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ANTIRETROVIRAL DRUG LOADED GOLD NANOPARTICLES RECENT TRENDS AND ITS APPLICATIONS

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ABSTRACT
Gold nanoparticles provide an excellent material for study the most stable, non-toxic and easy to synthesize nanoparticles and it exhibits various interesting properties such as aggregation type and quantum size effect. The optical behavior of gold nanoparticles depends on surface plasmon resonance (SPR). wide area from visible to infrared area. The spectrum is determined by mass oscillations transfer electrons. The range of the spectrum depends different properties of gold nanoparticles, size and a method has been developed to synthesize this material that can be changed by increased use chemical functional groups are innumerable. Many new sensations and special studies based on gold nanoconjugates. Gold nanoparticles have emerged as practical candidates for the delivery of various cargo carriers to the target place. This is a small carrier drug molecules including drugs for large biomolecules such as DNA, RNA and protein. Some drug molecules do not requires modification of the gold nanoparticle monolayer can be directly connected to gold for delivery physical absorption with ions or nanoparticles covalent bonds. To be sent by others charge carriers require functionality such as gold nanoparticles PEG lyation, peptide and amino acid conjugation or work with oligonucleotides. In addition, another prerequisite for effective delivery of therapeutic agents is their release. Various internal stimuli (glutathione, pH, and enzymes) and external stimuli (light, etc.) as investigated for effective release gold nanoparticles. Because of the abundance of information available and we choose the renewable level data is summarized over the past few years to illustrate this include the most promising programs Gold nanoparticles in drug delivery.

1. INTRODUCTION
1.1 Nanotechnology:
Nanotechnology refers to the design and application of components takes place on a nano scale: 10-1000 nm in size. Nanotechnology includes investigate the structural properties of nanostructures at the molecular and submolecular level with their electrical, optical and magnetic properties. Today, nanotechnology is an interdisciplinary field that requires engineering. Biomedicine, chemistry and

physics under one umbrella from oil and gas to cosmetics and nanomedicine, nanomaterials have ushered the world into a new era, the era of nanotechnology.[1]
The most various nanostructures are carbon nanoparticles, gold nanoparticles, liposomes and paramagnetic nanostructures. Gold colloids are now more and more available It is used in various fields such as chemistry, biology, engineering and medicine. In biomedical field, diagnosis, therapy and immunology.[1-3]

1.2 Gold Nanoparticles:

Gold nanoparticles provide an excellent material for study the most stable, non-toxic and easy to synthesize nanoparticles and it exhibits various interesting properties such as aggregation type and quantum size effect. The optical behavior of gold nanoparticles depends on surface plasmon resonance (SPR). wide area from visible to infrared area the spectrum is determined by mass oscillations transfer electrons. The range of the spectrum depends different properties of gold nanoparticles, size and a method has been developed to synthesize this material that can be changed by increased use chemical functional groups are innumerable. Many new sensations and special studies based on gold nanoconjugates. Gold nanoparticles have emerged as practical candidates for the delivery of various cargo carriers to the target place. This is a small carrier drug molecules including drugs for large biomolecules such as DNA, RNA and protein. Some drug molecules do not requires modification of the gold nanoparticle monolayer can be directly connected to gold for delivery physical absorption with ions or nanoparticles covalent bonds. To be sent by others charge carriers require functionality such as gold nanoparticles PEGlyation, peptide and amino acid conjugation or work with oligonucleotides. In addition, another prerequisite for effective delivery of therapeutic agents is their release. Various internal stimuli (glutathione, pH, and enzymes) and external stimuli (light, etc.) as investigated for effective release gold nanoparticles. Because of the abundance of information available and we choose the renewable level data is summarized over the past few years to illustrate this include the most promising programs Gold nanoparticles in drug delivery.[1-3]
A wide variety of medicinal products which originate from natural compounds and which are widely used to target and treat various appear diseases. The extraction of these complicated chemical molecules from plants, animals, microorganisms and minerals are common natural sources via several extraction processes, these compounds work as an initiator of future sinker molecules. Gold is inert and universally recognized as biocompatible. Until the recent past, it was only known as the metal. With the arrival of nanotechnology and the discovery of nanoparticles and the exploration of the physico-chemical properties of gold make it a supreme material for progress fields. A nanoparticle is defined as a tiny particle with a size ranging between 1 and 100 nm. The description of AuNPs was documented since 1996.
The term "nanoparticles" refers to highly heterogeneous atomic and multidimensional materials that allow materials to exhibit special photonic, electronic, catalytic, and therapeutic properties. Although this term can be applied to any material with a diameter smaller than 1 mm, approximately 1-100 nm, it is more commonly used to describe particles in biological laboratories. The configuration of nanoparticles includes primary organic molecules (liposomes, DNA, fatty acids, viruses, and micelles), inorganic molecules (iron oxide, gold, and carbon nanoparticles), or hybrids containing two or more of these elements. Nanoparticles are used for in vitro labeling of biomolecules or cells, transfection, and conventional imaging reagents. In living animal models, nanoparticles are very effective targets for medical imaging, drug delivery, and cell tracking. Studies have shown that AuNPs can be used to target different types of cells, stem cells and immune cells without compromising the therapeutic effect. Nanocarriers have the ability to absorb large amounts of drugs with poor pharmacokinetics or high intrinsic toxicity. Due to their immobility, implanted drugs are capable of extensive tissue distribution. Nanomaterials exhibit different physicochemical properties such as nano size, size distribution, surface to volume ratio, different surface structure, shape, chemical composition, and agglomeration. In the last decade, nanotechnology techniques have been used in cosmetics, medicine, food, construction materials,

