode via ultra sonification, and gold nanorods were electrochemically inserted within porous membranes. While the electrochemical approach is a unique method for producing AuNPs as well as anisotropic AuNPs, it is still being actively researched due to its

application, simplicity, and efficiency [42].

2.2.2. The Seeding growth method

GNP with sizes ranging from 5 to 40 nm and a narrow size dispersion were produced using this approach. Particle size may be properly organized by changing the seed-to-metal salt ratio. This approach has the advantage of being simple, rapid, and inexpensive, as opposed to using trisodium citrate as a source of OH ions in the seeding stage and sodium borohydride (NaBH4) as a reductant [28]. The most commonly practice to manufacture rod shaped gold nanoparticles are seed-mediated development. Which approach is based on the fundamental idea of first creating seed particles by reducing gold salts? This reaction is completed when reducing agents such as NaBH4 are present. The subsequently the next step included the seed particles transferring to a metal salt as well as a weak reducing agent such as ascorbic acid that inhibits further nucleation as well as speeds up the generation of AuNPs of rod shape. Geometry and Shape depends on the concentration of seeds and reducing agents [43].

2.2.3. Ultraviolet-Induced Photochemical Synthesis of AuNPs

Controlling the shape and size characteristics of the generated nanoparticles has a substantial impact on the potential chemistry related to the use of AuNPs in magnetic devices, photo catalysis, manufacturing, and aerosol. The light reduction procedure, as many studies have said, allows for the fabrication of single crystallite AuNPs. Photochemistry was used successfully to create AuNPs with adjustable size [44]. Photochemistry is also a viable way for producing anisotropic AuNPs. While a cationic micelle through a rod form is jumped to HAuCl4, UV light can diminish HAuCl4 to appear AuNRs. The light reduction of Au0 atoms is prevented in this situation by forbidden agglomeration. The photochemical route has also been carried out in the occurrence of poly-vinylpyrrolidone (PVP) TiO2 colloids and ethylene glycol, TiO2 serves equally as a photo catalyst as well as an additive of the AuNPs [45].

2.2.4. Ultrasound aided synthesis of GNP

An ultrasound wave generator was employed to provide a temperature-controlled water bath for the ultrasonic-aided reduction of gold precursor in the presence of 2-propanol. For repeatability and tunability, several stabilizers such as citrate, disulphide, and numerous dendrimers were utilised throughout this synthesis procedure [28]. Because the property derived as of sonic cavitations encourages chemical reactions under severe conditions, ultrasound has become a useful technology for the synthesis of extremely tiny nanoparticles. However, this approach produces nanoparticles with a wide range of sizes and shapes. Using this technology, Han and colleagues manufactured single-crystalline flexible gold nanobelts with a width of 30- 50 nm and a length of a number of Micrometers [46].

2.2.5. Laser ablation synthesis of GNP

In terms of size and form of properties, laser ablation has produced reproducible and accurate results. As a result, the pulsed laser approach that necessitates quick condensation and evaporation occurrences for gold characterizes a full physical method that may be efficiently used to provide GNPs using tunable assets. The research requires the reduction of HAuCl4 by a laser beam of 532 nm wavelength, resulting

in GNPs between 5nm and smaller in size. In this procedure, a solution of sodium dodecyl sulphate (SDS) was used as a model to evaluate the effect of different concentrations and laser on the form and size of the generated GNPs [29]. GNPs generated by this process assist in immune chromatographic test labelling. This technique varies from traditional technique for formation of nanoparticles [47].

2.2.6. The Biological method (Sundus)

GNP is produced in this manner by bacteria, enzymes, and plants.

Efforts have recently been undertaken to develop biological synthesis of AuNPs, which is a safe, reliable, and bio-friendly alternative to harsh chemicals used in chemical synthesis processes. Simple bacterial cells to sophisticated eukaryotes are among the biological resources employed in the creation of nanoparticles. Surprisingly, organisms' ability to synthesise metal nanoparticles has given rise to a new exciting approach to the creation of these biological Nano-factories [48]. A wide range of species, from bacteria to plants, algae, and fungus, have been found to successfully synthesise AuNPs.

