**CURRENT TRENDS OF SILVER NANOPARTICLE IN PHARMACEUTICAL APPLICATION**

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**GENERAL MECHANISM OF AgNPs FORMATION IN SOLUTION:**

Silver nanoparticles (AgNPs) are recently proved to be a decent tool with a varied range of industrial application in multiple fields drawing the attention of the current researchers. The metallic nanoparticles are reported to haveinhibitory effect on a wide spectrum of microbial species, which may be used as a possible substitute of antibiotics [1]. The use of AgNPs as a potential anti-inflammatory effect and in other medical application is also investigated and reported. possess Additionally the use of AgNPs in textile industry. [1,2]

**Synthesis of silver nanoparticles**

The usual process of top-down and bottom-up approach for the production of nanoparticle can also be applicable to produce AgNPs. In top-down technique, nanonised silver metals obtained from mechanical grinding are protected by suitable stabilising agents. Bottom-up approach includes metal reduction, electrochemical methods and decomposition. Various physical, chemical and biological methods extensively exercised for the production of AgNPs are discussed in this section [3,4].

**Chemical Approach**

Chemical reduction for the synthesis of AgNPs is one of the approaches that encompasses the reduction of silver ions (Ag+) in solutions of water or organic solvents into metallic silver in the presence of reducing agents and hydroxyl groups [5]. Silver precursors, organic or inorganic reducing agents and stabilizing agents are the three basic components required for the synthesis of AgNPs. This is a cost-effective approach which prevents excessive aggregation of particles and provides high yield. The shape and size of the particles is controlled by rate of reaction, nature of the reducing agents, the reactivity of the reducing agent to the redox potential of silver etc. [6].

**Physical approach**

Researchers have also turned to the physical technique as an alternative to chemical synthesis.Laser ablation, evaporation-condensation, and ultraviolet (UV) radiation are a few of the top physical processes used to create AgNPs. However, the majority of physical procedures are not only time-consuming but also expensive due to their high energy requirements. For the tube-furnace evaporation-condensation process, for example, a wide area is required, combined with the use of high energy, heat discharged to its surroundings, and a lengthy period to establish thermal stability. Consequently, new alternatives have been created in order to address such issues. To provide an example, Jung et al. (2006) tried to create nanoparticles by nucleating and growing them inside of a tiny ceramic heater [7]. This technique produces microscopic particles in high concentration by achieving thermal stability of the surface temperature more quickly and uniformly. Thermal decomposition, which forms monodispersed silver nanocrystallite from the reaction of silver nitrate (AgNO3) with sodium oleate at an enhanced temperature of 290 °C, is another better approach that has been investigated [8]. AgNPs' uniformity in size and shape is mostly controlled by the physical synthesis's use of heat, ac power, and arc discharge [2].

**Bio-synthetic approach**

However, the chemical production of AgNPs uses substances like sodium borohydride that may attach to the surface of the particles and contribute to whatever negative impacts the final product may have [9]. Additionally, the traditional method of creating AgNPs is expensive and needs a significant amount of energy because heat treatment is also necessary [10]. Researchers are looking at ways to produce nanoparticles that are more economical and environmentally benign in light of the current "going green" trend.

In order to produce silver nanoparticles in a sustainable manner, a variety of biological resources including plants and microorganisms (yeast, fungus, and bacteria) are employed. The presence of biomolecules in these sources' extracts, such as secondary metabolites and amino acids, proteins, vitamins, enzymes, and polysaccharides, aids in the reduction reaction [11,12]. For instance, Sahoo et al.had produced AgNPs as new antibacterial agents against upper respiratory tract infection using the cyanobacterium Chroococcusminutus as a biological reductant [13].

In another experimental investigation, green algae (Botryococcusbraunii) produced silver nanoparticles with cubical, spherical, and truncated triangular shapes with an average size of 88.87 nm [14]. AgNPs with an average size of 14 nm and a spherical shape were created using the endangered medicinal herb Withaniacoagulans. Results indicated that these particles might have an antibacterial and antioxidant effect on the tested microorganisms [15].

