International Journal of Advanced Research in Medicinal Chemistry
Volume 4, Issue 1 - 2022, Pg. No. 1-6
Peer Reviewed Journal

Research Article

A Review on Silver Nanoparticles from Lycurgus Cup as Drug Delivery System

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How to cite this article:
Agrawal A, Jai SD. A Review on Silver Nanoparticles from Lycurgus Cup as Drug Delivery System. *Int J Adv Res Med Chem* 2022; 4(1): 1-6.

Date of Submission: 2022-04-10
Date of Acceptance: 2022-05-25

A B S T R A C T

The Lycurgus Cup is one of the finest nanotechnology based cup, where colloidal microscope particles of gold and silver were impregnated on the glass and gives dichroic effects. Silver nanoparticles give greenish color on light scattering. Silver nanoparticles (Ag-NP) concept was used to decorate the different materials using nanotechnology. Concept of Silver nanoparticles was not limited to only decoration but its inherent properties were extensively studied and explore the different application of the silver nanoparticles in field of science. Some of the properties such as antimicrobial, drug delivery, catalyst are newly studied and reconnoitered. Ag-NP can delivery many therapeutics agents to target site of the disease. Green synthesis method is preferred from synthetic method of Silver nanoparticles. Silver nanoparticles is new era of drug delivery for delivering various therapeutics agents, it can have synergetic effects along with active pharmaceutical ingredients.

Keywords: Silver Nanoparticles, Lycurgus Cup, Nanotechnology, Drug Delivery, Antimicrobial, Colloidal Particles

Introduction

From ancient time to the middle ages, the history of the nanoparticles has been summarized by Daniel and Astrum. Because of their uniform size and sharp size distribution in nanometres; metallic nanoparticles have received much popularity. In the field of nanotechnology, metallic nanoparticles have shown number of properties and it has unlocked many new pathways in nanotechnology. Metallic nanoparticles have specialty with appropriate functional groups. It can be synthesized and modified that would allow them to bind with ligands, antibodies, drugs.[2] Metallic nanoparticle is nanosized metals with the size range of 10- 100nm. Metallic nanoparticles have unique characteristics such as surface Plasmon resonance and optical properties. Gold solution does have a golden yellow colour, for example, a solution of 20nm gold nanospheres has red ruby colour where 200nm nanospheres has bluish colour. The noble metals, especially silver and gold, have gained much attention to researchers in various branches of science and technology namely catalysis, photography, medical field as anticancer and anti-microbial agents. Faraday (1908) first recognized the existence of metallic nanoparticles in solution and Mie gave the quantitative explanation of their colour.

In medieval era, metallic nanoparticles were actually used to decorate cathedral windows. Due to unique properties of noble metal nanoparticles, it has made a special place in the field of nanotechnology. The most important feature of nanoparticles is their surface area to volume ratio, where it easily allows them to interact with other particles. In nanoparticles, high surface area to volume ratio makes diffusion faster and is feasible at lower temperatures. And this field has found more interesting, without disturbing and poisoning of healthy cells, we can directly treat affected cells and tissues. In fluorescence enhancement and surface enhanced Raman spectroscopy and in environment

refractive index sensing nanoparticles have found additional application in the enhancement of field sensitive optical process. The optical properties of metal nanoparticles play a key role due to the localized surface Plasmon with resonance wavelength in the visible region. Silver and gold nanoparticles are effective in inhibiting growth of gram-positive and gram negative bacteria. For the production of na,devices, living organism has huge potential. However, it requires much more experimentation. There is a drawback such as involvement of toxic chemicals makes it difficult for synthesis of metallic nanoparticles.

So, there is an alternate way of synthesising metallic nanoparticles by using living organisms such as fungi, bacteria, plants. Several studies have shown that metallic nanoparticles characteristics like (size, stability, physical, chemical properties, morphology) are strongly influenced by the experimental conditions, adsorption process of stabilizing agent, the kinetics of interaction of metal ions with reducing agents. In various industrial applications, metallic nanoparticles have attracted, because of their different physical and chemical properties from bulk metals. Various properties like mechanical strengths, high surface area, low melting point, optical properties and magnetic properties. Catalysts which are used in metallic nanoparticles are selective and highly active, has long lifetime for many chemical reactions. It has experimented that a DVD disk with storage capacity of 10 tetra bytes, which are approximately 2000 movies of convectional size. This is possible only due to the optical properties of gold nanorods embedded in the disk which are oriented randomly. To store data, Zijlstra and team used optical spectrum and different polarization directions.

