Chapter

# Silver Nanoparticles - Preparation Methods and Anti-Bacterial/Viral Remedy Impacts against COVID 19

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## Abstract

Silver has been an influential segment of pharmaceutical utilization for remedies & hygiene in the latest era. The first topic reviews the study on air sanitization ventilation & air sanitizer systems using laser ablated silver nanoparticles (inspired by 2020 Pandemic) directing to contamination of deadly biological particles. Intention of this investigation is to validate possible antiviral silver nanoparticles construction to be distributed by retention, to abate the aggravation of breathing organs flu. The underlying description of investigation consists of bibliometric reasoning of the review of the outcome of silver nanoparticles on the sterilization of viral ailments. The investigation will deliberate the approach of use of laser ablated silver nanoparticles for anti-actions. The chapter outcomes in the fascinating utilization of silver nanoparticles for pharmaceutical purposes for contagious diseases, viruses or bacteria and devotes to the upgradation of therapeutic education to safeguard health care workers from threatening viruses at therapeutic organizations. Morally, the investigation will obtain a hygienic scheme, which might be installed at every communal or individual places cost-effectively including silver nanoparticles (because of their therapeutic properties). The second section of investigation considers distinct techniques for manufacturing silver nanoparticles. The various schemes have been compared based on their pros & cons. The method of laser ablation for generating nanoparticles underwater is briefed. The intention of this part is to disclose the current & anticipation probabilities of the process - laser ablation, as a profitable and eco-favorable innovation for manufacturing silver nanoparticle in liquid solutions. The chapter is motivated by two of our reviewed papers i.e., "*Antibacterial and anti-viral effects of silver nanoparticles in medicine against covid 19*" and "*Methods for obtaining silver nanoparticles*".

**Keywords:** Air disinfectant, Air filters, Antibacterial, Antimicrobial, Antiviral, COVID-19, Laser Ablation, Pulsed Laser Ablation in Liquid, Silver nanoparticles

## 1. Introduction

The 2020 circumstances of COVID -19 pandemic, health & sanitization issues in communal buildings have increased recently. Infectious diseases resulted with the Corona Virus expansion were dominating challenge to humanity. That is why innovation into advance strain of practical sterilization strategies is the priority.

Disinfectants are reagents used to coat surfaces to reach out for microbes that either contaminate or eradicate them. Reagents are mostly used for the sanitization of diverse facades in communal premises and medical equipment. Disinfectants used in daily life can be handy to keep interacting surfaces clean by destroying biological microorganism on them and still pose no threat to human lives. Also, sterilizers must have a plentiful quantity for repeated utilization in short periods [1].

Presently, synthetic segments & oxidants like aldehydes, alcohols & sodium hypochlorite, hydrogen peroxides, iodine, and others, respectively, are favorably used for sanitization processes. In some events, these elements present numerous cons like metal corrosion, resistance to various bacteria, as well as other unfavorable environmental effects.

With the invention & promising features of nanomaterials, a wide range of options have been disclosed to overwhelming flaws. As interpreted by the International Organization for Standardization (ISO), "nanomaterials" are somewhat material particles of diameter varying between 1 nm & 100 nm. In present-day, distinct material nanoparticles are favorably utilized as efficient sanitizers. The preeminent attempts of scientists from nanotechnology, at the present day, are concentrated on enhancing their physiochemical features & increasing the results of their sanitizing ramification on emerging or modified viruses. Distinct nanoparticles of metals like copper (Cu), silver (Ag), and gold (Au), are now strongly preferred as antiseptics.

Products based on Ag ions and its other antimicrobial works are known since 1000 BC. They were commonly adopted by the archaic Indians in food & medicinal products as a remedy [2].

Antimicrobial effects of silver nitrate ($AgNO_3$) are generally well-known, but with Ag NPs onset, its beneficial properties have raised undoubtedly. This is briefed by the advanced physicochemical features that Ag NPs consists of. With a higher

| Component | Physicochemical features of Ag NPs | Disinfectant results |
|---|---|---|
| Ag/$TiO_2$ | Contraction in bandgap points to the noticeable active material | Noticeable active antibacterial results [3, 4] |
| Ag ZnO | $O_2$-, OH | Photo-oxidative elimination of bacteria [5, 6] |
| Ag NPs | Surface functionalization<br>Anti-viral | Photocatalytic, self-sanitization bacterial deactivation [7–10]<br>Eradication of aerosolized bacteriophage MS2 virus particles [11] |
| Ag polyamide | 40–60 nm of size | Viable discharge of $Ag^+$ ion for antibacterial ramification [12]. |
| LA/ZnO:Cu/Ag Bio-nanocomposites | Mechanical/structural, antibacterial & railing characteristics to UV light | Strengthening the lifespan of food [11] |
| Ag Co-NPs | Magnetic & antibacterial | Water Cleaning [13] |
| AgNP-SiO2 | Spherical morphology | Propelling & synergic antibacterial action of air sanitization [14] |
| Ag NPs/Chitosan | Porosity, moisture retention efficiency, blood-clotting proficiency | Injury healing strength [15] |
| Ag/BC | Porosity | Injury healing strength [8] |

**Table 1.**
*Prominent physicochemical features of silver nanoparticles & products as a preservative.*


**Figure 1.**
*Utilization of silver nanoparticles as a sanitizing agent at different communal places.*

surface/volume, ratio they have a great synergy with microbe surfaces and leads to great antimicrobial safety. The size, shape of Ag NPs portrays a vital aspect in this mechanism. These physiochemical features of Ag NPs are necessary and compatible to the seek for new technics to tackle any future pandemics like COVID-19.

These substantial physiochemical features of Ag NPs are also universally accepted in fields like ecology, industry, and many more. The table beneath briefs the investigation of distinct research teams, demonstrating their fields of utilization.

