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Gold nanoparticle: It's importance in biomedical fields

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Abstract: Nanoparticles are the substances which fall under the nano-range and are so small that they can easily circulate in the body. There are various types of nanoparticles like liposomes, dendrimers, fullerenes, virosomes, metallic nanoparticles, silica nanoparticles, spinel ferrite nanoparticles, magnetic iron oxide nanoparticles, silver nanoparticles, Out of all the other nanoparticles gold nanoparticles are one of the particles which are highly utilized in the research work because of their non toxic and compatible nature with the human body. They are also made in such a way that it can be used as a delivery system by loading the drugs into it and can then cross various membranes and barriers to deliver the drug at the right site and also, they can be used in various diagnostic and imaging process for tumors. Depending on the use gold nanoparticles comes in various shape like that of cage, shell, rod, sphere, all of these have separate manufacturing process which could be chemical as well as organic in nature. There are mainly two approaches which are followed for manufacturing of the gold nanoparticles top down and bottom up approach. Their characterization is done using techniques of UV spectrophotometer, X-ray Diffraction, High Resolution Transmission Electron Microscopy, Dynamic Light Scattering, Surfaced Enhanced Microscopy. They find their application in use against vectors, in cardiovascular disease, in catalytic application, in hepatoprotective application, application as an anti-oxidant, in the treatment of skin cancer, in the diagnosis and therapy of Alzheimer's disease.

Key words: Gold nanoparticle, microbial system, characterizations

1. INTRODUCTION

1.1. Nanoparticles: -

Novel Drug Delivery System (NDDS) is that branch of science that carries particles which is approximately 10^{-9} m. The development of nanotechnology cannot exist under the parameters which are conventional. The nano size range of the drug helps it to improve drug's immunogenicity, metabolism, solubility which leads to reduced adverse effects and dose. (Qunye He, 2020)

They are divided into following categories based on their chemical and physical properties: -

1.1.1. Liposomes

They are in a shape of vesicle which has an internal bilayer of phospholipid and an aqueous solvent. The phospholipid layer which also acts as a protective layer has a property which allows an increased penetration and also delivers hydrophobic as well as hydrophilic contents. (Daan J.A. Crommelin, 2019)

1.1.2. Dendrimers

They have a molecule which is symmetrical in nature with branch like extensions radiating outward and has a central core. These branches are known as 'generations' and this lies in a three-dimensional structure which allows delivery of drugs which are versatile in nature because of the conjugation of oligonucleotides to outward terminals and to form a multivalent system. (Mohammad Yousefi, 2020)

1.1.3. Fullerenes

These are ellipsoid, hollow or are tube like and are formed of carbon and the mostly known fullerene is Buckyball or buckminsterfullerene and they are made up of 60 atoms of carbon and these are arranged into a spherical shape resembling to that of a soccer ball(Raza *et al.,* 2015; Mehta *et al.,* 2016). They show these types of properties because of their ability of scavenging free radicals and then they are able to provide antioxidant effect. (Teresa Gatti, 2017)

1.1.4. Virosomes

It contains viral glycoprotein enclosed in an outer phospholipid membrane, it is protected from extracellular degradation by the viral envelope which makes it suitable for delivery of vaccines and it was helpful in the development of vaccines like human papillomavirus, influenza, hepatitis A, B etc. (CAO Zheng, 2013)

1.1.5. Metallic nanoparticles

Use of metals in nanoparticles is a common practice and the most widely used nanoparticles is gold because of its low toxicity, biomedical application, ability to detect tumor using near infra-red light, oxides of zinc and titanium are used in sunscreens which are inorganic in nature to reduce the white chalky appearance and still be able to protect from ultraviolet radiation and silver nanoparticles are being used because of their antiseptic effects. (Peter W. Hashim, 2019)

1.1.6. Silica nanoparticles

The mesopores form of the silica nanoparticles are one of the most essential components used by scientists. They are such a good candidate of the drug delivery because of their physiochemical properties which are totally unique, they also have a very prominent application in the optical and electrochemical biosensing. They are very capable of encapsulating big materials in the pores which can then be very easily delivered to the target. Their properties also enable them to be used in catalytic process and many more applications like that of bioimaging, catalysis, and biosensing and disease therapy. (Houman Kholafazad Kordasht, 2019)