Figure 1

The optical properties of gold, silver, lead, platinum nanoparticle arises from resonant oscillation of their free electrons in the presence of light, also known as Localized surface Plasmon resonance (LSPR). According to historical perspective, silver was considered as symbol of purity and it was valuable at that time as compare to gold. Since silver has many medicinal properties and it cures many diseases. It has anti-bacterial and antiseptic properties. In Ancient times, the noble metals were used to stained glass to produce the beautiful colors of drink cups such as Lycurgus cup. In 1890, Robert Koch, the bacteriologist discovered that K [Au (CN) 2] potassium gold cyanide at low concentrations had anti-microbial activity against the Tubercle bacillus, from there onwards gold is introduced in modern medicine. In 1727, John Herman Schulze first demonstrated that silver salts turned into black on exposure to light. In 1845, Michel Peyrone synthesized cisplatin (platinum containing anti-cancer drugs). In 1893, Alfred Werner elucidated the cisplatin structure whereas Roserberg studied the antitumor activity of cisplatin. In the 17th and 19th century, gold nanoparticles were used to treat fever and syphilis respectively.

Even before the fourth century AD, nanoparticles have been used in painting due to their optical characteristics. The most well-known example is the Lycurgus cup shown in Figure 2.

This cup is placed in British Museum in London. This amazing cup is the complete historical example. It is made of an extraordinary type of glass that is known as the dichroic glass. It can change colors when the light falls on it. When the light incidents on the cup at 90° then the opaque green color of cup change into the glowing translucent.

This cup consists of a very small amount of crystals of gold and silver in the molar ratio of 1:14. These metal crystals give it infrequent optical properties. This Lycurgus

Cup displays special color due to the presence of these nanocrystals. Up to the Middle Ages, gold in soluble form was used as excellent healing powers of many diseases such as dysentery, epilepsy and heart diseases, dysentery, epilepsy. It was also helpful in the identification of disease like syphilis. Daniel and Astruc Ages has been summarized the nanoparticles,s history since ancient times to the Middle age.

In various old churches, evidences of nanotechnology are easily available. A distinguished application of early nanotechnology was a ruby red color. During the middle ages, it had applications in stained glass windows. But the medieval artisans did not know that they were using nanotechnology. Jin and coworkers recognized a particular process to produce a very beautiful color effect. They explained the relation of particles and their colors that were

associated with specific particles. They summarized the relationship between the color of the stained glass, shape and size of NPs. Faraday prepared the first nanoparticle of gold. This gold particle is preserved in Royal Institution London.

In the German journal "Annalen der physic" (1908), Gustav Mie describes "how color of glass vary with size of metal". James Clerk Maxwell in 1867 gave a different concept of nanotechnology and proposed a tiny entity called Maxwell Demon". Color photography has been produced by him. According to Maxwell the color photography depends on the production of light sensitive nanoparticles.

Organic Nanoparticles

The organic nanoparticles include ferritin, micelles, dendrimers and liposomes show in Figure 3. The organic nanoparticles are not toxic, biodegradable and some organic nanoparticles have hallow sphere i.e. micelles and Liposomes. It is also familiar with name of nanocapsules which are heat and light sensitive. Organic nanoparticles are an ideal choice for drugs delivery due to these characteristics. Then nanoparticles are also widely used in target drug delivery. The Organic nanoparticles are also known as polymeric nanoparticles. The most known shape of organic or polymeric nanoparticles is nanosphere or nanocapsule. The matrix particles are former overall mass of which is solid and outer boundary of spherical surface adsorbs other molecules. In the later case, particles encapsulated the solid mass.