2.2.6.1. Bacteria

Microorganisms that produce both intracellular and external AuNPs. Bacterial cell walls with negative charges can electrostatically interrelate with positively charged Au (III) ions. Gold ions are distributed throughout the cell via enzymes and bimolecular synthesis during intracellular synthesis.

Table1: Different plant parts used in gold nanoparticles.

plant parts	plant name	bio-compound	time taken for synthesis process	synthesized aunps morphology	synthesized aunps size
leaves	Justicia glauca	lignans [(+)-pinoresinol, (+)-medioresinol], alkaloids, flavonoids, steroids (sitosterol-3-0-glucoside), terpenoids	1 hour	spherical, hexagonal	32 nm [49].
leaves	terminalia arjuna	Arjunetin, leucoanthoc-yanidins hydrolysable tannins	15 mins	spherical	20–50 nm [50].
leaves	cassia auriculata	proteins, oleuropein,	10-20 mins	spherical, anisotropic	50–100 nm [51].

		apigenin-7-glucoside, luteolin-7-glucoside			
fruit	Mangifera indica	terpenoids, flavonoids, and thiamine	2 mins	spherical,	17–20 nm [52].
flower	lonicera japonica	amino acids	8 mins	triangular, tetrahedral	8 nm [53].
flower	moringa oleifera	flavonoids, carotenoids, phenols, sterols, and amino acids	-------	-------	3–5 nm. [54]
peels	banana	------	spherical	20-25 min	50 nm [55].

Gold ions are also captured on the cell membrane by membrane enzymes during extracellular production. These enzymes on the membrane or reductase enzymes hidden out through the microbial cell can take out the bacterial cell's synthesis development outer surface [49]. Extracellular synthesis, on the other hand, is particularly intriguing because it does not require any additional downstream processing steps that are required for the separation of nanoparticles from the intracellular matrix [56]. NADH and NADH-dependent enzymes are both useful as nucleating agents or scaffolds in the synthesis process. The movement of electrons as of NADH through NADH-dependent enzymes is the basis for the reduction of Au (III) to Au0, which results in the synthesis of AuNPs [36]. The intracellular enzymes intercede synthesis of AuNPs through accomplish the reduction of Au (III) ions at the surface of membrane as well as mycelia. Similarly, Shewanella algae well passed out enzymes intercede bio reduction of AuCl4 ions to AuNPs that were established to be dispersed in bacterium periplasmic membrane [38]. Definite components produced by microbial cells, which are analogous to organic molecules proteins and enzymes, can act as capping agents for the stability of nanoparticles and, as a result, prevent their agglomeration [44]. Positive reductase enzymes found in microorganisms may reduce metal salts to metal nanoparticles with tight size distributions and monodispersed distributions [42]. The form and size of AuNPs may be easily modified by changing the critical growth factors.

2.2.6.2. Fungi

Fungi have also been exploited as a biological source for the manufacture of AuNPs. It leaked a large quantity of bimolecular Extracellular enzymes and metabolites, such as acetyl xylem esterase, 3-glucanase hemicelluloses, enzyme-1, and cell wall lytic, have been documented for the whole production of metallic nanoparticles [46]. Gold nanoparticles were used to create unicellular and multicellular fungus. Fusarium oxysporum, a fungus species, was employed in a study for the

extracellular production of Au-Ag alloy NPs via nitrate-dependent enzyme reduction and shuttle quinone. Verticillium has also been found to synthesise AuNPs intracellularly [48].AuNPs were create to be trapped in the cell membrane as well as the cell wall of fungi, signifying which Au^{3+} ions were bio-reduced through the reduction action of reductase enzymes in fungi the biosynthesis studies of AuNPs from Phanerochaete chrysosporium proved so as to lactase was the enzyme concealed through the fungi for extracellular synthesis of AuNPs as well as, for intracellular synthesis, ligninase was set up to be responsible [51].

