**TOPIC**

**" A REVIEW ON SILVER NANOPARTICLES"**

**HAS BEEN CARRIED OUT**

**BY**

**MS. SAYALI PRALHAD NANAWARE**

**UNDER THE SUPERVISION**

**DR.VISHAL BABAR**

**Dattakala College of Pharmacy**

**541/2, Off Pune- Solapur Highway, Swami-Chincholi**

**(Bhigwan), Tal - Daund, Dist. – Pune 413130, India**

**ABSTRACT**

**Silver nanoparticles (AgNPs) have been one of the most attractive nanomaterials in biomedicine due to their unique physicochemical properties. In this paper, we review the state-of-the-art advances of AgNPs in the synthesis methods, medical applications and biosafety of AgNPs. The synthesis methods of AgNPs include physical, chemical and biological routes. AgNPs are mainly used for antimicrobial and anticancer therapy, and also applied in the promotion of wound repair and bone healing, or as the vaccine adjuvant, anti-diabetic agent and biosensors. This review also summarizes the biological action mechanisms of AgNPs, Besides, we briefly introduce a new type of Ag particles smaller than AgNPs, silver Ångstrom (Å, 1 Å = 0.1 nm) particles (AgÅPs), which exhibit better biological activity and lower toxicity compared with AgNPs. Finally, we conclude the current challenges and point out the future development direction of AgNPs.silver nanoparticles, their origin, activity, and toxicity in cosmetic. The application of nanotechnology and nanomaterials can be found in many cosmetic products including moisturizer, hair care products, makeup and sunscreen.. A silvenanoparticle is the potent and broad spectrum antimicrobial agent. This review paper looks into use of nano silver and provides an overview of current activity in this area.**

**KeyWords : AgNPs , Silver Nanotechnology, Nanoparticles,Nanomaterials, biosynthesis, etc.**

# CONTENTS:

## INTRODUCTION

Nanotechnology is booming by leaps and bounds due to the emergence of nanomaterials (particularly inorganic nanoparticles (NPs) and nanorods) with unique functions and size dependent physicochemical properties differing significantly from their bulk counterpart[1].These properties take Ag-NPs to the top of the priority list, to be used in inks, in electronics, and for medical purpose[7].Furthermore, Ag-NPs are widely known for its antimicrobial properties against microbes such as bacteria, fungi, and virus[8]. Silver and its compounds have been used for antibacterial and therapeutic applications for thousands of years[1-2]. Ancient Greeks and Romans used silverwares to store water, food, and wine to avoid spoilage. Hippocrates used silver preparations to treat ulcers and promote wound healing. Silver nitrate was also used for wound care and instrument disinfection. In 1852, Sims sutured the vesicovaginal fistulas caused by delivery with fine silver wires which significantly decreased infection. At the beginning of the 19th century, silver preparations were developed for wound infection and burn care.

However, in the 1940s, the medical applications of silver gave way to the clinical introduction of antibiotics[1]. Herein, we review the achievements of AgNPs in the past decade, especially focused on the past five years. This review intends to provide a valuable reference for researchers who are interested in the biomedical applications of AgNPs.

## METHODS AND PREPARATIONS:

The Main Contents Include :

**1. Synthesis of AgNPs Methods:**

1.1 Physical

1.2 Chemical

1.3 Biological

Numerous studies focus on the synthesis of AgNPs with controlled size and shape, and a variety of specific synthetic methods have been developed, including physical, chemical, and biological methods[5].