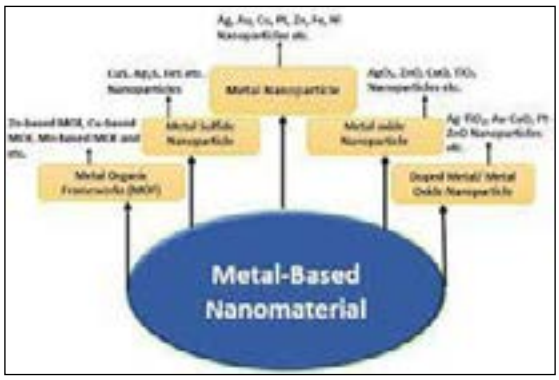

Figure 2

Inorganic Nanoparticles

Carbon is not present in inorganic nanoparticles. The inorganic nanoparticles are not toxic. The inorganic nanoparticles are biocomaptiable and hydrophilic. The inorganic nanoparticles are highly stable than organic.

The inorganic nanoparticles are classified into metal and metal oxide nanoparticles.

Metal Nanoparticles

Metals are used to synthesize Metallica nanoparticles by using destructive or constructive methods. The metal precursors are used to make the pure metal nanoparticles. The metal nanoparticles possess unique optoelectrical properties due plasma on resonance characteristics.

Metal Oxide Nanoparticles

The purpose of the synthesis of metal oxide nanoparticles is to modify the property of their respective metals nanoparticles such as iron nanoparticles are oxidized to iron oxide nanoparticles. The reactivity of iron oxides nanoparticles is increased as compared to the iron nanoparticles. Due to an increase in reactivity and efficiency of metal oxide, the nanoparticles of metal oxides are synthesized. The example of metal oxide nanoparticles are Zinc Oxide, Silicon Dioxide, Iron Oxide, Aluminum Oxide, Cerium Oxide, Titanium Oxide and Magnetite.

Ceramic Nanoparticles

Ceramic nanoparticles are also known as non-metallic solid. The ceramics nanoparticles are synthesized via heating or successive cooling. The ceramic nanoparticles may polycrystalline, amorphous, porous, dens or hollow form. The researcher focuses on these nanoparticles due to their wide application such as photodegradation of dye, photocatalysis, catalysis and imaging applications.

Biological nanoparticles or bionanoparticles Biological or Bio-nanoparticles is an assembly of atom or molecules which is prepared in the biological system having at least one dimension in the range of 1-00 nm. All bionanoparticles are naturally occurring nanoparticles. These nanoparticles are dividing into two categories intracellular structure and extracellular structure. Magnetosomes is an example of intracillular structure and lipoproteins and viruses are examples of extracellular structure. Magnetosomes, exosomes, ferritin, lipoproteins and viruses are examples of bionanoparticles.

Advantages of Metallic Nanoparticle

- Enhance Rayleigh scattering
- Surface enhanced Raman scattering
- Strong plasma absorption
- Biological system imaging
- Determine chemical information on metallic nanoscale substrate

Disadvantages of Metallic Nanoparticles

- **Particles Instability:** Nanomaterials can undergo transformation, as they are thermodynamically unstable and lie in the region of high energy local minima. This leads to deterioration of quality, poor corrosion resistance, main concerned is retaining the structure becomes difficult
- **Impurity:** While synthesising nanoparticles, nitrides, oxides, formation can aggravated from the impure

environment. As nanoparticles are highly reactive, there can also be high chances of impurity as well. In solution form, nanoparticles should be synthesized in form of encapsulation. So, it becomes a challenge to overcome impurity in nanoparticles

- **Biologically harmful:** nanomaterials has been reported toxic, carcinogenic and cause irritation as they become transparent to the cell dermis
- **Explosion:** exothermic combustion can lead to explosion, as fine metal particles act as strong explosives
- **Difficulty in synthesis:** while synthesizing nanoparticles, it should be encapsulated, because it is extremely challenging to retain the nanoparticles size in solution form.

Characteristics of Metallic Nanoparticles

- Large surface energies
- As compared to bulk they have large surface area to volume ratio
- Quantum confinement
- Plasmon excitation
- Increased number of kinks

Figure 3

General Application of Metallic Nanoparticles

Optical Function

Imaging sensor, display, solar cell, Photo catalysis, biomedicine, optical detector, laser-this are the applications based on the optical properties of metal nanoparticles. It is mainly dependent on some factors such as shape, size, surface area, doping, interaction with the surrounding. The optical properties of CdSe semiconductor nanoparticles can change with size. For different samples of gold nanospheres, the optical properties changes with enlargement of metallic nanoparticles. Surface absorption Plasmon Au & Ag can change into various colors by changing the particle size, form and shape of the particle and condensation rate.