2.2.6.3. Plants

Phyto nanotechnology is the method of biosynthesis of AuNPs in which plants or plant extracts, i.e. bio-compounds such as flavonoids, phytosterols, quinones, and so on, are used to reduce and cap AuNPs [57]. It is quick, affordable, and sustainable, and it reduces the number of further purification procedures necessary. Though any part of the plant can be utilised for AuNP production, leaves are the most typically employed [43]. Since, the bio-compound level varies in different parts of a plant, the depart used affects the synthesis of AuNPs. E.g. the leaves of Garcinia mangostana plant yield AuNPs faster than the fruit of the plant parts of plants, such as palm oil mill turmeric, nuts of Areca catechu, rhizomes of yam beans, latex of Hevea brasiliensis, galls of zebra wood, ginger, bark of bay cedar, seeds of cocoa, and pulp of green pepper, are carry out for the synthesis of AuNPs.

2.2.6.4. Algae

Gold nanoparticles were created using fresh algae and saltwater species. Previously, the synthesis of AuNPs was carried out using the marine red algae Turbinaria conoides, Gracilaria corticata, Laminaria japonica, Acanthophora spicifera, Cystoseira baccata, Galaxaura elongate, Sargassum wightii, marine brown algae Ecklonia cava, and Stoechospermum marginatum. Freshwater algal biomass, including Lemanea fluviatilis, Chlorella pyrenoidus, and Prasiola crispa, can all manufacture AuNPs. The hydroxyl and carbonyl groups found in algal biomass can be employed as reducing agents in the manufacture of AuNPs. These groups can also work as a capping agent for gold nanoparticles [58,59].

3. Characterization of gold nanoparticles:

3.1. UV–Vis absorption spectrophotometry

The UV-Vis absorption technique is utilised to detect Au (III) ion bioproduction [42]. The measurements are performed 10 minutes after the bioreduction procedure is completed [45].

3.2. Dynamic light scattering (DLS)

For the detection of the AuNPs obtained, they were purified through centrifugation. DLS is used for the detection of size, volume, distribution and average size of AuNPs [37]. The system of particle size is equipped through a green laser excitation source [33].

3.3. Differential Scanning Calorimetry (DSC)

DSC is detected for the curve of the gold nanoparticles and synthesized for the exothermic peak and endothermic peak. Consequently, the denaturation temperatures through DSC curve for these nanoparticles are in superior agreement [46].

3.4. Scanning electron microscopy (SEM)

SEM detects the morphological analysis of gold nanoparticles and also revealed the production of

AuNPs along with smooth surface spherical in shape [51].

3.5. Transmission Electron Microscopy (TEM)

TEM used for the detection of particle shape, size & elemental composition.

Owing to the TEM high resolution, it was not essential to purify the AuNPs earlier than measurements through centrifugation.

3.6. Fourier-Transform Infrared (FT-IR) Spectroscopy Studies

FTIR examination was carried out to classify various functional groups. The wavelength range of FTIR spectra was kept within 4000 – 400 cm-1[33].

3.7. Anti- bacterial study

Antibacterial was studied through the agar-well-diffusion method, in which bacterial suspension was added sterile nutrient Mueller Hinton agar at optimized temperature as well as on the Petri dish for solidification [27].

3.8. Particle Size and Zeta Potential Measurements

The particle size, polydispersity index and zeta potential were measured using a Malvern Zetasizer.

3.9. Stability Storage Study

Aliquots of the optimized formulation were stored in tightly closed containers at room temperature for 4 months.

3.10. Statistical Analysis Study

Graph Pad Prism software and one-way analysis of variance were used to analyses the statistical analysis research (ANOVA).

3.11. In Vitro Studies

The In Vitro studies were carried out with the dialysis bag method whereas drug loaded in the dialysis bag membrane with aqueous solution and samples was measured spectrophotometrically.

3.12. In Vivo Studies

The In Vivo Studies was conducted on male mice age 4–5 weeks and weight 20–25 g [60,61].

4. CONCLUSION

In current years, the conventional biomedical technique has been successfully substituted among Novel nanotechnology technique for Sensitivity, efficiency, high speed and accuracy measurement. With the different useful types of metallic nanomaterial's, AuNPs and of their intrinsic features. Various formulation and evaluation parameters like as U.V, FTIR, DSC Zetasizer, DLS, TEM, and SEM Gold Nano particles systems can simply be estimated. Thus, gold nanoparticle is an excellent choice of formulation.

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