**1. Synthesis of AgNPs Methods:**

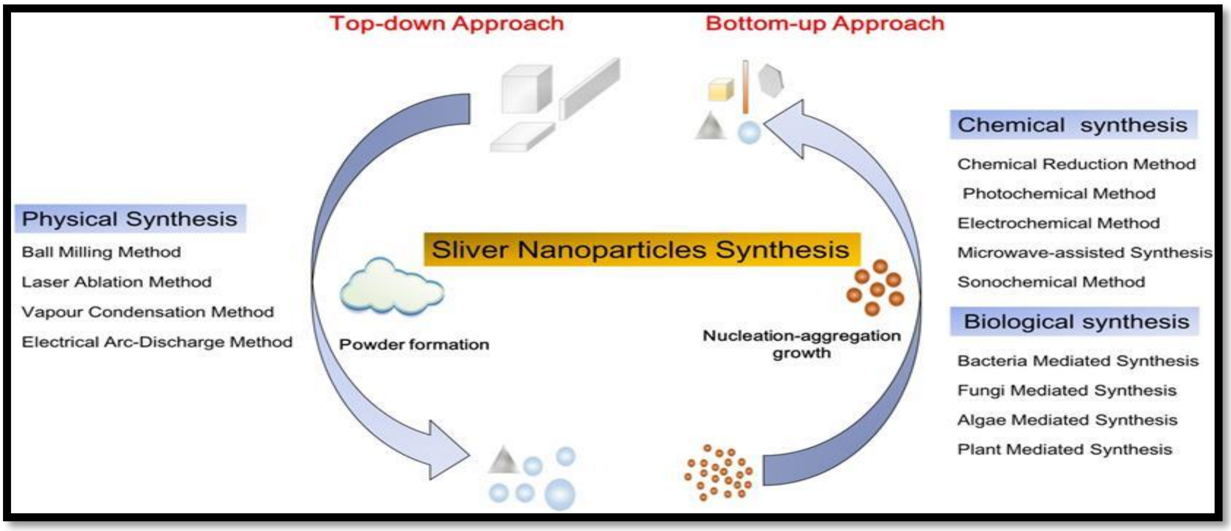


**Figure No. 1**

## 1.1 Physical Synthesis:

**Ball Milling Method**

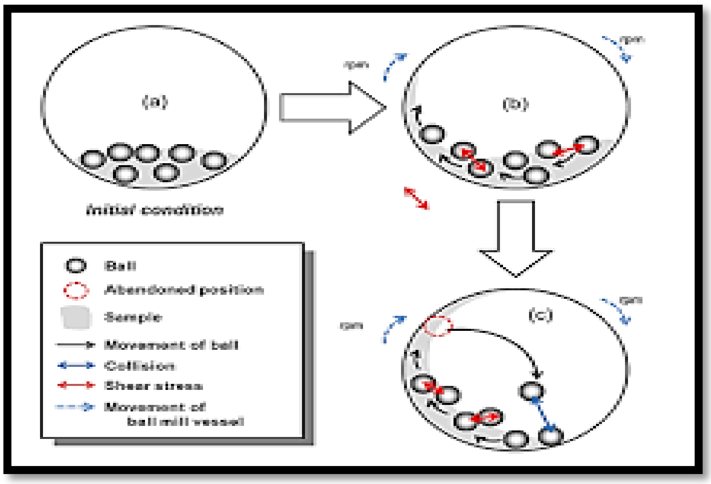


**Figure No. 2**

Mechanical ball milling technique is to put milling balls and metal materials with a specific mass ratio as well as gas (air or inert gas) in a container rotated at a high speed. The milling time, rotating speed and the atmospheric medium in the process of ball milling are playing essential roles in the morphology of metal materials. A suitable milling time is closely related to the production of particles with a satisfactory size. The smaller size of particles, the higher surface energy, therefore particles prefer to aggregate. The temperature of the powder in the ball milling process influences the diffusivity and phase of nanoparticles[8].