etc. It has been used in various industries like some useful applications are nano-capsules that are added to food to increase the level of nutrient absorption. Organic and polymeric nanoparticles are used to transfer vitamins into foods and beverages without affecting taste and appearance. One of the most important types of metal nanoparticles consists of precious metals such as gold (Au). AuNPs have attracted considerable attention due to their ability to interact with light through surface plasmon resonance (SPR). Recent advances in nanoscience have demonstrated the potential of gold nanoparticles (Au NPs) as building blocks for future plasmonic devices and other optical devices. Gold nanoparticles (NPs) have been used in various applications such as chemistry, materials science, physics, medicine, and life science, and should be expanded due to their multifunctional properties in therapy, detection, imaging, and surface modification. Metal nanoparticles such as gold have been widely used as nanomaterials for theranostic applications in cancer therapy. In the biomedical field, highly sensitive biomolecular assays are used to selectively destroy cancer cells through photothermal therapy, special cells, protein markers, and cellular therapy. The transport mechanism of these AuNPs drug molecules is mainly passive diffusion undetermined passive transport) or energy-dependent active transport systems. These are given orally, then absorbed through the gastrointestinal tract and usually distributed throughout the body through the venous system. In addition, these can be transported directly to vascular target organs, or can circulate once in the blood stream or for a long time depending on their size, shape, and surface, through protective mechanisms such as clearance by the reticuloendothelial system (RES). .properties of nanoparticles. In addition, it is chemically biocompatible and allows easy placement of various functional groups with different sizes, shapes, and configurations with different optical properties It can be synthesized by various physical, chemical, and biological methods from plants, fungi and bacteria, which is an active and important academic field. The challenge of finding particle size, shape, and surface chemistry for potential applications requires further research into the interaction of nanoparticles with cells or tissues.

1.3 Synthesis of AuNPs[4-9]

There are two basic strategies for the synthesis of AuNPs which are used which are "top-down" and "bottom-up" approaches. A top-down approach involves synthesis AuNPs starting from bulk material and breaking it up nanoparticles using various methods. In contrast to, a bottom-up approach synthesizes nanoparticles starting from the atomic level. Figure 1 shows the basic steps that They are involved in top-down and bottom-up approaches. Synthesis methods that involve a top-down approach include laser ablation ion sputtering UV and IR irradiation and aerosol technologies while reduction of Au3+ to Au0 is a bottom-up approach. Nanoparticles have been synthesized through various physiochemical processes, all of which have a great environmental impact. Gold nanoparticles are the most important of the aforementioned metal nanoparticles due to their long history of therapeutic applications. The most common form in the literature is gold nanoparticles. Since 1996, approximately 87,000 publications have been published. Nanoparticles of copper, silver, iron and titanium are all documented and should be studied separately (Daruich De Souza et al., 2019). Several different biological, physical, and chemical synthesis methods have been developed for the synthesis of gold nanoparticles.[4]

1.4 The formulation of AuNPs:

In the first stage, there is a gold precursor, which is usually and an aqueous solution of a gold salt is reduced to gold nanoparticles using a specific reducing agent such as citrate. In the second phase gold nanoparticles are stabilized using a specific covering agent. Limitations substances prevent the agglomeration of metal nanoparticles.

1.5 Chemical synthesis

1.5.1 Chemicals

Functionalization is disposable in the model of nanoparticles for a specific application and may rely on a surface charge, surfactants, functionality, and stabilizers. The Au0 (non-oxidized state) is the ultimate preferable state for nanoparticles. Thus, the principal stage involving the preparation of positively charged gold nanoparticles AuNPs is to reduce the oxidation of goldAu+1(aureus) or Au+3(auric) to Au0 by adding a reducing agent to the reaction; under intense stirring to form fairly uniform NPs in size. Then the saturation of the AuNPs solution to precipitate moderately. In order to minimize aggregate NPs, a stabilizing medium that adsorbs on the NP surface is typically applied (Daruich De Souza et al., 2019, Teimouri et al., 2018). The principle is the same but there are several methods to achieve.[5]

1.5.2 Chemical synthesis Methods:

Turkevich's method: This method for the synthesis of AuNPs was reported for the first time in 1951. It is one of the most commonly used techniques for the formulation of spherical AuNPs. AuNPs prepared when using this method, they have a magnitude in the range of 1–2 nm. The basic principle of this technique includes reduction of gold ions (Au3+) to form gold atoms (Au0)by using some reducing agents such as amino acids, ascorbic acid, UV light or citrate.

1. Turkevich-Frens method

This method is used to synthesize AuNPs and was developed in 1951 by J. Turkevich et al. to produce moderately colloidal AuNPs with sizes ranging from 10 to 20 nm. The diameter of the shaped NPs can be changed by varying the amount of reactant used or by using different styles or stabilizing factors. The main disadvantage was that only a limited number of AuNPs could be produced (Teimouri et al., 2018).[4]

2. Brust–Schiffrin method

The Brust–Schiffrin synthesis (BSS) of metal nanoparticles was described in 1994; this method can produce highly stable thiol functionalized nanoparticles (Perala and Kumar, 2013) and can be used to prepare AuNPs in organic solutions (Teimouri et al., 2018). In the end, AuNPs can be isolated as a solid and treated much like, the highly stabilized Brust-Schiffrin analogs (Booth et al., 2017).[4]

3. Martin method

Teimouri and colleagues advanced this method in 2010 by using NaBH4 as a reducing agent for the reduction of HAuCl4. HCl and NaOH are used as “stabilizing agents” in this process, and AuNPs are used as “colloidal dispersion.” The NPS scale is nearly monodispersed, and the diameter can be precisely adjusted from 3 to 5 nm (Teimouri et al., 2018). Microbes can produce biogenic nanoparticles both internally and externally, but extracellular processing is preferable for isolation (Sreedharan et al., 2019). The extraction efficiency of nanoparticles is influenced by the form, amount of extraction of nanoparticles, and concentration (Bosi et al., 2015). The majority of the methods reported for separating and detecting AuNPs required expensive instrumentation, such as field-flow analyzers. In comparison to these costly methods, the optical properties (fluorescence, absorbance, and dispersion) of NPs have been analyzed for AuNP testing utilizing low-cost instruments such as fluorescence and UV spectrometers. However, these approaches have a range of disadvantages, including the usage of organic solvents, lengthy sonication periods at low temperatures, and the need for intermediate evaporation steps. Selective methods for screening metallic NPs are in high demand and of vital importance. The use of eco-friendly sulfonate nano cellulose (s-NC) as a sorbent material is a simple and fast method for detecting gold NPs. The affinity of sulfur atoms to metals is central to the interaction between s-NC and AuNP. Through stabilizing the NP, the usage of cationic surfactant (+) has significantly aided the extraction of AuNPs. Because of its non-toxic properties and excellent qualities, nano cellulose (NC), extracted from plentiful renewable resources, is a good contender (e.g. compatibility, biodegradability,

lightness, high porosity, thermal stability and rigidity). Modified nano cellulose is a promising material for gold nanoparticle extraction (Jesús Dueñas-Mas et al., 2018).[4]