1.1.7. Spinel ferrite nanoparticles

They are one of the popular nanoparticles and are well known because of their applications in various fields from biomedical to industrial, wherein its use in industry is that of adsorbents, waste water management, in the making of electronic materials and catalysts. Its use in the biomedical field is that of magnetic resonance imaging (MRI), separation by the use of bio magnets, in the treatment of tumor by hyperthermia, in the release and delivery of drug. There are also equipped in the manufacturing of modern generation biosensors and sensors which are used in biomedical as well as industrial areas and they also have antimicrobial activity against pathogens and this activity is strong in nature. (Kebede K. Kefeni, 2019)

1.1.8. Magnetic iron oxide nanoparticles

These nanoparticles are of two types namely magnetite and maghemite which are superparamagnetic in nature which means that a particular temperature where there is no magnetic field applied externally then their magnetization becomes zero and this state is called superparamagnetic state. By the application of an external magnetic field the nanoparticles are easily magnetized because their susceptibility is very high, this property makes both of them an appropriate setup for magnetic based imaging, hyperthermia and targeting. In majority of the cases the small particle sized are preferred which have a great chance of crossing blood brain barrier and avoid the activation of the complement system. (Liron L. Israel, 2020)

1.1.9. Silver nanoparticles

It is one of the most famous types of nanoparticle which is widely used and is known by all. They provide their service in areas like biotechnology, magnetic fields, engineering, medicinal devices, electronics and many more. They have remarkable physicochemical properties which has been helpful in the screening as well as treatment of various diseases either in combination or alone (Bhatia *et al.*, 2013; Mishra *et al.*, 2018). They have also been designed in the form of a hybrid and have been used in food industry, cosmetics, sunscreen, medical devices, electronic, hygiene products and many more. They are being manufactured by the use of gamma radiation, chemical reduction and reduction by photochemical method. (Zahid Hussaina, 2019)

1.1.10. Gold nanoparticles

Gold nanoparticles have a higher compatibility with the human body due to which they are used for delivery of drug, treatment of cancer, imaging for biomedical purposes, diagnosis etc. they also have a higher level of stability and less amount of toxicity, and has a small dimension and interaction with a number of substances. They are able to soak infrared lights as they surface area which is larger in size and have optical properties they can also be loaded with numerous therapeutic agents and have shown a high amount of potential to be used as delivery system of drugs. They find their major applications in the field of biomedicines and recently it was seen that they were very much capable of crossing the barrier present in brain and also known as blood brain barrier. There is a possibility of their interaction with DNA which could lead to genotoxic effects. They are known for their ability to produce heat which is very helpful for the targeting and destruction of tumors leading to their use in photodynamic therapy. Chemical and biological methods are very common out of the various methods for the production of the nanoparticles. It is seen that the chemical method has an advantage as it offers better size and shape as compared to the biological method for the production of the nanoparticles. (Ramalingam, 2019)

2. Gold nanoparticles and their types

2.1. Gold nanospheres

Two nanometer to over hundred nanometer in diameter is the range in which they fall and can be synthesized by the technique known as that reduction in controlled manner in which the aqueous solution of $HAuCl_4$ is reduced by the use of the different reducing reagents which is taken depending on the condition in which the production is taking place . Out of many of the reducing agent Citrate is one of the most frequently used for the reduction of particles, it is able to produce gold nanospheres which are nearly monodisperse and it is possible to control their size by making variations in the ratio of gold or citrate. It is observed that small amount of citrate when taken tends to yield larger nanospheres. (Staci Adams, 2016)

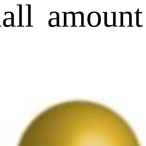

Fig. no. 1: Gold nanosphere

2.2. Gold nanorods

Their synthesis takes place by the use of template method, in this method gold particles are electrochemically deposited on the membranes of alumina template or their deposition could also take place in pores of the nanoporous polycarbonate. Determination of their diameter takes place by considering the pore diameter of the template membrane, and the control of their length. (Jie Zhou, 2017)