**Laser Ablation Methods**

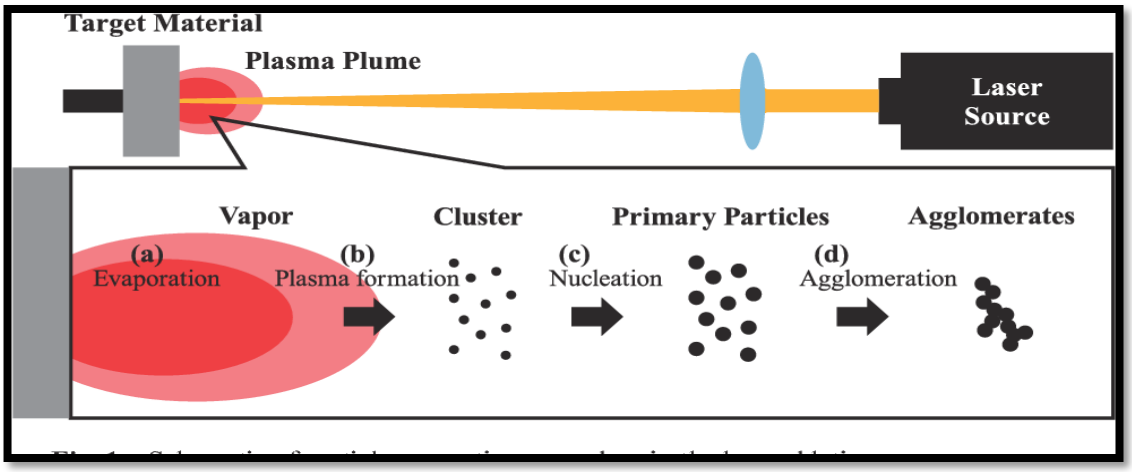


**Figure No. 3**

During the process of laser ablation, nanoparticles can absorb photons through multiple pathways, including plasmon excitations, interband transitions, and multiphoton absorption, which are closely related to pulse time, laser wavelength, and laser fluence.

These factors, as well as the type of aqueous medium, may affect the characteristics of NPs [9]. Different synthesis conditions, such as laser fluences, pulse wavelength, as well as solvent type, may affect the size of the NPs. The addition of organic stabilizers such as cetyltrimethylammonium bromide (CTAB) and PVP can enhance the dispersibility of AgNPs[11].

**Vapour Condensation Method**

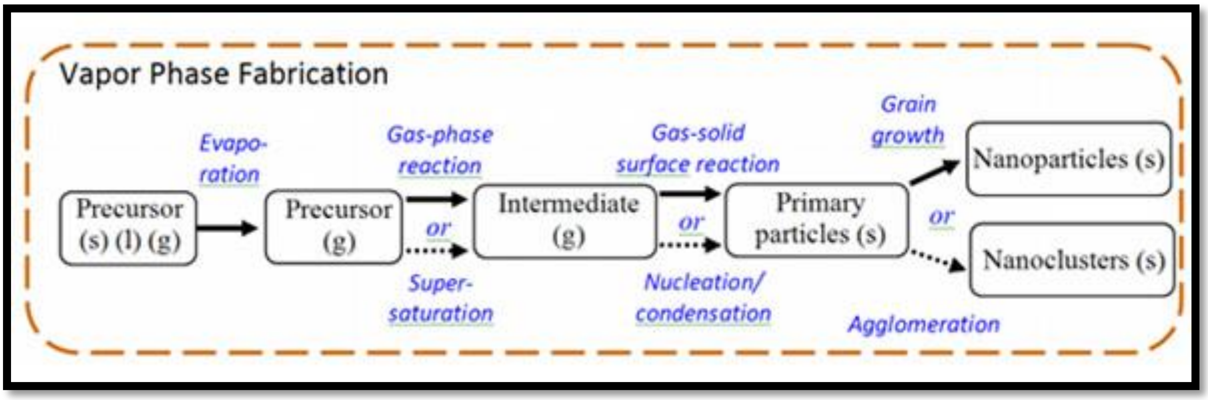


**Figure No. 4**

The basic and most commonly used physical vapor deposition processes are divided into two general categories: arc evaporation and sputtering. The former refers to the utilization of a cathodic arc source in a vacuum chamber or protective gases to obtain metal vapor and deposit it on a target coating material to form a thin, adherent pure metal or alloy coating. During this process, highly ionized metal vapor generates plasma[12]. And the latter refers to using a high-energy electrical charge to bombard the target coating material and deposit metal on the substrate.

In this process, ions and energetic atoms impact atoms and mechanically eject them from the target material. Recently, our team successfully synthesized a kind of very small silver particles which reached up to Ångstrom (Ång) scale for the first time with a self-developed evaporation–condensation system[21].