According to **Table 1**, Ag NPs play a crucial function in air and water sanitization, as well as a medical assistant in a few therapeutic actions. They radiate highly significant behavior in interaction with various bacteria & viruses like *Staphylococcus aureus*, *Pseudomonas aeruginosa* coli and many others [16]. The extraordinary activities of Ag NPs are due to binding capability to sulfur (S) and phosphorus (P), as well as functionalized biomolecules, directing to a rise in their physicochemical features and the competence to destroy various viruses [17].

**Figure 1** represents simplified promising operations of Ag NPs. Because of the multi-sphere utilization of Ag NPs, the vast sphere of the biomedical line, as an ingenious organization connected to the 21st century COVID-19 pandemic, that occurred globally and bringing the world to a halt. This review chapter is notably directed to the performance of Ag NPs as a purifying agent for isolating the escalation of Coronavirus, to quarantine Internal airborne ailments in which humans are likely to be contaminated with the viral atoms at communal places.

## 2. Silver nanoparticles

Silver is the exceptionally integral anti-microbial/bacterial (**Figure 2**) agent accessible way before the initiation of antibiotics [19]. Ag NPs are nanoparticles (NPs) of Ag constructed via nano-techniques of distinct size & shape in any proportion [20]. Approximately, three hundred and twenty tons of tiny silver is produced in a year and used worldwide at present [21]. For the past few decades, Ag NPs is the prime investigation theme because of their size, shape, antimicrobial effects, chemical stability, catalytic activity high conductivity, and other extraordinary features. Processes & methods like laser ablation, microwave processing, gamma irradiation, electron irradiation, chemical reduction, photochemical

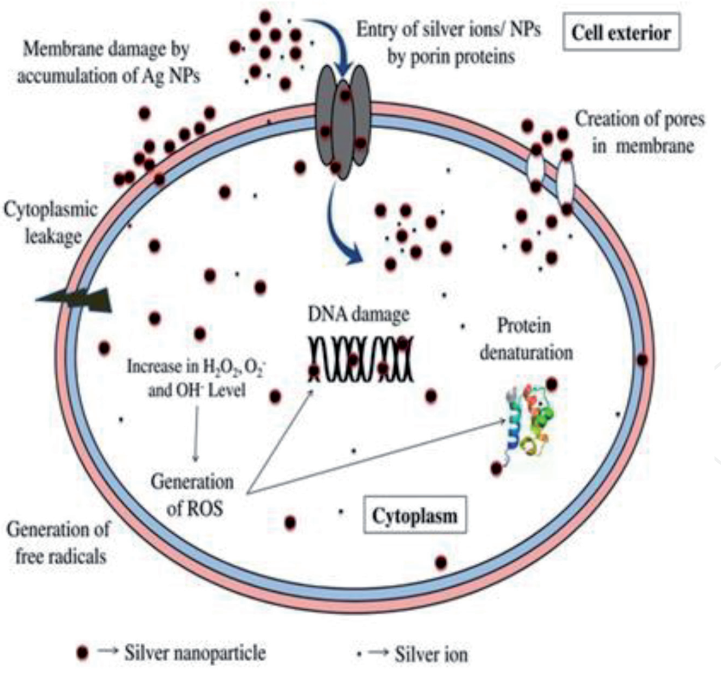


**Figure 2.**
*Biological process of antibacterial impacts of silver nanoparticles & silver ions [18].*

methods, and synthetic biological procedures are some prior researched techniques for constructed Ag NPs [22].

Nanotechnology is a fundamental research attention of present-day, managing design, synthesis, and molecule structures varying not more than 100 nm. NPs have several functions in medication, cosmetics, Eatables, optics, biomedical sciences, space industries, electronics, and in many other broad areas. Synthesized Ag NPs are valued for numerous medical functions such as [22, 23].

- Remedy to ulcerative colitis, acne & dermatitis
- Inhibition of HIV-1 replication
- Molecular imaging of cancer units
- Exposure of viral arrangements (SERS & Ag nanorods)
- Antimicrobial impacts for infectious organisms
- Lacquering of surgical mesh for pelvic repair & breathing mask patent, used in COVID-19.

Relying on the reducing agents and procedure there are 3 heyday mechanisms to develop Ag NPs.

- Physical techniques generally strive with laser impulse energy to dwindle Ag from volume to atoms and ions.
- Synthetic techniques utilize reducing chemical agents to reduce Ag ions from the bulk of metallic Ag.
- Biological techniques utilize reducing organic agents to reduce Ag ions from the bulk of metallic Ag [24].

## 3. Air decontamination

Currently, several human acts while the discrete modification practices direct a negative impact on air quality. Nowadays, the preeminent threat is to obtain a healthy air quality exempted from harmful particles like airborne bacteria/viruses, fine dust fragments, capricious biological elements & noxious gases. The eviction of threatening airborne microorganisms fascinate scientists because they are liable for chronic contagious disease and are genuine threats of airborne toxicity. Such microbes generate a need for air cleaning systems, which will lower the stability of several microorganisms in the air and will provide healthy air for inhalation. Mentioned microbes are the reason for several diseases like severe acute respiratory syndrome (SARS), anthrax, asthma etc.

Studies confirm that bioaerosols gather on air conditioner filters in massive amount & breed with high moisture [25]. Presently, several engineering solutions are available for bioaerosol removals like photocatalytic oxidation, UV irradiation with germicides, and aerial ozonolytic methods.

It is believed that a fruitful remedy for pandemics like COVID-19 also associates with the utilization of Ag NPs & Cu NPs (Copper nanoparticles) as a sanitizer agent. Enhanced air quality is obtained with Ag NPs sprayed on air filters [26]. Therefore, a belief is born, that nanomaterials & air filters coated with Ag NPs can be an engineering solution to pandemics.

Ag NPs coated with silica, in symmetric distribution, perform symbiotic antibacterial actions with gram-positive/negative, microbe in the air refining arrangements. Moreover, Ag NPs & $SiO_2$ infused together certifies a six-month steady solution & performs 99.99% antibacterial actions. Generating Ag aerosol NPs in a puffer as an antiviral assistant to Hay Bacillus & COVID-19 aerosols under expert medical guidance are favored applicable. Overall, we can claim that combined elements are beneficial for installing with air purifiers (**Figure 3**) in air refining devices [11, 14].

