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INNOVATION IN SILVER NANOPARTICLE SYNTHESIS METHOD AND APPLICATIONS IN MEDICINE

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ABSTRACT

Silver nanoparticles are continuously being employed in various fields due to their distinctive properties. Nano silver has shown immense activity in field of science against various diseases. As nano size of silver has shown advanced activities so different approaches are made to synthesize nano silver particles. Recently there are only main three synthesis methods to develop nanomaterials. The green approach to synthesize nanomaterials is the method of choice as it involves methods which are environment friendly. The conducted review includes study of different synthesis methods of Silver Nanoparticles and its application in medical field.

KEYWORDS: Silver Nanoparticles, Nanomedicine, Antimicrobial Therapy, Cancer Treatment, Green Synthesis.

1. INTRODUCTION

Nanotechnology, also known as nano science, is a scientific field that studies the chemistry of various nanoparticles. It has great potential in various fields of science and is being utilized globally on a large scale, earning it the title "key technology of the 21st century."

According to the European Commission, nanomaterials are natural, randomly created or manufactured materials containing particles in a free or aggregate state.

Key Features of Silver Nanoparticles:

- Size: 1-100 nm
- Increased surface area
- Unique properties compared to bulk silver
- Environment-friendly production through green synthesis
- Annual global production is approximately 500 tons
- Researchers have developed various methods to synthesize silver nanoparticles, including physical, chemical, and biological methods. see figure (1) These methods can be categorized into two approaches:

"Top-down" and "Bottom-up."

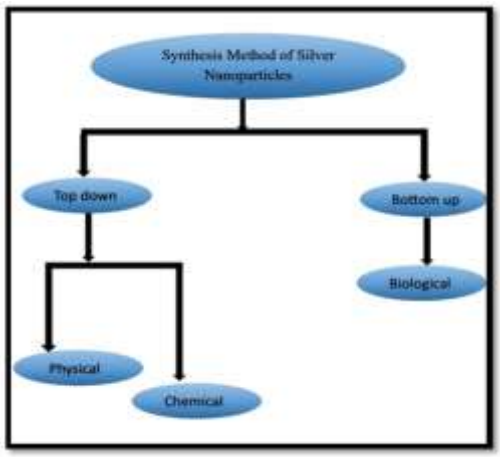

Figure (1) Synthesis Methods of Silver Nanoparticles

❖ **Top - down approach:** Involves breaking down bulk parent material into smaller nanoparticles with the help of different physical forces like ball milling, crushing, grinding, mechanical energy, electrical energy, laser ablation, and thermal energy. It includes

- Physical methods.

❖ **Bottom-up approach:** Involves forming complex clusters through nucleation and growth processes. The bottom-up approach includes two methods

- Chemical method
- Biological method

Chemical synthesis which utilizes energy sources such as photochemical, electrochemical, microwave-assisted, and sono-chemical methods. Biological synthesis, also known as green synthesis, is gaining popularity due to its environment-friendly production of silver

nanoparticles from living organisms like algae, bacteria, fungi, cellulose enzymes, flavonoids, alcohol, alkaloids, plants, and their parts.

Silver nanoparticles have made significant advancements in the medical field due to their remarkable properties and they are serving as effective.

- Antimicrobial agents
- Anticancer agents
- Wound healing agents
- Anti-diabetic agents
- Anti-viral agents
- Anti-tubercular agents
- Antifungal agents
- Anti-arthritis agents
- Vaccine production
- Dentistry

Silver nanoparticles have revolutionized various fields, particularly medicine, with their unique properties and environment-friendly production methods. Their applications continue to expand, making them an essential tool in modern science.

2. ADVANTAGES OF SLIVER NANOPARTICLES

- Silver nanoparticles have less tendency to induce anti-microbial resistance.
- Silver nanoparticles are cost efficient.
- The large surface area of nanoparticles provides several unique properties in field of science.
- Silver nanoparticles are time sufficient.
- Nano sized particles are sustainable.
- These are stable nano size particle.

3. SYNTHESIS METHODS OF SILVER NANOPARTICLES

3.1. Physical Method of Synthesis of Silver nanoparticles:

- This method involves the breakdown of parent bulk material under different physical energies to synthesize silver nanoparticles. The particle size is reduced by implementation of mechanical energy, light energy, electrical energy, thermal energy, milling, and melt mixing.