**Electrical Arc Discharge Method**

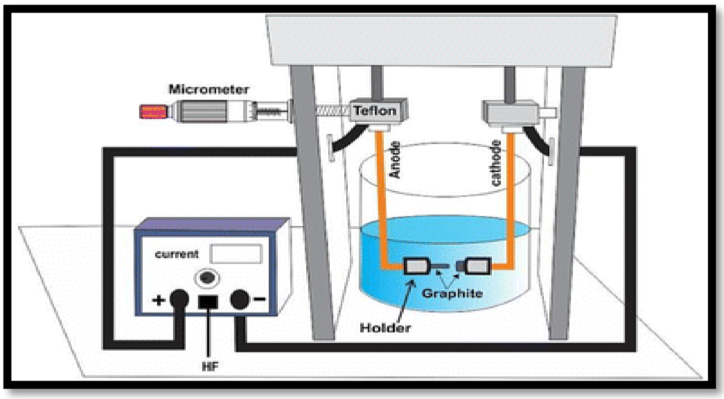


**Figure No. 5**

The electrical arc-discharge apparatus consists of DC power between two silver rods, which are immersed in dielectric liquids[13,14]. During the process of arc discharge, the silver electrode is etched in the dielectric medium, and the surface of the silver electrode is vaporized because of the high temperature near the electrode. Subsequently, the silver vapor is condensed into AgNPs and suspended in the dielectric liquid. This apparatus can obtain pure AgNPs with a simple and low-cost device.

**1.2 Chemical Method :**

**Chemical Reduction Method**

Chemical reduction is a reliable method for preparing colloidal AgNPs in organic solutions or water. AgNPs with desired shapes can be obtained by chemical reduction method, such as nanosphere, nanoprism, nanoplate, nanowire, nanocube, and nanorod. The chemical reduction method includes three components: salt precursor, reducing agent, and stabilizer. Silver precursors can be effectively reduced to AgNPs by different reducing agents with the presence of a stabilizer.

There are several alternative silver precursors continuously providing monomers for nucleation, such as silver nitrate[18], silver ammonia ( ie. Tollens reagent)[15], silversulfate[16], and silver chlorate[17].

Frequently used reducing agents may affect the growth of nuclei, including NaBH4, hydrazine, N, N-dimethylformamide, TSC, ascorbic acid, ethylene glycol, polysaccharides, and formaldehyde. The types and ratio of precursors and reducers, as well as the temperature and pH of the solution, may influence the characteristics of AgNPs[19-20].

**Photochemical Method**

The photochemical method refers to reduce the precursors to AgNPs under the illumination. The silver precursors and solution in the luminescent region produce reduced free radicals and hydrated ions, which can reduce $Ag^+$ to $Ag^0$*in situ* directly.

**Electrochemical Method**

Electrochemical method can form an electric potential in the electrolyte and reduce $Ag^+$ to $Ag^0$[22]. The nucleation and growth of AgNPs occur almost simultaneously under the external electric field. Electrochemical method can synthesize AgNPs with different sizes by adjusting the current density.

**Microwave-assisted Method**

Microwave-assisted method refers to rapid heating the silver precursor by microwave irradiation, which may promote the generation of nuclei *in site*[21]. Several factors may influence the microwave-assisted synthesis of AgNPs, including the concentration of precursor and the type of stabilizer, power input and irradiation time of the microwave, dielectric constant, refractive index of the medium and chirality of reducing agents[23]. Water and alcohol are ideal media for microwave heating stabilizer because of their high dielectric losses[24].

**Sonochemical Method**

Sonochemical method refers to the cavitation effect generated by ultrasonic irradiation, which produces a local hot spot and promotes the synthesis of AgNPs [25].

The instantaneous high pressure and microjet generated by ultrasonic irradiation can uniformly mix the solution and generate bubbles, which may suddenly collapse when the bubbles grow. The adiabatic compression of the gas phase in the bubble creates a local hot spot, which accelerates the contact of $Ag^+$ with the reducing agent and rapidly reduces it to AgNPs. Ultrasound prevents the agglomeration of nanoparticles in the aqueoussolution to decrease the size of AgNPs. Besides the high temperature, other factors such as pressure, pH, high-speed microjet, and high cooling rate may also contribute to the synthesis process. In summary, the sonochemical method is a simple, economical, and environment-friendly technique for preparing colloidal silver nanoparticles