**Figure 3** represents a schematic of the anti-viral impacts of Ag NPs coated on an air refiner. In the research paper, Herzong et al. manifested the probability of manufacturing an airway barrier with aerosolized Ag NPs featuring basic cytotoxicity [27]. Our research in this line confronts the Ag NPs originated products have a greater impact in safety and avoidance of viral ailments for upper respiratory section. It happens because, transfer of viral flu is observed primarily through inhalation, ingestion, and dermal routes.

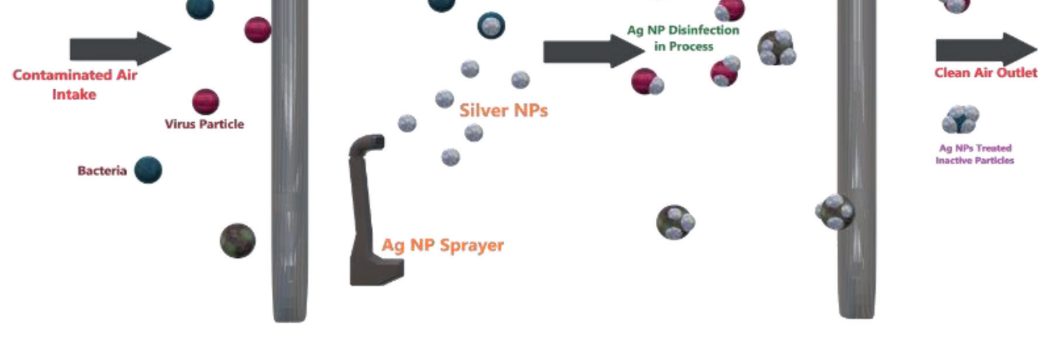


**Figure 3.**
*Anti-viral impact of silver nanoparticles on bioaerosols impregnated in the air filter. (Regenerated from reference [27]).*

So, sprayers originated from nanotechnology discharging airborne particles & Ag compounds have proven to boost good human health. Such ways substantiate a better air quality in communal places & provides enhanced protection against COVID-19 at its primary stage. Thus, mobile oxygen generating system & air coolers can easily be equipped with Ag NPs coated filters with improved efficiency & without being overpriced [28, 29].

## 4. Approaches for obtaining NPs

Many convincing procedures have been awarded for processing Ag NPs in the past years [30]. NP production is briefed under two elemental categories (**Figure 4**):

*Top-down Approach*: - Solid bulk material is applied with external force, forcing its break down into nanostructures.

*Bottom-up Approach*: - Its initiates from atomic scale & generates NPs, until appropriate size and shape is gathered [32].

Physical, Chemical, & Biological Methods to process the Ag NPs are explained below:

### 4.1 Physical methods

These could be defined as the green mechanism because of non-synthetic liquids in the tidy, thin films. Moreover, high consistency of NP distribution, is one of the pros of physically processed NPs as identify with any other methods [22]. This method consists of mechanisms like [30]:

- *Arc Discharge* - Condensation, nucleation, & construction of NPs pursues when marked component is volatilized via an arc discharge between electrodes [33].

- *High-Pressure Magneton Sputtering* - It falls under bottom-up process & inhabits in abridgment of super-saturated vapor via cold inert gas flow. This vapor atmosphere is acquired by discrete processes like thermal evaporation, laser ablation, magnetron plasma sputtering, and many other [34].

- *Laser Ablation* – A laser beam radiates to separate top layers of the bulk material with an absolute accuracy [35].

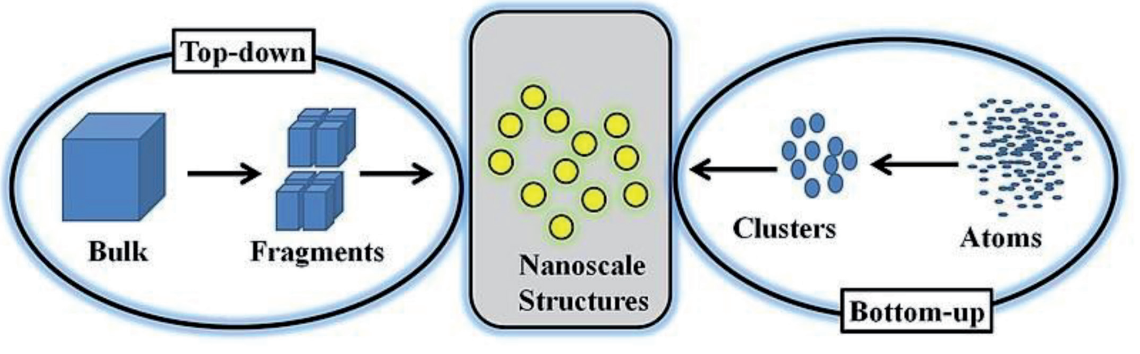


**Figure 4.**
*Representation of two elemental categories, 'top-down' & 'bottom-up' approaches for the nanoscale material processing [31].*

### 4.2 Chemical methods

A chemistry professor from Princeton - John Turkevich's work in the 1950s, gave a highlight to chemical methods. The chemical processing by natural and artificial reducing surfactants is the preferred method for constructing Ag NPs. Reducing agents like sodium citrate, ascorbate, elemental hydrogen, are generally employed for $Ag^+$ ions reduction in aqueous or non-aqueous solution. These agents shrink $Ag^+$ ions forming $Ag^0$ [36]. Protective agents are obligatory to stabilize breaking-up of NPs during their preparation and to restrict them to stay onto material surfaces [37]. To stabilize particle hike and to sustain them from sedimentation, accumulation, or losing surface properties, comprising functionalities to unite with molecule skin, the presence of surface-active agents like acids, amines, or alcohol are must [22]. This method comprises of [30, 38]:

- *Photochemical* – In an electron-contributing reagent, it requires UV irradiation of the solid forerunner solution. This process produces NPs subjected solid-state status & at low temperatures [39].
- *Microemulsion* – It is thermodynamically balanced colloidal diffusion of oil in water or vice-versa with a stabilizer. Ultralow interfacial tension, large interfacial area & monodispersed NPs, are pros of this technique [40].
- *Hydrothermal* - It is a solution reaction-originated approach which produce NPs at room-temperature to extremely high-temperature [41].
- *Chemical Reduction* - A usual process utilizing natural & artificial reducing agents like sodium citrate, sodium borohydride (NaBH4), elemental hydrogen, N-dimethylformamide (DMF), & poly (ethylene glycol)-block copolymers for $Ag^+$ ion break-down [22].
- *Electrochemical Mechanism* - A common process, containing a two-electrode mechanism for the electrochemical fusion. It has utmost preference over other bottom-up approaches because of pure quality of NPs received [42].

### 4.3 Biological methods

These are categorized under green synthesis and comprises polysaccharides, organic & irradiation techniques, preferred over other traditional practices requiring synthetic agents with hefty harms [43]. Because of benefits like organic surfactants (bacteria, fungi, yeast, and plant), cheap and eco-friendly techniques, a vast interest is gained by these methods. Even with natural surfactants, it has a usual reduction process [30]. Green synthesis pursues with:

- *Bacteria* – It is capable to weaken heavy metal ions & has its preferences for generating NPs. E.g.: *Pseudomonas stutzeri* and *Pseudomonas aeruginosa* [44].
- *Plants* - Metabolites in plant crude extract are capable of metal ions reduction into metallic NPs. E.g.: *A. indica*, *A. sessilis* [45].
- *Fungi* - They offer high tolerance NPs and are easy to handle. Its extracellular protein extract can stabilize NPs. E.g.: Fusarium oxysporum [46].
- *Algae* - These are single/multi-cellular organisms endured in surroundings. Processing at low temperature with high energy efficiency, less noxious to the environment are its pros. E.g.: *Chlorella Vulgaris*, Spirulina platensis [47].

## 5. Topnotch favored approaches

Pulsed Laser Ablation in Liquid (PLAL) subordinated to physical methods is the top-notch method for producing Ag NPs since it is a green method which utilize the least time & finances [48, 49]. Because of nucleation, advancement & cluster formation, it is a subordinate to the bottom-up process. Interacting with ultrashort laser beam pulses i.e., $10^{-13}$ *to* $10^{-8}$ sec , generates nanostructures from the metal bulk substrate in any medium, is called a laser ablation process [32, 50, 51]. It depends on aspects like laser wavelength (λ), repetition rate, frequency, pulse duration, the light absorption efficiency of material, transmission, and chemical composition of the liquid. The monochromaticity and directionality of the laser beam are vital characteristics for this process.

Moreover, produced Ag NPs are pure and are free of metal colloids contamination and have great quality because of non-utilization of any artificial or natural surfactant. Efficiency and features of produced Ag NPs are based on specifications, consisting of "λ", pulse duration, ablation time & the laser beam interaction with each NP inside the liquid [52, 53]. Spatial profiling of laser beam intensity or fine balancing of "λ" controls size distribution [54]. Essential specifications are briefed be/neath:

- *Pulse Duration*: In PLAL it can vary from *Femto-Nano* seconds. NPs originated via sputtering of the molten surface layer by the liquid's recoiling pressure around the processing metal. The temperature "*T*" of the laser beam spot is denoted with simple heat balancing equation:

$$T \approx \frac{Aj}{cph} \tag{1}$$

Here, A - absorptivity of marked material (A = 1- R) [R - reflectivity coefficient].

c - heat capacity of marked material,

ρ - density of marked material,

h - heat diffusion length inside marked material,

The heat diffusion length "*h*" is dependent on the heat diffusivity of the processed sample, expressed as:

$$h \propto \sqrt{at_p} \tag{2}$$

wherein, $a = \frac{k}{c}$, [*k* - heat conduction coefficient of marked material & "$t_p$" - laser pulse duration].

Larger the $t_p$, bulky is the layer of material which is heated by laser energy absorption. Moreover, for heating & evaporation of liquid adjacent to the laser beam spot, an unwanted bulk of energy is drained approximate to the one absorbed due to reduced thermal conductivity of liquids [54].

- *Laser Wavelength*: As most of constructed NPs can consume laser radiation (which can melt material), so, UV ranging "λ" are least preferred in PLAL [54].

- *Repetition Rate*: With every laser pulse, NPs are discarded from the processing sample surface. Therefore, higher the repetition rate of laser pulses, higher is the NP production [54].

In PLAL, laser beam is directed to a processing sample top-layer plunged into liquid. Supposedly, because of transparency and non-absorption of liquid, the laser beam radiation can focus directly on the target. The ideal facade of the liquid avoids surplus reflection at the interface "covering glass/air". However, the use of unstable liquids like acetone, ethanol, etc., demands covering the vessel with a transparent lid [54].

The laser ablation is successful only when tiny structures of processed metal are constructed by PLAL, see **Figure 5** [55]. In **Figure 5**, an *Ag* sample is immersed in distilled water and is synthesized under pulsed laser. Different types of lasers like Solid, Gas or chemical laser, can be used with distinct "λ" ranging from pico-femtosecond. Generated NPs have extraordinary features and are irreproducible by any other traditional methods [56].

**Figure 5** demonstrates the Ag NPs generation out of a bulk silver plate via high-power pulsed lasers in PLAL. Material properties affect the ablation at its best. Various laser parameters are used to composite NP characters like size, shape, surface properties, aggregation state, solubility, structure, and chemical composition, see **Table 2** [30].

When compared,

- The generation efficiency & the size of colloidal components of *"ns"* laser was larger than *"fs"* laser.