- Physical methods to synthesize:

3.1.1. Ball milling method

3.1.2. Laser ablation method

3.1.3. Physical vapor deposition

a. Electrical arc discharge method

b. Sputtering

3.1.4. Evaporation condensation method

3.1.5. Thermal breaking

- Advantages

1. Sample obtained with high purity.
2. Time saving method.

- Disadvantages

1. Requirement of higher energy.
2. Complex instruments.

3.2 Chemical method of synthesis

Recently most common method for silver nanoparticle production by transfer of electron under specified condition, silver ion is reduced to elemental silver.

This method uses Reducing agents (sodium citrate, sodium borohydride), Capping agents, Metal precursors, Energy sources (microwave, light, heat, sound).

- Chemical methods of synthesis:

3.2.1. Chemical reduction.

3.2.2. Pyrolysis.

3.2.3. Electrochemical

3.2.4. Micro-emulsion

3.2.5. Microwave assisted

- Advantages

1. Quick
2. High yield generating
3. Low cost

- Disadvantage

1. Chemical agent reduces medical efficiency of silver nanoparticles
2. Poisonous waste released leads to environmental pollution

3.3. Biological method of synthesis

This method of synthesis has gained attention of numerous researchers to produce silver nanoparticles by using plant and parts of plants like flowers leaves, bark, root, stem. Here biological components are also utilized like bacteria, fungi, algae, yeast etc.

Plants contains specific components that induces the synthesis of silver nanoparticles such as aldehydes, ketones, amides, terpenoids, carboxylic acid.

Microorganisms have the potential to develop metal tolerance in genes and metal bio concentration capability which help them to sustain in environment which has large concentration of silver.

- Advantages

1. Simple methodology.
2. Non-toxic
3. Silver nanoparticles have large surface area and high stability.
4. It involves eco-friendly methods to synthesize silver nanoparticles.

3.3.1. Plant-extract mediated synthesis

It utilizes leaf, flower, bark, root, or whole plant to develop the nanoparticles. Parts of plant consist of biomolecules like alkaloids, polysaccharides, tannins, terpenoids, phenols and nutrients which are environment friendly and responsible to induce the growth of silver nanoparticles.

- Green tea

Figure (4) Green tea

Green tea extract is used as reducing agent in this method. Anti-bacterial activity was shown by Green Tea extract silver nanoparticles against Gram Negative and Gram-positive Bacteria.

- Pineapple

Figure (5) Pineapple leaves

Pineapple leaf extract synthesized silver nanoparticles it showed antibacterial activity on strains of Gram-negative bacteria.

B) From flower:

- Rose petal extract

Antibacterial and antifungal activity show by the particles.

C) From Seeds

- Pumpkin seed

Figure (6) Pumpkin seed

It's effective dose can inhibit cancer cells in humans at some extent.

D) From Roots

- Ginger

Figure (7) Ginger

Ginger can show cytotoxic effect against breast cancerous cells. A sufficient amount of Ginger extract and AgNO3 were mixed a color change from pale yellow to dark brown indicated synthesis of silver nanoparticle.

4.3.2. From Microbes

- Fungi

Fungi can give high production of silver nanoparticles as they can release more proteins. The enzyme in fungal cell captures the silver ions from outside the fungus cell and leads reduction to silver metal with the help of enzyme in fungal cell such as anthraquinones.

Recent study developed silver nanoparticle by using endophytic fungus (Phyllostica Capitalensis). It also showed effective potential of phyllo-AgNPs against pathogenic micro-organism, Escherichia coli, Salmonella.

- Bacteria

Bacterial synthesis of silver nanoparticles is a best alternative to synthesize silver nanoparticles as this retained the potential to reduce heavy metal ions to metals.

Recently silver nanoparticles were synthesized by implementing Cynobacteria in synthesis process. Cyno-AgNPs were concluded to have highly effective antibacterial activity against gram positive and gram -negative bacteria.

- Algae

The biologically active substance present in Algae such as polysaccharides phenolic compound proteins and alkaloids lead to synthesis of silver nanoparticle. This synthesized silver particles have effective antifungal, antibacterial, antiviral, antioxidant, anti-cancer activities.

A study developed silver nanoparticles from micro-algae, aqueous extract of Asterary's was used to reduce AgNO3 to silver nanoparticle. It's antifungal activity was determined against fusarium sp.

4. MEDICAL APPLICATIONS OF SILVER NANOPARTICLES

4.1. As an Antimicrobial agent

Bacteria are becoming resistant to antibiotics such as Methicillin, Penicillin etc. Very minute particles called silver nanoparticles can help to combat resistant bacteria.