### 1.3 Biological Method:

**Bacteria Mediated Synthesis**

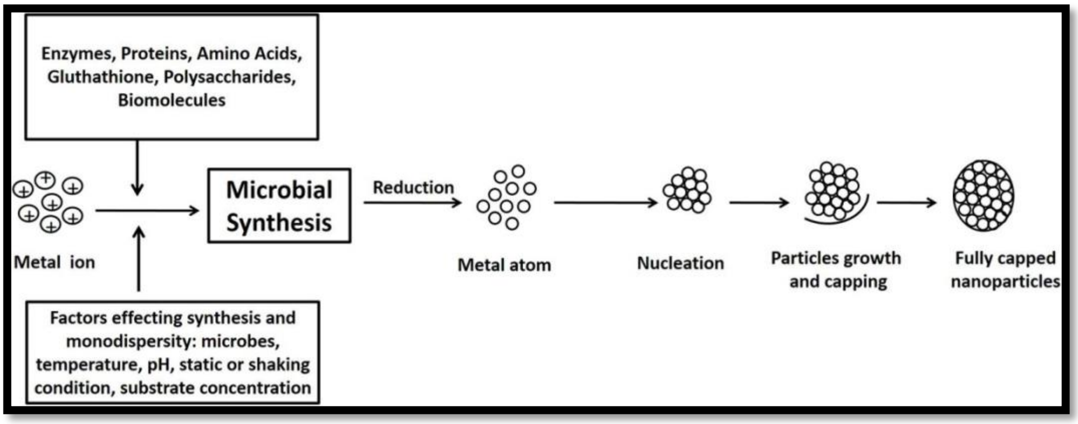


**Figure No. 6**

Some organic substances can also act as stabilizers and capping agents for AgNPs to prevent particle aggregation[26-27].

The mechanisms of bacteria-mediated synthesis of AgNPs still need to be further explored. In conclusion, bacterial-mediated synthesis of AgNPs is a simple, effective, and environmentally friendly method.

**Fungi Mediated Synthesis**

Fungi-mediated synthesis of AgNPs is an effective and straightforward approach[28-29]. According to the location of nanoparticles, fungi-mediated synthesis can obtain intracellular and extracellular AgNPs using mycelia and fungal cell-free filtrate, respectively[30-31] (**Table 3**).

Compared with intracellular synthesis, the extracellular synthesis of AgNPs using fungi is preferred due to the advantages of convenient collection and downstream processing. Plenty of fungi, due to their unique abilities of metal bioconcentration, high tolerance in the metal-rich environment, rapid mycelial growth, various extracellular enzymes secretion, and economic viability, are selected for biosynthesis of AgNPs[32], such as *Penicilliumpolonicum*[33].

**Algae-Mediated Synthesis**

Algae, as one of the most potential coastal renewable living resources, have received more attention in the biosynthesis of nanometer materials in recent years (**Table 3**). Algae contain a variety of biologically active organic matters, such as carbohydrates, polysaccharides, enzymes, proteins, vitamins, pigments and secondary metabolites[34-35-36.] These abundant organic compounds make algae an ideal candidate for biosynthesis of AgNPs. These active organic matters may be used as reducing agents to form size- and shape-controlled AgNPs, including spheres, triangles, cubes, rods, wires, hexagons, pentagons and wires. The roles of many algae in biosynthesis of AgNPs are verified, including *Cyanophyceae*, *Chlorophyceae*, *Phaeophyceae*, *Rhodophyceae* [37].

**Plant-Mediated Synthesis**

The plant-mediated synthesis of AgNPs is influenced by different reaction parameters such as temperature, reaction time, pH and concentration of plant extracts and precursors [38-39]. The AgNPs with different size and shape can be obtained by changing the synthesis parameters [38]. In summary, plant-mediated synthesis of AgNPs can be controlled by a variety of reaction conditions.

In addition, different parts of plant exhibit various abilities in the synthesis of AgNPs . The mechanisms of plant-mediated synthesis of AgNPs need more exploration. In conclusion, the plant-mediated synthesis of AgNPs using plant extract is a promising method due to its easy availability, nontoxicity, simplicity, cost-effectiveness and high reducing potential.

## AgNPs ROLE IN MEDICINE:

*Antibacterial Properties.* The Ag-NPs are famous for its potent antibacterial activity against various strains of bacteria including highly pathogenic bacteria species (gram positive and gram negative bacteria) [41].

Sondi and Salopeck-Sondi investigated the antibacterial activities of Ag-NPs against *E. coli* on Luria-Bertani agar plates. The *E. coli* bacterial strains were used as representative species for gram negative bacteria. After the analysis of the obtained results the authors reported that the antibacterial activity of Ag-NPs against *E. coli* was dose dependent (concentration). At optimized experimental parameters, they found out that Ag-NPs were adhered to the cell wall of the gram negative bacteria (*E. coli*) that caused the destruction of the bacterial cell [42]. In another reported study scientists conducted experiments on the size related properties of the Ag-NPs on different species of gram negative bacterial strains [43]. The results obtained from their study suggested that size of Ag-NPs is an important factor in preventing the bacterial cells from their normal functions.