1.6 Biological synthesis

Recently, attempts have been made for biological synthesis of pure AuNPs, safe and bio-friendly alternative to harsh chemicals used in chemical synthesis reaction. Biological resources are used in its synthesis. A nanoparticle is more complex than a simple bacterial cell eukaryotes interestingly, the ability of organisms. The synthesis of metal nanoparticles creates a new phenomenon this is an exciting approach to develop biological nano-factories. A large number of organisms from bacteria to plants, algae, and fungi have reported the synthesis of AuNPs. Biological synthesis of nanoparticles is a safe, dynamic and energy-efficient method to produce nanoparticles. This approach includes several biological sources, from prokaryotes to eukaryotes, to synthesize NPs in vivo. Metabolites (proteins, fatty acids, sugars, enzymes and phenolic compounds) from these sources play an important role in the bioreaction of metal ions to NPs and their stability. Biologically produced AuNPs are more stable than those produced by other means. AuNPs can be efficiently produced from chemical sources, but the main risk is the formation of byproducts (secondary products) that are dangerous for human health and the environment. New approaches to produce reliable nanoprobe products are currently being intensively explored by many biological systems, such as plants, bacteria, yeast, and fungi, to produce AuNPs.[5-10]

Bacterium:

Microorganisms have been reported to be excellent candidates for the synthesis of intracellular and extracellular AuNPs. The cell wall has a negative charge Bacteria can have a positive electrostatic effect Au(III) ion charge. During cellular synthesis, gold ions are transported intracellularly by enzymes and biomolecules synthesize AuNPs. Above on the other hand, gold ions are present during extracellular synthesis bound to the cell membrane by membrane enzymes. This enzyme or reductase enzyme in the membrane Bacteria that are secreted by microbial cells can carry out the process of synthesis outside the cell. Extracellular and the synthesis is more interesting as it is which requires downstream processing steps Au0 as nitrate reductase by Pseudomonas denitrificans. The results show that the movement is declining. Enzyme decreases after AuNPs are synthesized. Shahet Al reported that both NADH and NADH-dependent enzymes function in the nucleus agents for synthesis reactions. It was reported by Singh et al Rhodopseudomonas capsule NADH and NADH-dependent enzymes during extracellular synthesis AuNPs. Electron transfer from NADH has occurred an enzyme that causes the reduction of NADH from Au (III) to Au0, leading to the synthesis of AuNPs. Thermomonospora sp. (Order: Actinomycetes). It has been reported to activate cellular enzymes at risk Synthesis of AuNPs by achieving Au (III) reduction ions on the surface of the membrane and the mixture. Again, Shewanella algae perform intermediate enzymes efficiently bio reduction of $AuClP^{-}$ ions was found dissolve in the bacterial periplasmic membrane. Some materials produced by microbial cells, such as proteins, enzymes, and organic matter, can be packaged agents to stabilize nanoparticles and thus prevent them agglomeration. [11-20]

Green synthesis of Bacteria-AuNPs

Beveridge and Murray conducted their first research on the biosynthesis of gold nanoparticles (GNPs) using the bacteria Bacillus subtilis in 1980. Since then, a variety of microorganisms have been used to synthesize a variety of metals, nonmetals, metal oxides, and bimetallic nanoparticles, with more applications being considered. The use of marine bacteria to synthesize gold and silver nanoparticles has been active in recent years, as has the novel bacterial strain Marino bacteralgicola, which was isolated from marine waters in the Indian Sector's Southern Ocean. Furthermore, several bacteria, including strains of Bacillus, Cupriavidus, and Shewanella, were discovered to be capable of reducing Au(iii) to Au NPs.[21-30]

General approach of marine bacterium GNPs synthesis

A method that involves isolating the bacterium from water samples and growing it in broth for 24 h. Centrifugation is a method of harvesting biomass. Cell biomass is used to determine whether the enzyme responsible for GNP preparation is intracellular or extracellular. The cell biomass was washed twice in a phosphate buffer (pH 7, 0.05 M), then dissolved in 50 ml of distilled water and ultrasonicated (5 min, 30-second pulse) to break down the cell wall and release the enzyme into the aqueous system. The pellet is discarded by centrifugal solution and cell lysate supernatant (CLS). In a flask, (HAuCl4–1 mM) was mixed with (25 ml of supernatant) and stirred at 30 °C at 150 rpm for 72 h to produce AuNPs. Following an ultrasound, there was a notable shift of color from cell biomass. This shows that the enzyme is involved in intracellular processes in nature.[31-40]

The reaction condition:

The experiment was conducted using Ultrapure Millipore water (18.2 M). Inoculating newly grown bacteria into a liquid medium containing LB (Luria – Bertani) broth facilitates bacterial cell cultivation. Cleaning the cells three times with a PBS buffer solution was performed (pH 7.4). The final concentration of Au(iii) is 1.8 mm. At 30 °C, the mixture was incubated. After 12 h, cells and nanoparticles are removed by centrifuging at 4000×g for 10 min at room temperature (Liu et al., 2018).

Monodispersity.

By varying key growth parameters, the shape and size of AuNPs can be controlled. Synthesis of AuNPs using bacteria is a tedious reaction requires additional precautions during Bacterial handling and bacterial culture is time-consuming, requiring hours and days. This is flawed limit the use of bacteria for its synthesis AuNPs.

Fungi

These have also been used as a biological source Synthesis of AuNPs. Fungi secrete a number of biomolecules, including metabolites and extracellular enzymes. Hemicellulose, acetyl xylem esterase, 3-glucanase, reported cell wall enzyme Lithuanian β-1 et al. role during metal synthesis nanoparticles.[60] Several studies have been reported Synthesis of gold nanoparticles using unicellular and multicellular fungi.[61,62] Fungal species Fusarium oxysporum. was used for the extracellular synthesis of AuAg alloy NPs with a nitrate-dependent reduction reaction enzyme and quin transport.[63] Fungal species Vertically, AuNPs are reported to induce cellular synthesis. AuNPs were found to be entrapped required for the dissociation of nanoparticles from the cellular matrix. Research has demonstrated the presence of NADPH-dependent enzymes during extracellular synthesis reactions.