Thermal Function

When nanoparticle diameter is less than 10nm, the melting point is also lower than a bulk metal. With low boiling point, electronic wiring can be made with nanoparticles.

Electrical Function

Can be used to make high temperature superconductivity material. In conductance one step can be shown, at constant applied voltage, the mechanical thinning of a nanowire and electric current measurement. So the main point here to be noted is that, the number of electron wave modes supporting to the electrical conductivity is becoming smaller with decreasing diameter of the wire. Only one electron wave mode is observed in electrically conducting carbon nanotubes which transport the electrical current. Electrically conducting carbon nanotubes touch the mercury surface at different times, as their length and orientation are different and this leads to transport of electrical current.

Application of nanoparticles in food and agriculture

The nanotechnology provided new techniques for water filtration and desalination but it will be more economical. By using nanotechnology food industry can also be developed. For example, by using nanotechnology new functional material and new instruments design for food preservation and bio-security are developed. Bayer Company introduced airtight plastic packing with the help of nanotechnology. Food is preserved in this plastic packing. From nanotechnology, genetics modifications in the constitution of the crop plant can bemade.

Application as chemical catalyst

In chemical reactions, nickel, lead, silver and platinum have been used as distinctive metal catalysts. Though, below the 200 °C, the dissociative adsorption of molecule of hydrogen and oxygen cannot be carried out on the surface of gold. In hydrogenation and oxidation reactions the gold material is used as catalyst because gold nanoparticles are not reactive during such reaction. However, Haruta discovered that gold nanoparticles work successfully as catalyst. (154) This state found in cluster structures. In the physical properties, quantum size effect appeared. Metals that have the ability to form clusters that is un-stabled to the atmosphere. However, clusters of gold are highly stable that is why, gold particles can be used as catalysts. In catalyzed oxidation reactions, the catalytic activity increase with the decrease in size of the gold nanoparticle.

Used as Fuel Cell Catalysts

Fuel cell is a device that directly converts chemical potential energy into electric energy. A PEM (Proton Exchange Membrane) cell uses hydrogen gas (H2) & oxygen gas (02) as fuel. The products of fuel cell are water, electricity, heat.

Elimination of Pollutants

As metallic nanoparticles is highly active in terms of physical,

chemical and mechanical properties. They can be used as catalysis to prevent environment pollution arising from coal and burning gasoline. As they react with toxic gases such as carbon monoxide and nitrogen oxide.

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Applications in energy harvesting

Fossil fuels are nonrenewable nature, that's why recent approach informed about the limitations and inadequacy of fossil fuels in the coming years. Therefore, scientists are trying to shift their research approaches to

- The resources that can easily available
- Generate renewable resources
- Low cost material

For these purposes scientists found the NPs as the best aspirant due to the following characteristics

- large surface area
- photo catalytic applications
- catalytic nature
- optical behaviour

Therapeutic Applications of Metallic Nanoparticles As anti-Infective Agents

The anti-viral properties of AgNps are more effective then chemically synthesized silver nanoparticles. In one study, metallic nanoparticles have been described as a HIV preventative therapeutic. In a couple of studies, it has been shown that as virucidal agent silver acts directly on the virus by binding to the glycoprotein gp120. This binding in turn prevents the CD4 dependent virion binding which effectively decreases HIV- 1's infectivity and it has also been reported that metallic nanoparticles has been effective antiviral agents against herpes simplex virus, influenza, respiratory syncytial viruses.

As Anti-Angiogenic

It is well known that angiogenesis is the development of new blood vessels and occurs during normal development and in some disease states. It plays a main role in number of diseases such as cancer, rheumatoid arthritis. In normal conditions, angiogenesis is tightly regulated between various pro-angiogenic growth factors (VEGF, PDGF, TGF-B) and anti-angiogenic factors (platelet factor 4, TSP-1). Under diseased conditions, angiogenic is turned on. Some reviews have reported that these agents have serious toxicities such as fatal haemorrhage, thrombosis, hypertension. It may be overcome if these nanoparticles alone can be efficacious as an anti-angiogenic agent.