Fig. no. 2: Gold nanorods

2.3. Gold nanoshells

Their main use is in optical imaging; this is done by the use gold nanoparticles which are used as a contrasting agent but they have a fixed amount of applications in studies conducted in humans. In 700-900 nm of the near-infrared region, absorbance of biomolecules takes place, which provide a comparatively clear picture for the use of the optical imaging. They can be designed and made with the Surface Plasmon Resonance (SPR) with the use of slight modification which takes place in the composition by modifying the shell thickness and SPR peak ratio the composition of Gold nanoshell can be changed. (Guohui Wu, 2009)

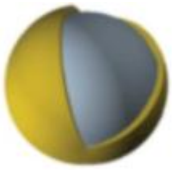

Fig. no. 3: Gold nanoshells

2.4. Gold nanocages

They are having a characteristic governable pore that area unit present on the surface and area unit synthesized via galvanic replacement reaction between binary compound truncated silver nanocubes and aqueous solution of $HAuCl_4$. These silver nanostructures area unit generated via controlled morphologies of polyol reduction, whereby $AgNO_3$ is reduced by ethylene glycol to get silver atoms then nanocrystals or seeds. By the introduction of adequate silver atoms in the seeds the required nanostructures can be produced by dominating the crystalline silver seed structures within the presence of polyvinylpyrrolidone that is a polymer which is capable of by selective binding to minimum of one hundred surfaces. (Eun Jung Lee, 2016)

Fig. no. 4: Gold nanocages

2.5. SERS (Surface Enhanced Raman Scattering) nanoparticles

It has multiple advantages over existing technologies as it is an optical technique, techniques like fluorescence and chemiluminescence has a higher sensitivity, has a performance which is superior in the case of biological matrices, has a higher level of multiplexing, and robustness and blood. The use of the 13 nm gold nanosphere which is modified with Cy3 capped and labelled alkylthiol oligonucleotides strands are used as a probe for the monitoring of the presence of a specific DNA strand target. The main reason for the selection of this Cy3 group was because of its larger Raman cross-section. (Dan Song, 2019)

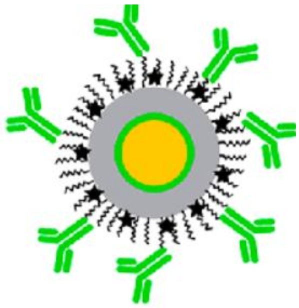

Fig. no. 5: SERS nanoparticles

3. Approaches for synthesis

As it is well established that the size of the nanoparticles is between 1-100 nm and they can only be synthesized using two methods. The first one being top-down method wherein the bulky particles are taken and are broken down into the size of nanoparticles. As we all know that the conventional method of synthesis of gold nanoparticle include reduction of gold by the use of the reducing agent prime example being that of citrate which was given in 1951 by Turkevitch, other reducing agents which can be used are hydrazine, gallic acid and hydrogen peroxide. (Yogita Kumari, 2019)

There is also a method which is size selective in which functionalized thiol liquid ionic in nature are used as one of the major components. All these methods are very efficacious but the uses of organic liquids make them unsuitable for diagnostic purpose like that of detection of proteins, nucleic acids and saccharides. (Dan Song, 2019)

Also the use of the solvents which are non-polar in nature and are chemicals which are toxic in nature has a limiting effect of these nanoparticles in the field of the clinical department, these chemicals includes sodium borohydride, oleyl amine, citric acid, hexadecyltrimethylammonium bromide are known to be irritable, harmful, hazardous or flammable hence there is a need of the development of the biocompatible, eco-friendly, non-toxic methods. Synthesis done using yeasts, bacteria, actinomycetes and viruses which can be used for the clean synthesis of gold nanoparticles and this helps to connect microbial biotechnology with that of the nanotechnology. (Capek, 2016)

These methods have numerous advantages such that of the high biocompatibility and reproducibility and also there is no use of the solvents which are toxic or organic in nature. The use of these organisms is helpful as they are easy to handle and can be manipulated easily (mainly genetic manipulation).