General approach of fungus AuNPs synthesis

Endophytic fungal isolates are grown for 21 days at 25 °C-28 °C in potato dextrose broth (PDB). In PDB, mycelial biomass is created, then extracted by filtration, and the traces of the media components are removed by washing with distilled water. Incubate the biomass in 100 ml of distilled water for 48 h at room temperature. Gold nanoparticles are generated by combining a 1 mM HAuCl4 aqueous solution with a fungal suspension filter (Osonga et al., 2020). The solution was then recovered using centrifugation (10,000 rpm for 10 min). Finally, the filtered gold nanoparticles were washed with distilled water. The initial stage of myco-synthesis of gold nanoparticles is detected by a visual color change in the reaction flasks and verified by UV–Vis spectroscopy.[41-45]

The reaction condition:

pH, cell growth rate, and temperature all had an effect on the morphology and size of gold nanoparticles during development. The optimal temperature for the production of gold nanoparticles was identified by adjusting the incubation temperature of the cell-free filtrate from 28 to 55 °C. The

ideal pH for gold nanoparticle formation was identified by changing the pH of the cell-free filtrate using buffers ranging from pH 5–9.

Green synthesis of fungi-AuNPs

Another way, green synthetic approaches for the preparation of various types of nanoparticles are critical for the preservation of long-term growth. Because of the scalability and cost-effectiveness of fungal growth on an industrial scale, extracellular or intracellular extracts of fungi are suitable materials for the synthesis of metal nanoparticles. Fungi can produce gold nanoparticles in one of three ways: extracellular, fungal autolysate, or intracellular. The size and distribution of the fungi differ depending on the strain and the experimental conditions. Fungi have an advantage over other microorganisms in that they can produce a large number of extracellular enzymes capable of reducing metal salts to nanoparticles. Fungi can also be easily prepared in the laboratory as well as on a large scale, as mycelia can withstand harsh conditions in bioreactors. Marine endophytic fungi have been found coexisting with marine algae. Several Scholars have been able to synthesize antioxidant gold nanoparticles from Penicilliumcitrinum, an endophytic fungus isolated from the seaweed Sargassumwightii, in recent years. The advantage of using M. phaseolina to create gold nanoparticles is that its oxidoreductase activity is higher than that of other fungal species, which is economically useful since less enzyme is needed for the generation of gold nanoparticles.[46-50]

Algae

There are a few studies which have demonstrated the synthesis of gold NPs using algae. A few species of both marine and fresh algae were used in these studies. Among the marine red algae, Gracilaria corticata, Acanthophora spicifera, and Galaxaura elongata, and marine brown algae, Stoechospermum marginatum,Ecklonia cava, Sargassum wightii, Cystoseira baccata, Laminaria japonica,and Turbinaria conoides have been previously reported to carry out the synthesis of AuNPs. On the other hand, biomass from freshwater algae including Prasiola crispa, Lemanea fluviatilis, 103 and Chlorella pyrenoidusa104 can also synthesize AuNPs. Previous studies have shown that hydroxyl and carbonyl groups present in algal biomass can act as reducing agents for carrying out the synthesis of AuNPs. It has also been shown that these group can also act as the capping agent for gold nanoparticles. Table 1 shows the list of various organisms that have been reported to carry out successful synthesis of AuNPs.[4-55]

Biomolecules

Molecules synthesized by living organisms to speed up their biological processes of the body are known as biomolecules and these include macromolecules such as amino acids, nucleic acids, carbohydrates, and lipids. Previous studies have reported the synthesis of gold nanoparticles using chitosan which does not only act as a reducing agent but also as a stabilizing agent during synthesis reaction. Apart from that, starch is another polysaccharide used for the synthesis of AuNPs. In an alkaline environment starch can be degraded into short chains having carboxyl groups and the –OH group of carboxylic acid can reduce Au3+ ions to gold nanoparticles. Among proteins, consensus sequence tetratricopeptide repeat proteins and corn protein, α-zein can be used to carry out the synthesis reaction of AuNPs. The biological method of synthesis of AuNPs can conveniently overcome the complications of biosafety of the chemicals used for the generation of AuNPs. Advantages and Limitations of Biological Synthesis. Synthesis of AuNPs using biomass from bacteria is an advantageous process as some species of bacteria are not affected by the presence of heavy metals. Also, the extracellular synthesis approach produces pure nanoparticles as compared to the intracellular synthesis process which requires additional purification steps. Conversely, culturing of bacteria is a slow and tedious process.[56-60]

Table 1. Various Types of Living Organisms That Can Carry either Intracellular or Extracellular Synthesis of AuNPs

Name of Organism	Intra/ Extracellular	Reaction Type
Bacteria		
Deinococcus radiodurans	Extra/intra	Reduction
Bacillus Extra Reduction	Cereus	

The synthesis reaction of AuNP can take a long time of hours and even days. On the other hand, fungi produce large amounts of proteins and reactive compounds. Therefore, the reaction process can be easily measured above. Furthermore, it is simple compared to bacteria to culture and grow fungi. But preparing biomass from Fungi require careful steps for the synthesis reaction is complicated to separate mycelia from culture filtrates. Manipulation of the genetic makeup of eukaryotes to produce desired proteins is also challenging. Also, some species of fungi are pathogenic. Synthesis of AuNPs using plants based material is a facile and uncomplicated process. Various attributes of AuNPs such as shape and size can be regulated by controlling the reaction parameters. Additionally, the reaction process is fast and economical. The disadvantage of using plants for the synthesis of AuNPs is that the identification of reactive components is difficult as plant biomass comprises a large number of organic components. Synthesis of AuNPs from algal biomass is also easy and simple, but algae take a lot of time to grow so the overall process can become tedious and time consuming. Biomolecules on the other hand contains various functional groups which can aid in the synthesis of AuNPs. Contrarily, as different biomaterials show different reducing ability it is imperative to first determine their reducing ability before using them in the synthesis reaction.[61-65]