Furthermore they also reported that smaller particle can easily adhere to the cell wall of the bacterial cells thus hampering their normal behavior such as permeability and respiration along with the release of the Ag ions from the Ag-NPs particle.

Furthermore in an another published study, researchers conducted experiments for elucidating the dose dependent properties of Ag-NPs on gram negative and gram positive bacteria; the authors reported that gram negative bacteria (*E. coli*) can be inhibited at relatively low concentration as compared to the gram positive bacteria (*S. aureus*) (see Figure 5). Shrivastava et al. revealed that the antibacterial activity of the Ag-NPs is both size and dose dependent; furthermore they also proposed

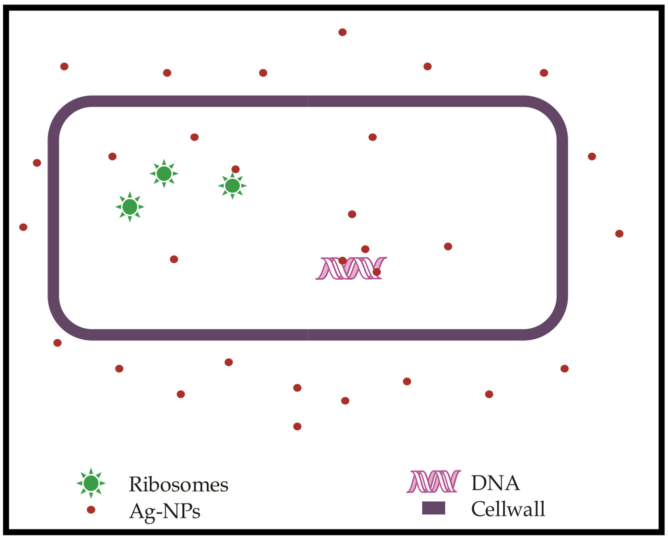


**Figure No. 7**

Figure: Schematic of antibacterial activity of Ag-NPs. Ag-NPs get adhered to the cell wall of bacterial cell through sulphur present in the protein comprising the bacterial cell wall, ultimately causing bacterial cell death. Ag-NPs also hamper protein synthesis along with directly causing damage to the interior of the bacterial cell by directly penetrating the cell wall and cell membrane.

The possible mechanism for the antibacterial activity of AgNPs, which states that the antibacterial activity of the AgNPs is governed by the adhesion and penetration pattern of the Ag-NPs into the cell wall of the bacterial cell, ultimately resulting in abnormal function [86]. In a study published by Pal et al., the authors revealed that the antibacterial activity of the Ag-NPs is structure (morphology) dependent [44].

*Antifungal.* Fungi are considered to play a vital role in causing fungal infections, especially in hospitals[45]. Along with the antibacterial activities of the Ag-NPs numerous studies had been reported on the antifungal activities of AgNPs, which reveals that Ag-NPs could be used as effective antifungal agent because Ag-NPs exhibit excellent antifungal properties against various species of fungi.

In a report published by Kim et al. they tested the antifungal activities of the Ag-NPs against different fungal strains such as *Trichophyton mentagrophytes (T. mentagrophytes)* and *Candida albanicans*(*C. albanicans*) fungi and revealed that Ag-NPs exhibited good antifungal activity.

Furthermore they also proposed the possible mechanism for the antifungal activity of AgNPs, which states that Ag-NPs cause abnormalities in the cell wall of the fungi which results in the abnormal functions (retarding the normal budding process) of the fungal cells (*C. albanicans*) [46-47-48]. In another published paper researchers found out that catheters coated with Ag-NPs can result in complete inhibition of fungi (*C. albicans*).

Recently, scientist reported the antifungal activities of Ag-NPs synthesized by tollens method. From the obtained results they revealed that the yeast cells proliferation can be inhibited with the help of Ag-NPs along without causing any harm to human fibroblastic cells. Another reported work states that Ag-NPs have exhibited antifungal activities against different strains of fungi such as *C. albicans* and*C.glabrata Trichophyton rubrum(T.rubrum)*buttheactivityisdosedependent.

In short due to the reported literature available on the antifungal activity of Ag-NPs, it can be concluded that Ag-NPs can be used as antifungal agent against various strains (species) of fungi and can be helpful in overcoming various fungal infections caused by fungi.