Figure number 6 shows the production of the gold nanoparticles by different methods

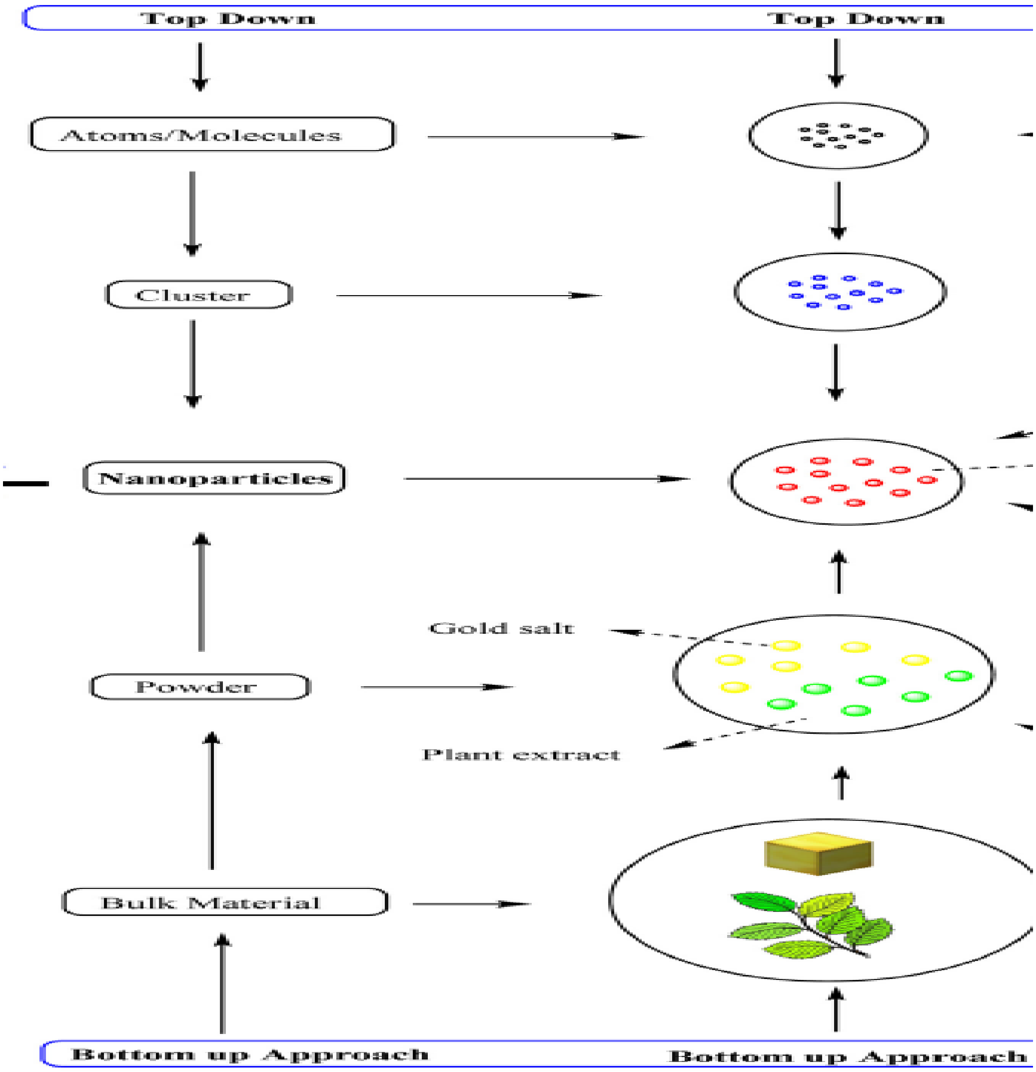

Fig. no. 6: Manufacturing of the gold nanoparticles by different methods (Dan Song, 2019)