- The manufactured colloids by *"ns"* pulses were extra scattered than *"fs"* pulses.

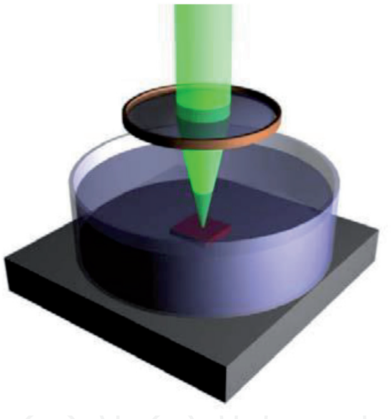

**Figure 5.**
*Diagrammatic representation of PLAL process with metal immersed in distilled water [54].*

| Wavelength | 532 nm | 800 nm | 1064 nm |
|---|---|---|---|
| **Laser Type** | Nd: YAG (ns*) | Ti: Sapphire (fs**) | Nd: YAG (ns*) |
| **Mean Diameter of NPs** | 2–3 nm*** | 400 nm*** | 2–5 nm*** |
| **Absorbance** | 0.28 | > 0.05 | < 0.1 |
| **Quantity & Type of Liquid** | 170 ml**** (Pure water) | 5 ml**** (Deionized water) | 25 ml**** (Pure water) |

*Nanosecond
**Femtosecond
***Nanometer
****Milliliter.

**Table 2.**
*Different laser parameters for obtaining Ag NPs via PLAL, based on the theoretical research [57–59].*

- The ablation demonstration for *"fs"* ablation in air was lessened than distilled water but *"ns"* pulses did not have any change of ablation energy in either of the mediums.
- The self-absorption capability of Ag is higher at lower wavelengths [57, 60].

## 6. Nosocomial epidemic (hospital-acquired infections)

The predominating threats in the biomedical line are the penicillin-immunity of the living beings, product advancement behavior and its services in terms of hazardous, healing timespan & aftereffects on the mortal cells. Also, the revelation of infection-inducing non-bacterial microorganisms, supervising infection administration & avoiding nosocomial infections (**Figure 6**) are main confronting puzzles for the science [61].

A survey by WHO concluded that moderately 8.7% of world population has suffered from nosocomial disease, and approximately 1.4 million people suffered Hospital-Acquired Infections (HAI) [62]. Eastern Mediterranean & south-east Asian regions are HAI sensitive rather than the other regions. Nosocomial Infections covers categories likes surgical wounds, urinary & lower respiratory tract infections. The latter was particularly pronounced for the 2020 COVID-19 infections.

Avoidance of HAI demands a coordinated & overseen plan in which peculiar features must be calculated. The transmission of bacterial/viral microorganism from person to person is diminished by individual cleaning like handwashing, hand gloves, masks, working clothes, shoes, & sterilization of medical apparatus [63].

Also, higher the bacterial/viral protection, higher is the impact on wellbeing. Many theories have been executed worldwide for restricting HAI's. It is noted that Ag NPs utilization is highly emerging solution to quarantine the Nosocomial Infections, also, an efficient nano-weapon to multidrug resistance microorganisms [64].

The unmanaged & enormous use of penicillin and their bacterial hostility is a present-day menace for medicinal industry, which also consists of Ag NPs induced antibiotics [65]. Ag NPs obtained from bio-methods using *B. marisflavi* resulted high antibacterial actions against bacteria leading to nosocomial infections [66].

In therapeutic institutions, medical apparatus is the usual source of spreading infection. The quick fix to this problem could be the coating apparatus with Ag NPs to bypass bacterial contagion. Ag NPs are productively utilized in catheters

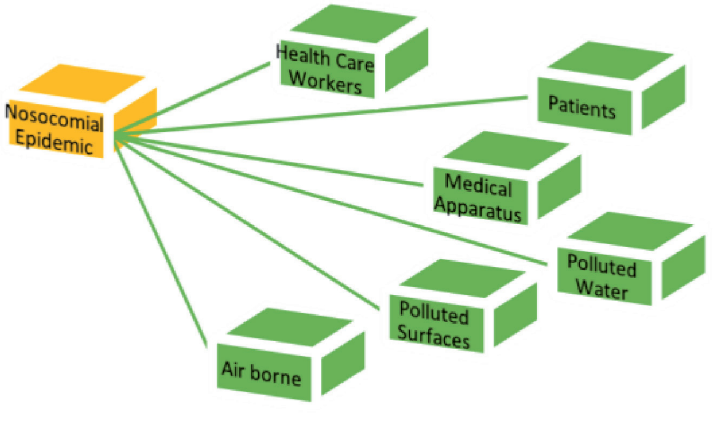


**Figure 6.**
*Elements subjected to nosocomial infections.*

for enhanced antimicrobial actions & zero thrombogenicity [67]. The writers also questioned the impact of Ag NPs on blood clotting, and the outcomes are fascinating. It should also be understood that the antimicrobial impact of Ag NPs coated titanium instruments is modified by UV light exposure [68].

Exploration in this branch had concluded an overall bacterial termination of Methicillin-resistant *staphylococcus aureus* (MRSA) as a result of Ag NPs synergic effect as a photocatalyst & visible light was accomplished [5, 69]. An identical energetic bactericidal effect was detected with stents & catheters used in cardiovascular operations [70]. So, it can be believed that the Ag NPs are advantageous ingredient to isolate differential ailments occurring in therapeutic organizations. Also, precautions should be taken to avoid their noxious impact on humans.

## 7. Anti-action operations of AgNPs

Many researchers have examined & published the antibacterial performances of Ag NPs. The bacterial cell membranes consist of sulfur (S) comprising proteins & involves amino acids. On inner & outer membrane Ag can blend in with them preventing bacterial expansion. Ag NPs also produce Ag ions which blends in with Deoxyribonucleic acid's (DNA's) phosphorus (P) and with "*S*" consisting of proteins, inhibiting the enzymes movement. Characteristics like "size" & "shape" of NPs guides to evaluate Ag NP's antimicrobial behavior. NPs of size <20 nm will execute a better attachment of "*S*" comprehending protein of membrane ending in cell death of bacteria as a result of maximum permeability via membrane [71].