**PHYSICAL AND CHEMICAL PROPERTIES of AgNPs:**

Precise particle characterisation is required following synthesis since a particle's physicochemical characteristics may have a big influence on those particles' biological characteristics. It is vital to describe the manufactured nanoparticles before use in order to solve the safety concern and utilise the full potential of any nano material for human welfare, in nanomedicines, or in the health care business, etc. [16,17]. Before determining toxicity or biocompatibility, it is necessary to examine the distinctive properties of nanomaterials, such as size, shape, size distribution, surface area, form, solubility, aggregation, surface charge, redox potential, surface functionalization, and composition etc. [18].

**STABILIZATION OF AgNPs:**

The measure issue associated with the stability of AgNPs is particle agglomeration. Capping agents and surfactants as stabilizers such as chitosan, cellulose, and diverse polymers like polyethylene glycol (PEG), polyvinylpyrrolidone (PVP), polymethacrylic acid (PMAA) can be used to reduce agglomeration and regulating the size of the nano materials. Electrostatic or steric repulsion between the NPs can be used to stabilise AgNPs in suspensions. Anionic species, which cover AgNPs and give their surface a negative charge, such as citrate, halides, carboxylates, or polyoxanions, are typically used to stabilise electrostatic fields. For instance, polyethyleneimine (PEI) can be used to coat the surface with a positive charge. By measuring the zeta potential, it is possible to keep track of these charging-coatings in AgNPs. AgNPs can interact with large molecular groups like organic polymers and alkylammonium cations to provide steric stability. By adjusting the pH, temperature, reaction time, pressure, and the biological reducing agent, one may regulate the synthesis, shape, size, and characteristics of the NPs using a green technique. [19,20]

**CHARACTERIZATION of AgNPs:**

Numerous analytical methods have been used to characterize the synthesised nanomaterials, including scanning electron microscopy (SEM), transmission electron microscopy (TEM), atomic force microscopy (AFM), X-ray diffractometry (XRD), Fourier transform infrared spectroscopy (FTIR), X-ray photoelectron spectroscopy (XPS), dynamic light scattering (DLS), and others [21.22].

AgNPs are invisible to conventional optical microscopy because of their nanoscale size. Because they have a significantly greater resolution and are based on the application of an electron beam, electron microscopy (EM) methods are a common choice for the imaging and characterization of NMs. Transmission electron microscopy (TEM) and scanning electron microscopy are the two most important methods (SEM). TEM pictures show the morphology and condition of the particle aggregation in addition to the size and shape of the particles. Even the layers of atoms in crystalline materials may be seen clearly with high-resolution TEM.

However, the first objective is to create a suitable sample since TEM specimens must be dry and no more than hundreds of nm thick. Solvent evaporation in solutions can result in surface changes and unwanted particle coagulation. Chemical fixing and a straining operation are frequently required for biological tissues and other complicated samples in order to preserve their pristine condition and to increase contrast. In order for the electron beam to pass through the samples, they must also be sliced into thin slices and embedded in resin. [23].

When an electron beam interacts with a specimen surface in a scanning electron microscope (SEM), secondary electrons, backscattering electrons, and distinctive X-rays are seen. One can acquire a 3D picture by focused ion-beam SEM. Although SEM samples do not have to be as thin as TEM samples, it is occasionally required to cover the sample with conductive material in order to prevent the buildup of static electric charge on the sample during electron irradiation. But there's a chance that some of the surface knowledge may get forgotten. [24].

The use of environmental SEM (ESEM), which enables the imaging of samples under vacuum, might be a solution to this issue. The lower resolution is a disadvantage [23]. The size and form of NMs can be directly seen using EM methods, but because so few samples are examined, it takes a long time and a lot of effort to count thousands of particles in order to achieve a representative result. It is also crucial to use energy-dispersive X-ray spectroscopy (EDS), an analytical technique for identifying elements. TEM or SEM are typically used with it to provide an element distribution of the AgNPs. Additionally, it is a very helpful technique for determining the presence of AgNPs in complicated samples. [25,26].

Since AgNPs' optical characteristics are distinct from those of bulk metal, UV-Vis provides the opportunity to characterise AgNPs. As demonstrated by Leopold and his collaborator using TEM and UV-Vis to characterise freshly synthesised AgNPs [27], the maximum absorption wavelength in a UV-Vis spectrum is typically associated with the average particle size, while its full width at half-maximum (FWHM) can give information about particle dispersion. It is also favoured as an additional way to attribute quality [28,29] and to identify the presence of AgNPs due to its low cost and simplicity of handling [26].

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