4. Synthesis of gold nanoparticles

4.1. Preparation of gold nanoparticles by microbial system

4.1.1. By bacterial synthesis

Bacteria both gram- negative and gram- positive are observed to take up and absorb ions of heavy metal. They are very easy to handle and to manipulate but they do not have proper shape and size as that of industrial scale synthesis. By learning the molecular mechanism of the organism, we will be able to have a better control of shape, size and crystallinity of that nanoparticle but there are only a very few groups of bacteria which are able to reduce selectively the metal ion. There are many organisms which are used to produce hexagonal, cubic and spherical which lies in range from 5-200 nm (using organism like *Shewanella algae, Pseudomonas aeruginosa, Rhodobacter capsulatus*). *Rhodopseudomonas capsulata* is a type of bacterium belonging to prokaryotic class which was known to reduce Au (3^+) to Au (0) that to at room temperature. These particles lie in the range of 10-20 nm that to in 7.0pH but when the pH was changed to 4 the formation of gold nanoplates were seen. *Bacillus megatherium* dried powder can also be used to reduce Au (3^+) to monodisperse gold nanoparticles and then by the use of dodecanethiol was used to cap the ligand to stabilize the particles and that due to the presence of thiol group formation of small spherical nanoparticles 0.8nm in size was observed. (Kalimuthu, 2020)

4.1.2. By fungal synthesis

This synthesis of nanoparticles has more advantages over the microbial systems because of the fact that mycelial mesh is able to handle higher flow pressure and the force of mixing in bioreactors or other chambers. In this the gold nanoparticles are of 20 nm approximately that to on the surface of the fungus and on the cytoplasmic membrane of the mycelium of fungus. *Verticillium luteoalbum* is used to generate spherical particles with a diameter less than that of 10 nm when incubated at pH 3 with Au (3^+) but hexagonal and triangular particles were synthesized at pH 5. Due to the presence of enormous secretory components the generation of nanoparticles takes place extracellularly as a result it reduces the number of nanoparticles lost in reduction and capping. Shankar et al. discovered that species of *Colletotrichum* reduces Au (3^+) to gold nanoparticles rapidly, this is also true for the fungus species of *Trichothecium* which also rapidly converts Au (3^+) to gold nanoparticles. TEM image proves that hexagonal, triangular, rod-like gold nanoparticles had an average size of 5-200nm. (Kalimuthu, 2020)

4.1.3. By yeast synthesis

Saccharomyces cerevisiae which is also known as baker's yeast is helpful in the preparation of gold nanoparticles with the help of the aldehyde group which is present in the reducing sugar which is present in their cell wall. *Pichia jadinii* is responsible for producing gold nanoparticles which are triangular, spherical and hexagonal in nature which are less than 100 nm intracellularly, and these particles are mainly distributed in the cytoplasm. *Yarrowia lipolytica* are known for the synthesis gold nanoparticles on their cell wall. In a pH dependent manner, the reduction of the Au (3^+) occurs like when the incubation pH is 2, they tend to form triangular and hexagonal crystals of gold whereas between pH 7 to 9 production of purple and pink color particles takes place and belonging to an average size of 15 nm. (Kalimuthu, 2020)

4.1.4. By actinomycetes synthesis

They are primarily known for the synthesis of the metabolites which are secondary in nature like antibiotics but actinomycetes ability to form gold nanoparticles has opened a new dimension in their use. They fall under the classification of prokaryotes but they share some of the important traits with that of the fungi. *Thermomonospora* was reported to synthesis monodispersed gold nanoparticles where an average size of 8 nm. *Rhodococcus* which is an alkali tolerant actinomycetes accumulates 5-15 nm gold nanoparticles intracellularly with the help of reductase present on both the cell wall and the membrane of cytoplasm which reduces Au (3^+) to Au (0). (Kalimuthu, 2020)

4.1.5. By algae synthesis

Synthesis of gold nanoparticles can also take place by the use of the algae. *Sargassum wightii was* the first of the marine algae which was used to synthesis the gold nanoparticles that to in relatively shorter period of time as that of the other organism, as 95% of the existing Au (3^+) was converted within 12 hours. *Tetraselmis kochinensis* can produce gold nanoparticles intracellularly within 48 hours when exposed to the ions of Au (3^+). Purple color confirms the production of the 15 nm nanoparticle. *Nitzschia diatom* which is a unicellular, aquatic, photosynthetic microalgae are able to form gold nanoparticles by showing a particular color of ruby red. Incubation of 8 hours was enough for the formation of the Au (3^+) ion. (Kalimuthu, 2020)