**Figure 7** represents the interaction mechanism of Ag NPs surface-to-volume ratio on bacteria/virus. Nanomaterials has a nature, that smaller the NPs, greater surface interaction is exposed and contributes to better microbicidal effect [72, 73].

Shape of NPs also plays avital role to interact with the membrane walls. Analysis in [74] directs to large anti-activities towards *E. coli* bacteria with abbreviated triangles of Ag NPs better than those of spherical & rod-shaped NPs. It is also mentioned that Ag NPs <10 nm creates holes in the cell wall as a result of these holes the cytoplasmic is dispensed into the medium, responsible for controlling cell death without interaction between intracellular and extracellular proteins and bacterial nucleic acids. The writers of [75] declares that the interaction of Ag NPs with virus cells directs to an escalation in actions of their programmed cell death i.e., apoptosis.

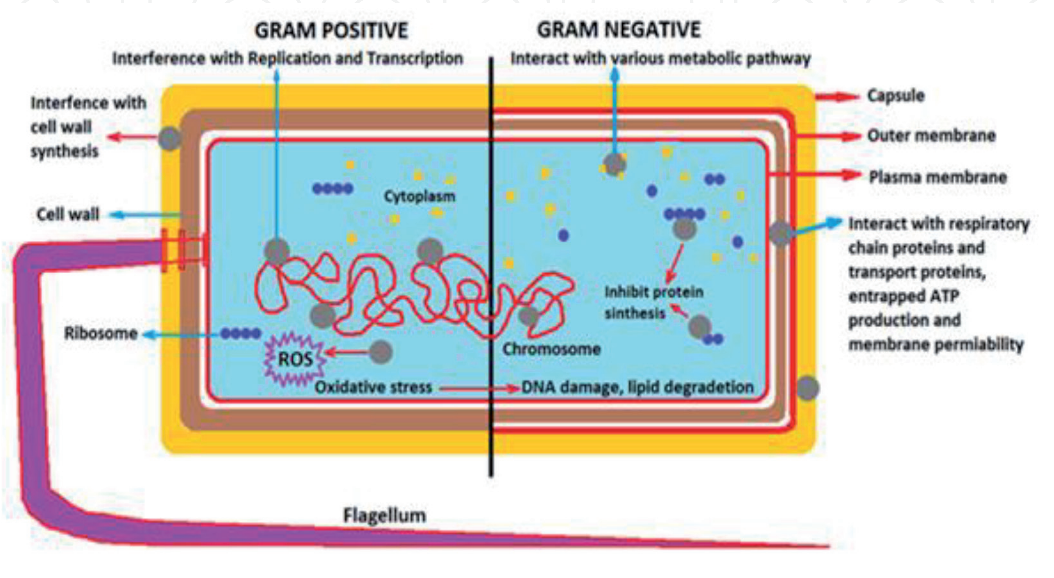


**Figure 7.**
*Demonstrating antibacterial features of silver nanoparticles.*

In simple words, Ag NPs are fascinating disinfectants better than merchandise like Acticoat™ & Silverline® for wound dressing & polyurethane ventricular catheter, respectively [70]. Moreover, Ag NPs are utilized in several merchandise-like surgical masks, toothpaste, hand wash, shampoo, detergent as well as humidifiers but their toxicity to human lives is still a top concern.

## 8. Early-stage treatment via respiration approaches with Ag NPs for COVID-19

Numerous drug manufacturing experiences the well-known antimicrobial features of Ag NPs. The anti-bacterial/viral features of Ag are very well researched in the scientific world [76, 77].

To investigate and validate the anti-action features Ag NPs as a purification segment for medicinal benefits, and their functions for treatment & anticipation of viral disease for inhalers, was the prime intuition of this investigation. Viral & Bacterial ailments threats to respiratory supported patients in intensive care units (ICU) due to ventilator-associated pneumonia (VAP), are basic scenarios that are present day discussion topic. The nasopharynx and/or bronchial tree of the breathing organs (respiratory system) are vulnerable to be infected by any infections even by a regular bacteria/virus (**Figure 8**) [78, 79].

The sinking of the microorganism to the lower vent of the breathing organs aggravates the conditions, intensifying the immune response and consequence huge damage (**Figure 9**) [81, 82]. Therefore, a superior proficient approach to diminish the bacterial/viral growth at the very starting i.e., in the upper breathing organs. For example, patients with slight symptoms or patient's arrival at ICU in the therapeutic institution before any VAP infection.