4.2. As Anti-cancer agent

- Breast cancer

AgNPs inhibit cancer cell growth this proves to be helpful in overcoming multidrug resistance in breast cancer cells. Silver nanoparticles bind to the folate receptors of breast cancer cells and producers cytotoxic effect leading to cell deaths.

- Lung cancer

The silver nanoparticles inhibit several cell functions of lung cancer cell line. Scientists used green-synthesized silver nanoparticles (AgNPs) from various plants to combat lung cancer cells. These plants include Eucalyptus, Cotton.

4.3. As Anti-bacterial agents

Bacteria have very low ability to become resistance to silver nanoparticles as compared to normal antibiotics this can help to overcome the bacterial resistant to antibiotics. The antibacterial mechanism of silver nanoparticle is as follows generate hole on bacterial cell, develops gap or space on the cell wall leads to destruction of the membrane permeability.

- Tuberculosis

Silver nanoparticle antibacterial agents are found to be effective and valuable tool to improve T.B. therapy and overcome drug resistance in the therapy of TB.

- Pneumonia

Staphylococcus-aureus is a bacterium that causes pneumonia. In a study AgNPs were snythesized by using Trichoderma Harzianum via green synthesis. Inhibitory growth activity of silver nanoparticle was observed for the above the bacteria.

4.4. As Antifungal agent

In recent time silver nanoparticles are observed to possess effective antifungal activity and can be incorporated to treat various fungal infection causing organism like C. Albicans, Aspergillus, P. notatum.Silver nanoparticle destroy fungal cell in following ways silver nanoparticles (AgNPs) kill fungal cells by damaging cell walls and surface proteins, disrupting DNA and RNA.

- Candidiasis: Scientists used extracts from Diospyros sylvatica to create tiny particles (AgNPs) that were found to exhibit antifungal activity against C. Albicans.

4.5. Antiviral agents

Various study revealed the increased antiviral efficiency of silver nanoparticles as compared to already present drug or medicine used in viral infection treatment.

- Coronavirus

Effect of silver nanoparticles was observed on the biological process of COVID 19 virus, by binding to GP 120 protein sub-unit of COVID, this binding supresses S subunit of COVID and prevents binding and fusion to host cell by virus.

- HIV

Scientists are exploring a new approach to simplify HIV treatment by Loading HIV meds into tiny particles (NPs) for a single-dose therapy. This will Improve treatment effectiveness and reduce multiple pill burden.

4.6. In Neurological disorders

Silver nanoparticles due to their very small size can easily cross the blood brain barrier and can be useful in treatment of brain disorders like Alzheimer's disease, Parkinson.

- Parkinson

Silver nanoparticles can relieve the neurotoxicity which is caused due to Parkinson’s.

- Alzheimer

Nanoparticles can lower down the succession of Alzheimer Pathology. Silver nanoparticle developed from Pimpinella Anisum-I. Seed extract showed inhibitory activity on amyloid fibrils and can be given to reduce side effects of Alzheimer.

4.7. Dentistry

By addition of silver nanoparticles in various dental implants like root canal fillers, implantable devices can show effective results against bacterial growth inhibition.

4.8. Wound Healing

Silver nanoparticles are increasingly used in wound dressing and topical formulation to treat infection and has shown reduced infection rates and improve efficiency to treat chronic wound like burns, diabetic ulcer.

4.9. Bone: During the bone transplantation there is a threat of bacterial infection in bone. Silver nanoparticle has shown remarkable antibacterial activity so this can be used as antibacterial agents during the bone transplantation to prevent infection.

4.10. Arthritis

M1 macrophages secret inflammatory cytokinins and this are responsible for inflammation in Rheumatoid arthritis. The Folic acid synthesized silver nanoparticles can induce M1 macrophage reduction and polarization of M2 macrophage in Arthritis therapy.

5. CONCLUSION

The synthesis of silver nanoparticles has witnessed significant innovations in the upcoming modern times, advancing their applications in medicine. This review highlights the advancements in top-down and bottom-up approaches, including physical, chemical, and biological methods. The biological synthesis method, in particular, has emerged as a promising eco-friendly, alternative and safe method as compared to physical and chemical methods. The applications of silver nanoparticles in medicine have shown remarkable potential, including: Antimicrobial and antibacterial properties, Anticancer and Antiviral activities, Wound healing, Dentistry, Anti-arthritis. Continued research and development are essential to unlock their full potential, for to be used on large scale and address existing challenges.

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