Plants

Phytonotechnology has gained attention with time it involves an environmentally friendly, cheap and fast process Synthesis of nanoparticles. There are a number of studies Biosynthesis of AuNPs using different plants or Reduction of plant extracts involving the use of harmful biological components from plants and Capping of AuNP, reduction of waste generation and limiting the need for additional purification steps. Numerous biological components present in plants such as flavonoids, phytosterols, quinones etc. play a role in the synthesis of AuNPs because of the functional groups which accelerate the reduction and stabilization of AuNPs. Although almost every part of the plant has been reported to successfully carry out the synthesis of AuNPs, leaves are most commonly used. Differences in levels of different compounds present in different plants and also in them Different parts of the plant affect the synthesis of AuNPs. For example, one study reported a differential effect in the level of phenolic content present in the leaves and fruits of Garcinia mangostana plant on the synthesis of AuNP. As The leaves are rich in phenolic content so rate AuNP synthesis was faster in the presence of leaves than the fruit. Furthermore, the recent synthesis of gold Nanoparticles using the medicinal plant Acorus calamus and Cassia auriculate has been reported. reactive compounds: Lignans [(+)-pinoresinol, (+)-medioresinol], alkaloids, flavonoids, steroids (sitosterol 3-0-glucoside), and terpenoids are present in the leaves.[4-68]

Green synthesis of plant extract-AuNP

Nature is rich in plant species that have the advantage of low price, high productivity, environmental friendliness and precise purification compared to other environmentally friendly biological methods. The green route of using plant extracts as reducing agents and stabilizers for the preparation of gold nanoparticles has recently gained interest for several reasons.[71-75]

Plant preparation-General approach for AuNPs.

The direct method involves choosing individual parts depending on the type of plant. For example, collect Euphorbia fischeriana root extract as general antioxidant, Punicagranatum pulp extract as antimicrobial, A. noeanum leaf as antibacterial, and papaya juice as Sensing L-Lys.For example, after chemotherapy, cancer cells become desensitized to repeated drug exposure, and nanoparticles

can increase cellular drug accumulation due to their ability to target and deliver more specific drugs agents and stabilizers. Polyphenols, flavonoids, reducing sugars, polysaccharides, alkaloids, amino acids, vitamins, ketones, phenols, and proteins are examples of plant extract biomolecules. For biosynthesis, a plant must be selected that contains at least one of the above-mentioned chemicals that convert metal ions into elemental metals. First, reduce Au3+ to Au0, then precipitate and stabilize AuNPs by covering the outer surface of gold to prevent aggregation.

1.7 Physical:

A number of advantageous characteristics of spherical AuNPs have been identified, including size- and shape-related optoelectronic capabilities, a high surface-to-volume ratio, great biocompatibility, and minimal toxicity. It was found that contact angle heavily relies on the nanoparticle size. According to the results, the contact angle for de-ionized water droplets ranged from 24° to 67° and for DEG (droplet-based electricity generator droplets), it ranged from 15° to 60°, for nanoparticle sizes that ranged from 14 to 620 nm. AuNPs exhibit several significant physical features, including surface plasmon resonance (SPR) and the ability to quench fluorescence. In aqueous solution, spherical AuNPs exhibit a spectrum of colours (e.g., brown, orange, red, and purple) as the core size grows from 1 to 100 nm, and often exhibit a size-relative maximum absorption between 500 and 550 nm. Furthermore, particles with high charges can cause double layers to form in aqueous environments, and they can be discrete, dispersed, or suspended in the solution. As opposed to the bulk shape, the energy levels of electrons in a substance in nano-form are not as continuous. The containment of the electronic wave function in up to three physical dimensions separates them. This causes a change in surface area and electron containment; the change in material properties is controlled in the same way that melting point, fluorescence, electrical conductivity, and magnetic permeability are Ion coaters are an easy and direct method for generating uniform gold nanoparticles with a narrow size distribution by combining an ion coater on glycerin with a viscous liquid capture medium. A low-cost, low-energy synthesis technique that does not require additives or reducing/stabilizing agents. It is based on a physical low vapor deposition method rather than the conventional hydration process chemical reactions in liquids. The surface plasmon resonance level appears at 530 nm in the absorption spectrum with the formation of gold nanoparticles; red shift with particle size indicates that gold nanoparticles are successfully grown using ion plating. Recently, researchers have focused on new methods of synthesis of different shapes and controlled particle sizes. There are optical physical properties related to AuNP anatomy and physiology.

1.8 Stabilization of AuNPs is performed using various capping/stabilizing agents.

At the beginning of the application of the Turkevich method were finite due to the limited range of AuNPs which can be synthesized by this technique. With passage several advances have been made in the basic method allowed researchers to expand the range of particle sizes synthesized using this method. It was founded in 1973 that by changing the reducing and stabilizing ratio agents, AuNPs of specific sizes ranging from 16–147 nm can be produced.[31–33]. The basic method involved in the Turkevich method.

This method was first reported in 1994 and involves two reactions to synthesize AuNPs with a range of sizes. 1.5–5.2 nm using organic solvents. Method involves using phase transitions such as tetraoctylammonium bromide to transfer gold salts from an aqueous solution to an organic solvent (eg toluene).The gold is then reduced using a reducing agent sodium borohydride and alkanethiol. Alkanethiol stabilizes AuNPs. This reaction causes an orange color change chocolate.

Figure 2B shows a schematic diagram here are the basic steps involved in the Brust method. The growth of seeds is average the previous two methods can only synthesize spheres. AuNPs; however, it can also be configured numerically rod-like geometry and shape.

Method for the preparation of monodispersed gold nanoparticles:

Method for the preparation of monodispersed gold nanoparticles the presence of excess ligaments (digestion representative).The process basically involves heating the colloid Heat for 2 minutes at high temperature (~138ºC). then heat at 110ºC for 5 hours using alkanethiol. Temperature is a major

factor to determine the size distribution of gold colloid. In addition to this method, other methods are also applicable Using ultrasound waves for the synthesis of AuNPs.

1.9 Stabilization of AuNPs

Nanoparticles can be stabilized using a stabilizing agent which basically assists in maintaining repulsive forces to overcome Van der waal forces in the solution of nanoparticles to avoid agglomeration. During the chemical synthesis of AuNPs sodium borohydride or sodium hydride, sodium citrate or ascorbic acid may act as capping and stabilizing agents for AuNPs.