## MEDICAL APPLICATIONS OF AgNPs

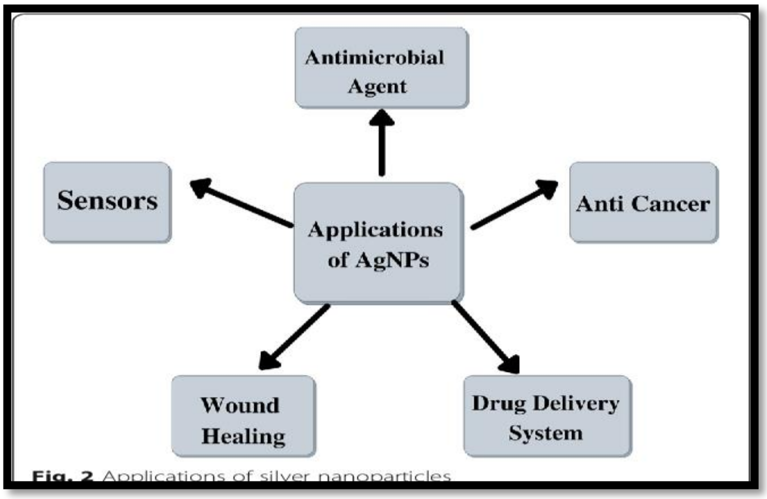


**Figure No. 8**

**a. Antimicrobial**

Silver nanoparticles are well-known as the most universal antimicrobial substances due to their strong biocidal effect against microorganisms, which has been used for over the past decades to prevent and treat various diseases.

**b. Anticancer**

Silver Nanoparticles serve as antitumor agents by decreasing progressive development of tumor cells. This might be because of their inhibitory actions in several signaling cascades liable for the development and pathogenesis of cancer.

**c. Wound Repair**

Recently, silver nanoparticles are attracting interest for a clinical application because of its potential biological properties such as antibacterial activity, anti-inflammatory effects, and wound healing efficacy, which could be exploited in developing better dressings for wounds and ulcers.

**d. Bone Healing**

The potential use of osteo-conducive biomaterials in the promotion of bone fracture healing has attracted wide attention. This study investigated if silver nanoparticles (AgNps) could promote the proliferation and osteogenesis of mesenchymal stem cells (MSCs), and improve bone fracture healing.

**e. Dental Application**

Silver nanoparticles (AgNPs) have been successfully applied in several areas due to their significant antimicrobial activity against several microorganisms. In dentistry, AgNP can be applied in disinfection, prophylaxis, and prevention of infections in the oral cavity.

**f. Vaccine Adjuvant**

Vaccination is one of the most effective methods to prevent infectious diseases and manage healthcare costs. Traditional vaccines have good immunogenicity due to the complex nature of the formulation and the presence of adjuvants.

However, purified preparations lack immunogenicity, which makes the addition of adjuvants essential.

Adjuvants can simultaneously reduce the amount of antigen required, shorten the time needed for a protective threshold of antibody production and improve the intensity of the elicited responses, stimulate long-term memory responses to reduce the requirement of repeated vaccinations.

## CONCLUSION

Over decades, AgNPs have been studied rapidly and extensively due to the unique physical, chemical, optical, electronic and catalytic properties. These properties are closely related to characteristics of AgNPs, especially the size and shape.

AgNPs with different characteristics can be produced by physical, chemical and biological routes. External energy sources such as light, heat, electricity, sound and microwave can be used in the synthesis process. Various factors should be considered in the synthesis of AgNPs with expected size and shape.We review the synthesis methods of AgNPs and compare the advantages and disadvantages to help understand how to obtain nanoparticles with controlled size and shape. AgNPs have broad prospects in medical applications. Among them, antimicrobial and anticancer properties have received more attention.

In this review, we separately introduce the synthesis method and anticancer properties of Ång- scale silver particles in the relevant sections.

Compared with AgNPs mentioned in this review, we prepared pure and fine silver particles with Ångstrom size. This ultra-fine size may be a threshold for silver particles in the medical applications, that is, Ång-scale silver particles exhibit broad-spectrum anticancer activities without obvious cytotoxicity. This exciting discovery inspires us to explore more promising applications of Ång-scale silver particles in nanomedicine.

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