4.2. Manufacturing of gold nanoparticles by using plant parts

In this type of synthesis, the nanoparticles are not synthesized using hazardous chemicals and hence no toxic by-products are produced, this is an eco-friendly way of manufacturing of nanoparticles and hence doesn't have any adverse effect on human beings and environment. The conventional method has an edge as by that we can get nanoparticles in desired range, size and morphology but these methods are complicated, costly and are outdated. The green synthesis on the other hand produces less waste, it is fast, has simple procedure for manufacturing. (Kalimuthu, 2020)

This synthesis takes up bottom-up approach in which we metal atoms assemble and then forms clusters leading to the formation of nanoparticles. During the synthesis the nanoparticles are made stable by the biological compounds which are present in the materials used for the synthesis as they help by acting as reducing and capping agent hence leading to the control in shape and size of the nanoparticles and this have further application in the biomedical fields. (Tariq Khan, 2019)

The table number 1 shows the use of parts of the plants for the synthesis of gold nanoparticles.

Table no.1: Plant parts used in green synthesis (Kalimuthu, 2020)

Plant part	Name of plant
Marine plants	*Sargassum muticum*
Fruits	*Couroupita guianensis*
Fruit peels	*Punica granatum*
Leaves	*Tridax procumbens*
Seeds	*Syzygium cumini*

5. Characters of gold nanoparticles

5.1. Localized Surface Plasmon Resonance

The first property of gold nanoparticle is the Localized Surface Plasmon Resonance (LSPR), application of which can be seen in the field of immunotherapies for the purpose of treatment or diagnosis. This property is due to the collective oscillation near the surface of the gold nanoparticles of the electrons because of the input of light at a narrow frequency range. LSPR leads to the strong scattering of light with absorption. Confinement of photon makes strong electromagnetic field on the surface of the gold nanoparticles. These particles are sensitive to shape, size and surface chemistry of gold nanoparticles. This property gives it numerous applications mainly in the field of biomedical imaging. LSPR is measured in UV visible spectroscopy for shape and size and also its affinity and stability of the molecules associated with gold nanoparticles. (Hai Chen, 2018)

5.2. Zeta potential

Compounds such as amine, citrate, thiols are used to modify as well enhance the surface to get the colloidal gold nanoparticles. Thiols includes compounds like Poly Ethylene Glycol (PEG), mercaptopurine and glutathione are considered to have a positive effect in the stability of the gold nanoparticles for its use in the biological application as it has strong bonds of gold-sulfide. The modifications that take place on the surface affect the zeta potential and LSPR. The use of zeta potential is to confirm the charge of the gold nanoparticles which is helpful in the surface modification of the molecules.

5.3. Transmission Electron Microscopy (TEM) and Dynamic Light Scattering (DLS)

Gold nanoparticles colloidal stability is seen by the use of the high-resolution Transmission Electron Microscopy (TEM) and Dynamic Light Scattering (DLS) wherein DLS is use for the measurement of the hydrodynamic diameter with interaction of the ligands which are surface bound, aggregation of gold nanoparticles and both DLS and TEM gives us the information of the dispersion of the gold nanoparticles. (Ramalingam, 2019)

5.4. Fluorescence Resonance Energy Transfer (FRET)

The ability of the gold nanoparticles for the fluorophores comes from the deactivation pathway based on the overlapping in between other excited fluorophores spectrum of emission and the gold nanoparticles. Fluorescence Resonance Energy Transfer (FRET) occurs in the slightest presence of gold nanoparticle even that of 1nm due to the non-radiative and radiative rate of decay of the fluorescent molecules which effects the gold nanoparticles. These gold nanoparticles behave as an electron acceptor to grab the fluorophores of the Photon-induced Electron Transfer (PET) by charging/discharging of the core of gold for its use in the fabrication of the sensors. (Huang, 2010)