1.10 Other Common Functionalization Methods

Several molecules other than proteins, amino acids, and nucleic acids have also been used for the functionalization of AuNPs for diverse applications. One study has reported the functionalization of AuNPs with anti-human IgG to develop a technique for the detection of human IgG in blood serum samples and the results were found to be consistent with enzyme-linked immunosorbent assay (ELISA).

1.11 Applications of AuNPs in Drug Delivery:

Gold nanoparticles have lately been exploited as an excellent applicant for delivering numerous drugs to their target sites. These payloads range from small drug molecules to bigger biomolecules such as RNA, DNA, and proteins.

Nano-sensors and biomarkers

It is important to calculate the ionizing radiation dose of therapeutic radiation based on accurate and fast radiation measurements. A new and highly sensitive nanosensor for gamma detection is being developed, with a single strand of DNA acting as "radiation sensitive data" and gold nanoparticles as "signal messengers". Under optimal conditions, the radiation nano-sensor has excellent linearity in the dose scale of 0-100 Gy. Used to calculate the dose of ionizing radiation absorbed in the Chernobyl disaster (Wang et al., 2020). MicroRNAs (miRNAs) are small coding RNA molecules of 19 to 22 nucleotides. It can be used as a biomarker due to its early detection properties and can be found in various body secretions and collected samples. For example, studying the expression of kidney microRNA can help detect the cause of kidney failure (diabetic nephropathy) early (Khan et al., 2015). It has not been documented in obesity (Alshammary and Khan, 2021) or type 2 diabetes (Alharbi et al., 2021). However, it is very difficult to identify due to its unique characteristics or small quantity. The use of positively charged gold nanoparticles significantly improves the performance of miRNA biosensors (Gauglitz, 2020, Nossier et al., 2020, Hong et al., 2018, Miao et al., 2018).

Colorimetric sensing of AuNPs

The colorimetric application of AuNPs in sensing is one of the most promising analytical approaches for the recognition of analytes and the detection of biomolecules such as amino acids, peptides and proteins, nucleic acids, inorganic ions, and enzymes. The basic mechanism is that even if the distance between antiparticles is smaller than the average diameter of AuNPs, the color changes from red to blue, which is easily detected by the eye. The coupling path to the sensor can be divided into two strategies: red shift and blue shift in absorption, which causes aggregation and fragmentation of AuNPs. A UV spectrophotometer can be used to record the results (Qin et al., 2018).

Antimicrobial agents

The use of gold nanoparticles as a novel antibacterial agent can provide a viable alternative to current methods for limiting or inhibiting the growth of many pathogenic species. Gold nanoparticles synthesized using Solanum nigrum leaf extract are expected to have free radical scavenging activity as well as antibacterial antistatic properties. These nanoparticles have been

shown to have DPPH and hydroxyl radical scavenging capabilities. These nanoparticles significantly inhibit the growth of pathogenic Staphylococcus saprophytica and Bacillus subtilis (Gram-positive bacteria), as well as Escherichia coli and Pseudomonas aeruginosa (Gram-negative bacteria) (Muthuvel et al., 2014). The antibacterial efficacy of cannabinus hibiscus root extract against P. aeruginosa and Staphylococcus aureus was investigated with gold nanoparticles. The antibacterial effect is stronger in the case of P. aeruginosa, which may be due to the electrostatic interaction between positively charged nanoparticles and negatively charged microbial cells.

HIV

HIV is a virus that damages the immune system. Untreated HIV affects and destroys CD4 cells, a type of immune cell called T cells. Over time, as HIV destroys more CD4 cells, the body becomes more susceptible to various types of diseases and cancers.

HIV is transmitted through body fluids such as:

Blood semen Vaginal and rectal fluids mother's milk the virus is not transmitted through air or water or through casual contact.

Because HIV attacks the DNA of cells, it is a lifelong disease, and while there is currently no drug that can eliminate HIV from the body, many scientists are trying to find one. But with medical care, including a treatment called antiretroviral therapy, it is possible to manage HIV and live with the virus for many years.

If people with HIV are not treated, they may develop a serious illness called acquired immunodeficiency syndrome, also known as AIDS. At this stage, the immune system is too weak to respond to other diseases, infections and conditions. If untreated, life expectancy in the final stages of AIDS is about three years. Trusted Source With antiretroviral therapy, HIV can be successfully managed and life expectancy can be similar to that of people without HIV. An estimated 1.2 million Americans are currently living with HIV. One out of seven people do not know that they are infected with this virus. HIV can cause changes throughout the body.

AIDS is a disease that can develop in people with HIV. It is the most advanced stage of HIV. But just because a person has HIV does not mean they will develop AIDS. HIV kills CD4 cells. A normal CD4 count in healthy adults is 500 to 1,600 per cubic millimeter. A person with HIV whose CD4 count falls below 200 per cubic millimeter will be diagnosed with AIDS. A person with HIV may also be diagnosed with AIDS if they develop an opportunistic infection or cancer that is rare in people who do not have HIV. An opportunistic infection such as Pneumocystis jiroveci pneumonia is one that occurs only in a severely immunocompromised person, such as someone with advanced HIV infection (AIDS). If left untreated, HIV can progress to AIDS within a decade. There is currently no cure for AIDS, and without treatment, life expectancy after diagnosis is about 3 years. This may be shorter if the person develops a severe opportunistic illness. However, treatment with antiretroviral drugs can prevent AIDS from developing. If AIDS develops, it means that the immune system is severely weakened, that is, weakened to the point where it cannot successfully respond to most diseases and infections. It makes a person living with AIDS vulnerable to a variety of illnesses, including:

Pneumonia
Tuberculosis
Oral thrush, a fungal condition in the mouth or throat
Cytomegalovirus (CMV), a type of herpes virus
Cryptococcal meningitis, a fungal condition in the brain
Toxoplasmosis, a brain condition caused by a parasite
Cryptosporidiosis, a condition caused by an intestinal parasite
Cancers including Kaposi's sarcoma (KS) and lymphoma.

Early symptoms of HIV

The first few weeks after someone contracts HIV is called the acute infection stage. During this time, the virus reproduces rapidly. The person's immune system responds by producing HIV antibodies, which are proteins that take measures to respond against infection. During this stage, some people have no symptoms at first. However, many people experience symptoms in the first month or so after contracting the virus, but they often don't realize HIV causes those symptoms. This is because symptoms of the acute stage can be very similar to those of the flu or other seasonal viruses, such as:

they may be mild to severe
they may come and go
they may last anywhere from a few days to several weeks.