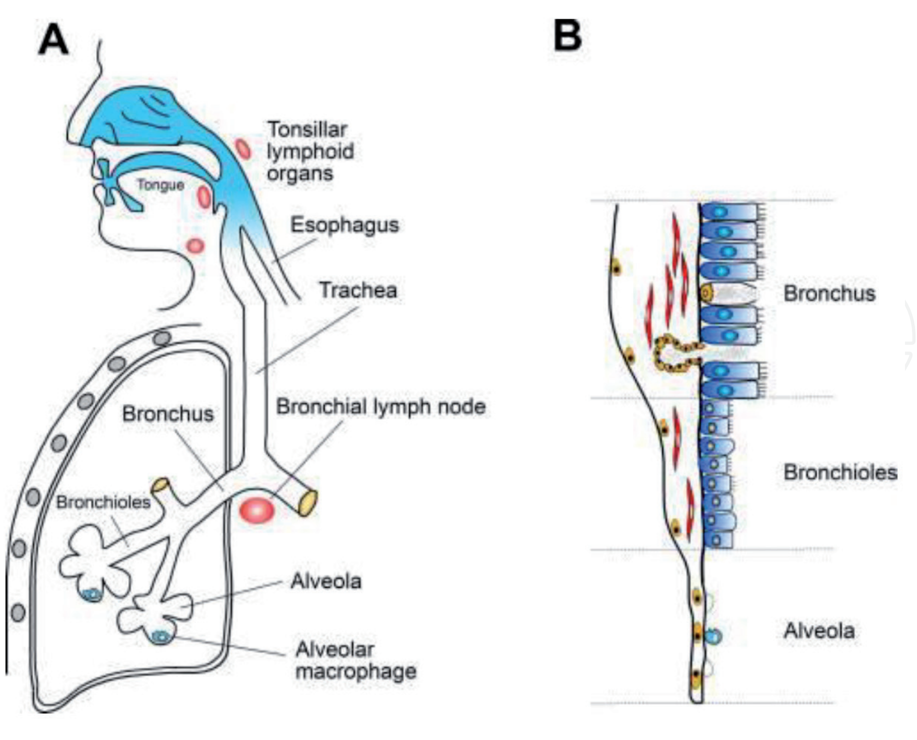


**Figure 8.**
*Entry points of influenza into respiratory system. (A) The description of the human airways. Microbes first infects the upper vents and the rough cells in the bronchus and bronchioles. The adaptive resistance is initiated in lymph nodes along the airways. (B) The respiratory epithelia are especially equipped to defend from incoming pathogens by a layer of mucus (bronchus), ciliated cells (bronchus and bronchioles), and alveolar macrophages (alveoli).*

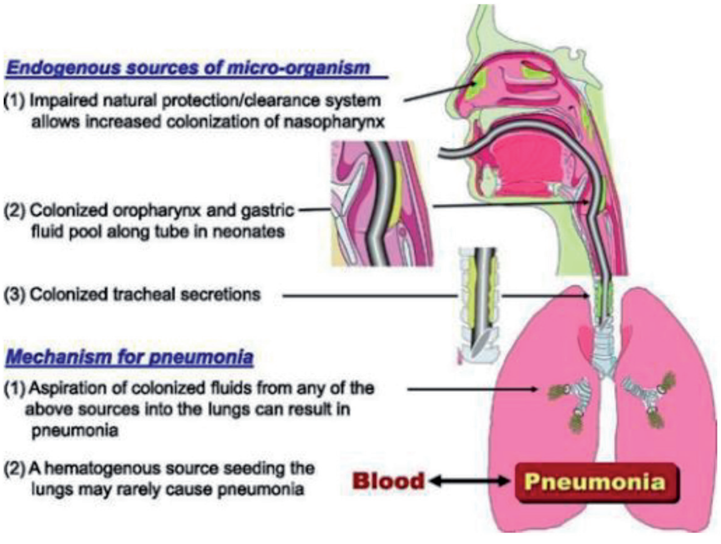


**Figure 9.**
*Microbes of HAI - VAP [80].*

An adequate solution for upper & lower respiratory system remedy is briefed in the paper. It is mandatory that for intake, the difference between ionic Ag solution & colloidal Ag and Ag particles suspensions/solution in water has the relevant structure.

- In ionic Ag, the atomic Ag ions are soluble in water.
- Colloidal Ag are nanosized Ag pieces ranging from 1 to 100 nm diameter [80].

There is a debate on colloidal particles being more persuasive than ionic Ag for anti-viral features [83], as described in **Table 3** for Human Immunodeficiency Viruses (HIV). Evaluation the anti-action of colloidal Ag will help understand the quantity of Ag NPs for healthy inhalation.

Minimum Inhibitory Concentration (MIC) should be developed to calculate the authorize dosage of any effective agent. The delicacy of MIC (μg/ml) to NP size, is problematic to settle conclusions from disclosed studies.

NPs >10 nm are ultimately resulting than those >25 nm [83, 84]. Higher density was noticed with the small sizes of NPs which leads extraordinary synergy with microorganisms. That is why, the MIC of NPs > 10 nm must be tiny than that of large sized NPs and is experimentally absolute (see **Table 4**) [80]. With every publication the value to MIC has varied with the NP size. It has been stated in the research of the effect of Ag NPs size on anti-viral efficacy in HIV treatment. These results are concluded by assuming that because the virus size is ≥ 100 nm for e.g., HIV has a size of 120 nm. And to interact and act on the virus the AG NPs must be tiny for the virus particle (approx. of 10 nm). These assumptions were made by direct imaging of NPs [85].

| Element | IC50* |
|---|---|
| Silver Nanoparticles | 0.44 mg/mL (± 0.3) |
| Silver sulfadiazine (ions) | 39.33 μg/mL (± 14.60) |

**The half maximal inhibitory concentration.*

**Table 3.**
*Anti-action impacts of Ag ion & Ag NPs against HIV-1 [83].*

| Specimen | MIC (μg/mL) | |
|---|---|---|
| | *Bacteria* | |
| | *E. coli* | *S. aureus* |
| 7 nm Ag NPs | 6.25 | 7.5 |
| 29 nm Ag NPs | 13.02 | 16.67 |
| 89 nm Ag NPs | 11.79 | 33.71 |