6. Evaluation of gold nanoparticles

- Evaluation of gold nanoparticles can be carried out using UV-Visible spectra wherein the particle size can be seen between 200 to 900 nm using UV-Visible spectrophotometer. Instruments like Shimadzu UV-1800 are used.
- X-ray diffraction is another method for the characterization of the nanoparticles. Instruments like Rigaku Miniflex-2 are used.
- High Resolution Transmission Electron Microscope (HR-TEM) is also used for the characterization of the gold nanoparticles. Instruments like JOEL-JEM 2100 are used. (R. Ranjana, 2019)
- To find the average distribution and size of nanoparticles use of Dynamic Light Scattering (DLS) is used which uses instruments like Tri-Blue particle size analyzer. (JyothiKumara, 2019)
- By the use of SEM analysis characterization can be carried out in which the 2D images of the various samples can be analyzed and they are considered to give more valid and accurate data. (Mekprayoon, 2019)

7. Application of gold nanoparticles

Serial No.	Type of Nanoparticle	Application	Reference
1.	Gold nanoparticle synthesized by the use of *Lycopersicon esculentum*	It has a good antibacterial activity for *Staphylococcus aureus.*	(Ahmad, 2017)
2.	Gold nanoparticle synthesized by the use of *Mentha piperitta*	It has a good antifungal activity against *Penicillium italicum*	(Ahmad, 2017)
3.	Gold nanoparticle synthesized by the use of *Artocarpus heterophyllus*	It showed more antibacterial activity than ampicillin loaded gold nanoparticles.	(Ahmad, 2017)
4.	Gold nanoparticle synthesized by the use of *Momordica cochinchinensis*	It had more antibacterial activity towards *Pseudomonas aeruginosa*	(Ahmad, 2017)
5.	Gold	It has more antibacterial activity towards	(Ahmad, 2017)

	nanoparticle synthesized by the use of *Couroupita guianensis*	*Bacillus cereus*	
6.	*Trianthema decandra* synthesized Gold nanoparticle	It has an excellent antibacterial activity against *Yersinia enterocolitica, Escherichia coli*	(Ahmad, 2017)
7.	Gold nanoparticle synthesized by the use of *Helianthus annuus*	It showed good antifungal properties.	(Ahmad, 2017)
8.	Gold nanoparticle synthesized by the use of *Phyllanthus emblica*	Excellent antibacterial activity against *Pseudomonas aeruginosa.*	(Ahmad, 2017)
9.	Gold nanoparticle synthesized by the use of *Beta vulgaris*	It has a good antibacterial activity against *Proteus vulgaris*	(Ahmad, 2017)
10.	For the diagnosis and treatment of cancer	Probes made up of nanoparticles enter the body and gets accumulate at the site of the tumor and thus this is helpful in the screening of tumor by making illuminating gold nanoparticles and the same can be loaded with the drug for the treatment of the tumor. They are protected from degradation by the use of the co-polymer.	(Kalimuthu, 2020)
11.	Use in immunotherapies	It is used for the targeted delivery of the drug to the immune system in the case of cancer.	(Rupara, 2019)
12.	Use in vaccines	Studies have suggested that when gold nanoparticles are conjugated with the active molecule it leads to the generation of immunity like that of the vaccine, but these studies are in their preliminary phase in animal models.	(Rupara, 2019)
13.	Gold nanoparticle use in biosensing	It works by directly transferring electrons between the active site and the electrode leading to electrochemical biosensing	(Borran, 2018)