Early symptoms of HIV can include:

fever
chills
swollen lymph nodes
general aches and pains
skin rash
sore throat
headache
nausea
upset stomach

Because these symptoms are similar to common illnesses like the flu, the person who has them might not think they need to see a healthcare provider, and even if they do, their healthcare provider might suspect the flu or mononucleosis and might not even consider HIV. Whether a person has symptoms or not, during this period their viral load is very high. The viral load is the amount of HIV found in the bloodstream. A high viral load means that HIV can be easily transmitted to someone else during this time. Initial HIV symptoms usually resolve within a few months as the person enters the chronic, or clinical latency, stage of HIV. This stage can last many years or even decades with treatment.

HIV symptoms can vary from person to person.

What are the symptoms of HIV?

After the first month or so, HIV enters the clinical latency stage. This stage can last from a few years to a few decades. Some people don't have any symptoms during this time, while others may have minimal or nonspecific symptoms. A nonspecific symptom is a symptom that doesn't pertain to one specific disease or condition. These nonspecific symptoms may include:

headaches and other aches and pains
swollen lymph nodes
recurrent fevers
night sweats
fatigue
nausea
vomiting
diarrhea
weight loss
skin rashes
recurrent oral or vaginal yeast infections
pneumonia
shingles

As with the early stage, HIV is still transferable during this time even without symptoms and can be transmitted to another person. However, a person won't know they have HIV unless they get tested. If someone has these symptoms and thinks they may have been exposed to HIV, it's important that

they get tested. HIV symptoms at this stage may come and go, or they may progress rapidly. This progression can be slowed substantially with treatment. With the consistent use of this antiretroviral therapy, chronic HIV can last for decades and will likely not develop into AIDS, if treatment was started early enough.

Epidemiology of HIV/AIDS

he global epidemic of HIV/AIDS (human immunodeficiency virus infection and acquired immunodeficiency syndrome) began in 1981, and is an ongoing worldwide public health issue, according to the World Health Organization (WHO), by 2023, HIV/AIDS had killed approximately 40.4 million people, and approximately 39 million people were infected with HIV globally. Of these, 29.8 million people (75%) are receiving antiretroviral treatment. There were about 630,000 deaths from HIV/AIDS in 2022. The 2015 Global Burden of Disease Study estimated that the global incidence of HIV infection peaked in 1997 at 3.3 million per year. Global incidence fell rapidly from 1997 to 2005, to about 2.6 million per year. Incidence of HIV has continued to fall, decreasing by 23% from 2010 to 2020, with progress dominated by decreases in Eastern Africa and Southern Africa. As of 2020, there are approximately 1.5 million new infections of HIV per year globally.

According to the World Health Organization (WHO), the prevalence of HIV in the Africa Region was estimated at 1.1 million people as of 2018. The African Region accounts for two thirds of the incidence of HIV around the world. Sub-Saharan Africa is the region most affected by HIV. In 2018, an estimated 61% of new HIV infections occurred in this region, and as of 2020, more than two thirds of those living with HIV are living in Africa. HIV rates have been decreasing in the region: From 2010 to 2020, new infections in eastern and southern Africa fell by 38%. Still, South Africa has the largest population of people with HIV of any country in the world, at 8.45 million, 13.9% of the population as of 2022. As of 2022, it is estimated that the adult HIV prevalence rate is 6.2%, a 1.2% increase from data reported in the 2011 UNAIDS World Aids Day Report.

In Western Europe and North America, most people with HIV can get treatment and live long and healthy lives. By 2020, 88% of people living with HIV in the region know their HIV status, and 67% have suppressed viral loads. In 2019, approximately 1.2 million people in the United States had HIV; 13% did not realize they were infected. As of 2016, there were approximately 63,110 cases of HIV in Canada. In 2020, there were 106,890 people living with HIV in the UK and 614 deaths (99 of these due to comorbidity with Covid-19). In Australia, as of 2020, there were approximately 29,090 cases.

Around the world, HIV disproportionately affects certain key populations (sex workers and their clients, men who have sex with men, people who inject drugs, and transgender people) and their sexual partners. These groups account for 65% of global HIV infections and 93% of new infections outside sub-Saharan Africa. In Western Europe and North America, men who have sex with men account for about two-thirds of new HIV infections.

In sub-Saharan Africa, 63% of new infections are women, with young women (aged 15 to 24) twice as likely as men of the same age to be living with HIV.

HIV originated in non-human primates in Central Africa and reached humans several times in the late 19th or early 20th century. A reconstruction of its genetic history suggests that HIV-1 group M, the strain most responsible for the global pandemic, may have originated in Kinshasa, the capital of the Democratic Republic of the Congo, around 1920. In 1983, the HIV virus was discovered and identified as the cause of AIDS.

HIV Prevention:

Treatment options for HIV

Regardless of viral load, treatment should begin as soon as possible after HIV diagnosis.

The main treatment for HIV is antiretroviral therapy, a combination of daily medications that prevent the virus from reproducing. These help protect CD4 cells, keeping the immune system

strong enough to fight disease. Antiretroviral therapy helps prevent HIV from progressing to AIDS. It also helps reduce the risk of HIV transmission to others. When treatment is effective, the viral load will be "undetectable". The person still has HIV, but the test results do not show the virus. However, the virus is still in the body, and if that person stops taking antiretroviral therapy, the viral load will rise again, and HIV can start attacking CD4 cells again.