In Tumour Therapy

It has been studied that naked gold nanoparticles inhibited the activity of heparin-binding proteins such as VEGF165 and bFGF in vitro and VEGF induced angiogenesis in vivo. Further work in this area has been reported that onto the surface of AuNPs heparin binding proteins are absorbed and were subsequently denatured.The researchers also showed that surface size plays a main role in the therapeutic effect of AuNPs. Mukherjee and colleagues also experimented the effect of gold nanoparticles on VEGF mediated angiogenesis using a mouse ear model injected with an adrenoviral vector of VEGF (Ad-VEGF- mimics the resulting angiogenic response found in tumours). A week later, the Ad- VEGF administration, mice treated with AuNPs developed lesser edema than the same treated mice. Eom and Colleagues revealed the anti-tumour effects of 50nm AgNps In vitro and In vivo.

In Multiple Myeloma

Researchers (Washington university school of Medicine in St.Louis, journal Molecular cancer Therapeutics) have designed a nanoparticle based therapy that is effective in treating mice with multiple myeloma. Multiple myeloma is a cancer that affects plasma cells. Mukherjee and group demonstrated that a gold nanoparticle inhibits the VEGF and bFGF dependent proliferation of multiple myeloma cells.

In Leukaemia

B-chronic Lymphocytic Leukaemia (CLL) is an incurable disease predominantly characterized by apoptosis resistance, by co-culture with an anti-VEGF antibody, found induction of more apoptosis in CCL B cells. In CLL therapy, gold nanoparticles were used to increase the efficacy of these agents. Gold nanoparticles were chosen based on their biocompatibility, very high surface area, surface functionalization and ease of characterization. To the gold nanoparticles, VEGF antibodies were attached and determined their ability to kill CLL B cells.

In Rheumatoid Arthritis

Scientists from the University of Wollongong (Australia) have built a new class of anti-arthritic drug which could be used by gold nanoparticles and it has fewer side effects. Rheumatoid arthritis is an autoimmune disease that occurs when the immune system not function properly and attacks a patient's joints. New research has shown

that gold particles can invade macrophages, stop them from producing inflammation without killing them. Journal of inorganic biochemistry it has been published that by reducing the size of gold into smaller nanoparticles (50nm) was able to cause more gold to immune cells with lesser toxicity.

In Photo Thermal Therapy

Gold nanoparticles absorb light strongly as they convert photon energy into heat quickly and efficiently. Photo-Thermal Therapy (PTT) is an invasive therapy in which photon energy is converted into heat to kill cancer.

In Radiotherapy

Tumours loaded with gold, this absorbs more X-rays as gold is an excellent absorber of X-rays. Thus deposition of more beam energy and results in a local dose which increase specifically to tumour cells. Gold nanoparticles have been more useful to treat cancer.

Conclusion

Metallic nanoparticles in this 21st century are highly demanded because it can be synthesised through various routes. Metallic nanoparticles synthesis is important because of their ideal electrical, optical, magnetic and chemical properties. And it has been proved that by Radiolytic and photolytic methods it offers several advantages, as it is easy to synthesize nanoparticles of narrow size distribution. Moreover, ultrafast lasers and electron pulse radiolysis can be employed in combination for nanoparticles preparation. The novelty of this technique is, along with the formation of metal nanoparticles, growth kinetics can also be studied. Recently, seed method was used to synthesize bigger size uniform particles. Cd and Ag metal nanoparticles were prepared in viscous medium and in aqueous solutions.

To stabilize metal nanoparticles viscous medium was used Uniform particle size can be prepared by bombarding the particles by laser irradiation in ethylene glycol and glycerol media. Metallic nanoparticles have wide range of applications such as imaging agents, delivery vectors, synthetic inhibitors and sensors.

In nanobiotechnology, one of the major challenges is to improve the efficacy of nanoparticle therapeutic and to reduce the toxicity level. New treatment strategies are being explored with the rapid development in nanomaterials that has the potential to overcome existing problems using noble metallic nanoparticles.

Prior to wide spread use, the impact on human health needs to be fully understood. Nanotechnology can play an excellent role in individualized medicine. Although more research is necessary for that. Noble metal nanoparticles can be effective in therapeutic and diagnostic agents as they show new properties at the atomic and supramolecular scales (1-100nm).

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