14.	Use against vectors	It is seen that gold nanoparticles when combined with *Cymbopogon citratus* leaf extract is toxic to *Aedes stephensi* and *Aedes aegypti*.	(Benellia, 2018)
15.	Use against *Plasmodium* parasite	Auronafin is a gold nanoparticle which has drug in it which is currently being studied for its anti-parasitic action against plasmodium and the nanoparticles can inhibit the growth of these plasmodiums.	(Benellia, 2018)
16.	Use against *Leishmania* parasites	Gold nanoparticles incorporated with natural rubber are seen to decrease the population growth rate in *Leishmania brasiliensis*.	(Benellia, 2018)
17.	Use against *Toxoplasma* parasites	Gold nanoparticles incorporated by antibodies have toxic effect against toxoplasma parasites.	(Benellia, 2018)
18.	Use against *Cryptosporidium* parasites	Gold nanoparticle probe is used for the detection of *Cryptosporidium parvum* by the assay of immune-dot blot.	(Benellia, 2018)
19.	Use against microsporidian parasites	Gold nanoparticles incorporated with bacteriocin leads to the decrease in the number of the microsporidian parasite.	(Benellia, 2018)
20.	Use against helminth parasites	Gold nanoparticles has a vermifungal activity against cestodes.	(Benellia, 2018)
21.	Use against *Trypanosoma* parasites	Gold nanoparticles are capable of binding to both cysteine and arginine residue which in turn control nucleophile and electrophile which in turn blocks the arginine and guanidinium group responsible for phosphoryl transfer in between ATP and ADP.	(Benellia, 2018)
22.	Diagnosis of Alzheimer's disease	It is used to detect the pathology and molecular mechanism of the disease and the release of pharmacological substance at the site of the action for therapeutic action.	(Kalimuthu, 2020) (Gupta, 2019)
23.	In the treatment of skin cancer	It is based on the enhanced permeation and retention of gold nanoparticles to the site of cancer in skin where drug release can take place.	(Hashim, 2019)

24.	Application as an anti-oxidant	They have an anti-oxidant activity because of their ability to donate electron DPPH free radicals.	(Khan, 2019)
25.	In hepatoprotective application	Gold nanoparticles loaded with drugs are seen to increase glucathione peroxidase and superoxide dismutase which repairs the damaged hepatic cells.	(Khan, 2019)
26.	In catalytic application	They have a good catalytic reduction ability.	(Khan, 2019)
27.	In cardiovascular disease	By the use of Surface Enhanced Raman Spectroscopy (SERS) nanoparticles it is easy to diagnose and imaging of CRP which is one of the biomarkers for the cardiovascular diseases.	(Kalimuthu, 2020)

8. Conclusion

Nanoparticles are the molecules which are used heavily in researches because of their size which lies in the nano-range and hence falls in the novel category of drug delivery system. These nanoparticles are divided into categories which depends upon their chemical and physical nature like liposomes, dendrimers, fullerenes, virosomes, metallic nanoparticles, silica nanoparticles, spinel ferrite nanoparticles, magnetic iron oxide nanoparticles, silver nanoparticles, gold nanoparticles.

Out of all of the above gold nanoparticle is least toxic and is much more compatible with the body as compared to any other nanoparticles. They are synthesized using only two theories of synthesis that is either top down or bottom up approach. Gold nanoparticles are present in different structures like nanospheres, nanorod, nanoshell, nanocages and Surface Enhanced Raman Scattering. Gold nanoparticles can be synthesized by following approaches like bacterial synthesis, fungal synthesis, yeast synthesis, actinomycetes synthesis, algae synthesis, green synthesis, traditional synthesis. Gold nanoparticles have properties like Localized Surface Plasmon Resonance which can be used for immunotherapies and in treatment or diagnosis. Other property is that they should be colloidal in nature as in the presence of high amount of salts and proteins they tend to aggregate which could be resolved by the use of the compounds like amines, citrates, thiols. They are characterized by the techniques like UV spectrophotometer, X-ray Diffraction, High Resolution Transmission Electron Microscopy, Dynamic Light Scattering, and Surfaced Enhanced Microscopy. These gold nanoparticles are used in various applications like that of antibacterial activity, antifungal activity, gets accumulate at the site of the tumor and thus this is helpful in the screening of tumor by making illuminating gold nanoparticles, targeted delivery of the drug to the immune system in the case of cancer, when gold nanoparticles are conjugated with the active molecule it leads to the generation of immunity like that of the vaccine, but these studies are in their preliminary phase in animal models, use against vectors, in cardiovascular disease, in catalytic application, in hepatoprotective application, application as an anti-oxidant, in the treatment of skin cancer, in the diagnosis and therapy of Alzheimer's disease, use against *Trypanosoma* parasites, use against helminth parasites, use against microsporidian parasites, use against *Cryptosporidium* parasites, use against *Toxoplasma* parasites, use against *Leishmania* parasites, use against *Plasmodium* parasite.

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