**Table 4.**
*MIC of colloidal Ag for antibacterial effects [80].*

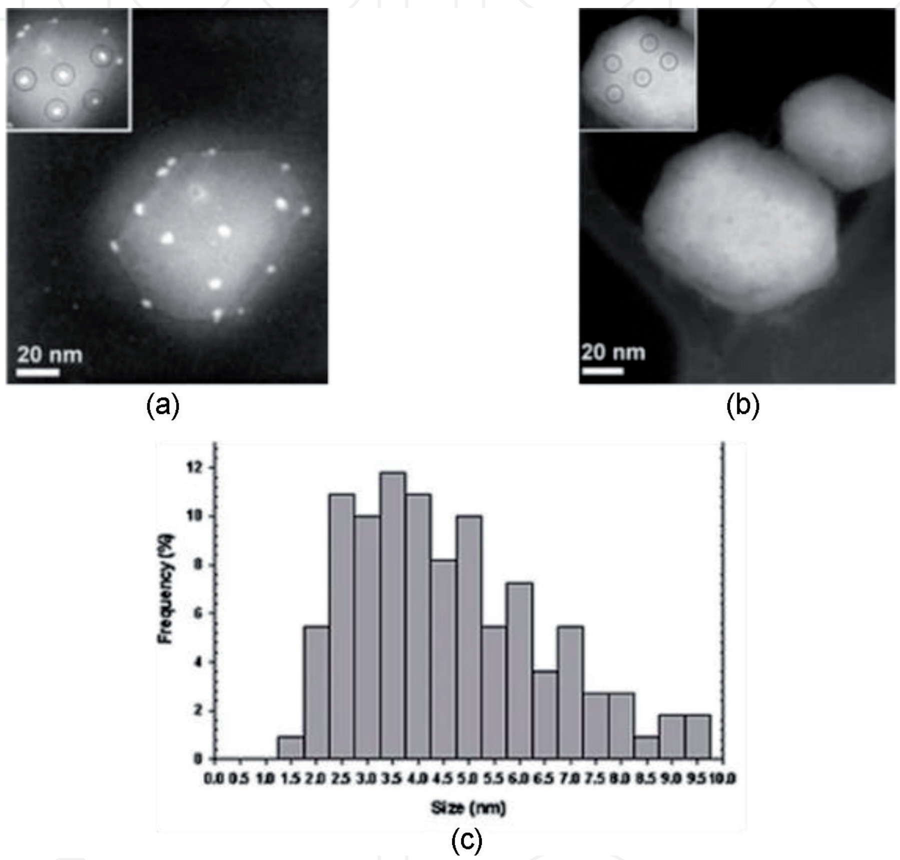


**Figure 10.**
*a) HIV-1 virus commuting silver; b) HIV-1 viruses without commuting silver; c) complex size distribution of Ag NPs commuted with HIV-1 virus, resulted via tested preparations [85].*

Fascinating fact is that the culminating virus attachment for NP impact ranged between 3 and 7 nm (see **Figure 10**) [85]. Hence, the size-dependency for NP interaction to virus is stated.

In this chapter we have discussed miniscule measure of Ag NPs utilization in the biomedical work, whereas worldwide testing rooms are actively researching on it. In overall it could be said that, presently, the anti-bacterial/viral features of colloidal Ag are definite but in case of respiratory disease, a lot of must be researched deeply. Also, the MIC size of colloidal Ag ranging between 10 μg / ml and 25 μg/ml (indirect conclusions, requires deep study to specify) & 3–7 nm, respectively, have impressive suppression on viral infections.

Expecting, these formulations can be persuasively precautionary & remedy in beginning of respiratory viral ailments, including COVID-19/SARS-CoV-21. Such remedy could be helpful for bacterial ailments like prevention of clinical VAP & in ICU's and only half dosages compared to other anti-bacterial.

Until now, high assumptions are made from Ag NPs applications, but their over concentration can be threatening to human lives [86]. For example, excessive concentration can cause high blood pressure [87]. However, the hazardous of AG NPs is not that higher because of their nano size and possibly end in the urine [88].

The adequate & conservative utilization of Ag NPs should be concrete, as their catastrophic consequences are known only through animal & In vitro tests.

## 9. Ending

Because Ag NPs have chemical stability and retains uncommon features, they are used in fields like therapeutic, environment, food industry, biotechnology, microelectronics, and many other. Moreover, there antimicrobial assistance has compelling vigilant ramifications against microbes. Ag NPs are an elemental ingredient to configuration of products with antimicrobial actions due to their non-toxicity to mortal bodies but only in low mixtures. These uncommon features of Ag NPs have interested many researchers for innovating modern techniques to obtain their different size & shapes. Many leading research teams are enhancing the Ag NPs manufacturing methods using chemical reduction, laser ablation, electron beam exposure, concentrated microwave exposure, and other.

The PLAL (branch of Physical methods) tends to occur any exceptional environmental side-effects by producing pure & clean metal NPs with uncommon characteristics, without any organic/inorganic chemical agents. Laser wavelength ($\lambda$) & intensity are vital parameters required for NP construction. For example, green lasers can construct NPs with better efficiency than infrared (IR) lasers and *"ns"* pulsed laser generates strong heat.

The hasty incorporation & flexibility of chemical methods into distinctive surroundings is the motivation for scientists to keep up with the mechanistic conditions of the anti-microbial/viral/inflammatory impacts of Ag NPs. This takes place with the alteration in the form, NP size by altering the reaction requirements, reagents and stabilizing surfactants used.

Whereas biological methods for NP synthesis possess vast alternatives for using natural & artificial stabilizing surfactants. Use of bio-organisms for NP extraction might commit to the surrounding purification. Surface chemistry & morphology, size, shape, coating agent, NP agglomeration & dissolution rate, particle reactivity in solution, and ion release efficiency, are the dependencies for biological actions of Ag NP.

The fascinating use of Ag NPs in medicinal purposes especially against contagious ailments as a result of their extraordinary microbicidal spectrum. In recent years, studies have confirmed Ag NPs impact on viruses, which was expected to be opposing. Contact infection between Health Care Workers and patients could be prevented effectively with Ag NPs, must be advised. Optimistic results have been obtained for Ag NPs contribution in enhancing the microbicidal effects of biocompatible medical devices. Expectations have aroused for contribution of effectual utilization of Ag NPs in modification of medical science for treatment of contagious ailments.

With the time the research in this line has reached to a far point but there is a lot more to be researched like to improve & interpret the last-longing benefits of NPs on mortal souls. Also, the optimal accumulation on the distinct points of the ailments in sufferer without noxious impact on living beings. It requires all hands joined from around the globe to put their efforts for research in enhancing technologies for generating NPs with various features, as well as carrying out therapeutic observations & particular objective investigation.

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