Antiretroviral therapy (ART):

Antiretroviral therapy (ART) is the cornerstone of prevention and management of HIV infection. To evaluate new data and treatments and incorporate this information into updated recommendations for initiating therapy, monitoring individuals starting therapy, changing regimens, and preventing HIV infection for individuals at risk. New evidence collected since the International Antiviral Society-USA 2016 recommendations via monthly PubMed and EMBASE literature searches up to April 2018; data presented at peer-reviewed scientific conferences. A volunteer panel of experts in HIV research and patient care considered these data and updated previous recommendations. ART is recommended for virtually all HIV-infected individuals, as soon as possible after HIV diagnosis. Immediate initiation (eg,rapid start), if clinically appropriate, requires adequate staffing, specialized services, and careful selection of medical therapy. An Integrase strand transfer inhibitor (InSTI) plus 2 nucleoside reverse transcriptase inhibitors (NRTIs) is generally recommended for initial therapy, with unique patient circumstances (eg, concomitant diseases and conditions, potential for pregnancy, cost) guiding the treatment choice. CD4 cell count, HIV RNA level, genotype, and other laboratory tests for general health and co-infections are recommended at specified points before and during ART. If a regimen switch is indicated, treatment history, tolerability, adherence, and drug resistance history should first be assessed; 2 or 3 active drugs are recommended for a new regimen. HIV testing is recommended at least once for anyone who has ever been sexually active and more often for individuals at ongoing risk for infection. Preexposure prophylaxis with tenofovir disoproxil fumarate/emtricitabine and appropriate monitoring is recommended for individuals at risk for HIV. Advances in HIV prevention and treatment with antiretroviral drugs continue to improve clinical management and outcomes for individuals at risk for and living with HIV.

When to Start

Recommendations for initiating antiretroviral therapy (ART) are summarized in Box 1. In patients with established HIV, ART should be initiated as soon as possible after diagnosis.[1]The question of when to start ART is focused now on whether immediate ART (same day to14 days after diagnosis) is preferred. The World Health Organization endorsed ART initiation within 7 days of new diagnosis (including same day), citing improved viral suppression.[4] Rapid initiation of ART requires improving linkage to care and addressing structural barriers (eg, staffing and services availability) within clinics and ART distribution systems.

Rapid ART Start

Randomized trials in Lesotho, Haiti, and South Africa showed significant improvements in viral load suppression at 10 or 12 months and retention in care with rapid initiation of therapy.[5-7] In 1 study, individuals were randomized to early ART with simplified counseling and point-of-care CD4 cell assays or to standard care. In the intervention group, 80% began ART within 14 days and 71% started ART the same day of eligibility, compared with 38% and 18%, respectively, in the control group. Virologic suppression at 1 year was improved in the intervention group (85% vs 75%).8 Several cohorts examined the feasibility, outcomes, and challenges of rapid ART start.[9] Meta-analyses of 8 cohorts showed an improvement in the proportion of patients starting ART within 3 months but no benefit on retention in care.[10] A statistically nonsignificant trend toward worse viral suppression was observed for those who started ART rapidly in 1 cohort.[10] San Francisco implemented a citywide rapid ART program in which newly diagnosed persons were linked to care within 5 days from diagnosis and offered treatment on the day of their clinic visit. Of 265 newly diagnosed persons, 97% were linked to care (30% within 5 days) and 81% started ART; time from

diagnosis to HIV RNA level below 200 copies/mL decreased by more than 50% and time from first care visit to ART decreased from 27 days to 1 day.11,12 A large HIV clinic in Atlanta implemented rapid access to ART on the day of the initial visit. Median time from initial diagnosis to HIV-1 RNA level below 200 copies/mL decreased from 67 to 41 days; however, the program was not sustainable because of increased patient load and inadequate funding for staffing.[13] Despite the success of rapid ART initiation in some settings, starting ART on the day of diagnosis requires coordination between testing and treatment settings and access to resources that may limit treatment uptake. All elements of conventional treatment initiation must be in place at the treatment site but provided in a way that ensures immediate access.[12] ART initiation, including rapid start, is recommended for all infected ambulatory patients committed to starting ART (unless the patient has symptoms that suggest an opportunistic infection for which immediate ART is contraindicated) or for those with unclear HIV diagnosis (eg, discordant serologic or rapid test results) (evidence rating AIII). Because of concerns about transmitted drug resistance (eg, K103N mutation), immediate ART should not be nonnucleoside reverse transcriptase inhibitor (NNRTI)–based (evidence rating AIII). Dolutegravir/tenofovir alafenamide (TAF) (or tenofovir disoproxil fumarate [TDF])/ emtricitabine (or lamivudine) or bictegravir/TAF/emtricitabine or boosted darunavir TAF (or TDF)/emtricitabine (or lamivudine) are recommended for rapid initiation (AIII). Patients requiring abacavir should not begin until the result of testing for the HLAB*5701 allele is available (evidence rating AIa).

When to Start ART in the Setting of Active Opportunistic Infections and Malignancies

Recommendations for initiating ART in the setting of active opportunistic infections (OIs) remain unchanged.[1] ART should be started within the first 2 weeks after diagnosis for most OIs (evidence rating AIa). Data further support the recommendation to start ART within the first 2 weeks of initiation of tuberculosis treatment for patients with CD4 cell counts below 50/μL and within the first 2 to 8 weeks for those with CD4 cell counts of 50/μL and above (evidence rating AIa). For patients with cryptococcal meningitis in high resourced settings with access to optimal antifungal therapy, frequent monitoring, and aggressive management of intracranial.

Pressure, ART should be started within 2 weeks of diagnosis.[14,15] Careful monitoring for immune reconstitution inflammatory syndrome. For individuals diagnosed with an essential concurrent HIV malignancy, ART should be started immediately. Early adverse effects of ART can be monitored and controlled during cancer staging, and a nuclear test is done.

Primary OI prophylaxis

With the universal recommendation of ART, the incidence of Pneumocystis pneumonia and major AIDS-related OIs has declined. compared to 1.45 and 0.4 per 100 person-years in the United States, respectively Stats.[16] For individuals with viral suppression while taking ART. The incidence and overall mortality of Mycobacterium avium complex disease are sufficiently low.[17,18] that primary Mycobacterium avium complex prophylaxis is no longer recommended (evidence rating AIIa).

Primary prophylaxis for Pneumocystis pneumonia is still recommended for patients meeting CD4 criteria (evidence rating AIa).[17,19]

Primary prophylaxis for cryptococcal disease is not recommended. In settings where incidence is low (evidence rating AIII).

Conclusion:

Gold nanoparticles consider as a promising future for scientists and researchers, especially in the medical field. Biosynthesis from plants, bacteria, and fungi delivers the desired result with minimal damage compared to other constructing methods. HIV treatment has found its way with the use of gold nanoparticles.

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