



Synthesis of Silver Oxide Nanoparticles and its Antimicrobial, Anticancer, Anti-inflammatory, Wound Healing, and Immunomodulatory Activities - A Review

Sheraz Muhammad¹, Asif Ali^{2*}, Sana Zahoor¹, Xie Xinghua³, Jehangir Shah¹, Muhammad Hamza⁴, Muhammad Kashif¹, Sumayya Khan¹, Behram Khan Ajat Khel¹, Arshad Iqbal¹ and Marwa Tariq¹

¹Department of Chemistry, Abdul Wali Khan University, Mardan, KPK, Pakistan

²School of Chemistry and Chemical Engineering, Beijing Institute of Technology, Beijing, China

³School of Chemical Engineering, Anhui University of Science and Technology, China

⁴Department of Chemical Engineering, Ming Chi University of Technology, Taiwan, Republic of China

***Corresponding Author:** Asif Ali, School of Chemistry and Chemical Engineering, Beijing Institute of Technology, Beijing, China.

Received: June 04, 2023

Published: June 30, 2023

© All rights are reserved by **Asif Ali, et al.**

Abstract

The unique characteristics and potential uses of silver oxide nanoparticles (Ag₂O NPs) have generated considerable interest in the field of nanotechnology. The present review offers a comprehensive survey of the various synthesis techniques utilized in the fabrication of Ag₂O nanoparticles, and investigates their multifaceted biological properties. The article presents a comprehensive analysis of diverse physical and chemical techniques employed for the synthesis of Ag₂O NPs. Additionally, the study highlights the characterization methods utilized to evaluate the structural and chemical attributes of the synthesized nanoparticles. This study provides a comprehensive analysis of the biological properties of Ag₂O nanoparticles, encompassing their antimicrobial, anticancer, anti-inflammatory, wound healing, and immunomodulatory activities. The elucidation of mechanisms of action, including the generation of reactive oxygen species and interactions with cell membranes and DNA, is also discussed. Additionally, this study addresses the toxicological implications and possible environmental consequences linked to Ag₂O nanoparticles. The review concludes by emphasizing the diverse utilization of Ag₂O nanoparticles in various domains, including biomedicine and environmental restoration. The present study provides a thorough examination of the synthesis, biological activities, mechanisms, and applications of Ag₂O nanoparticles. This investigation enhances our comprehension of their potential and establishes a foundation for further exploration in this captivating field of nanotechnology.

Keywords: Synthesis; Silver Oxide Nanoparticles; Characterizations; Biological Activities; Application; Future Perspectives

Introduction

Nanotechnology is the study of structures with dimensions between 1 and 100 nanometers (nm), which are characterized by unique qualities and functionalities as a result of their tiny sizes [1,2]. Incredible day-to-day growth has unbolted up creative applied and basic frontiers in nanotechnology. These frontiers may

be found in a new sector of study known as materials science and engineering. Some examples of these frontiers include quantum dots, Nano biotechnology, surface-enhanced Raman scattering (SERS), and applied microbiology. Nanoparticles are attracting a lot of attention because of the enormous surface to volume ratio and very tiny size (in nm) that they have. This ratio and size lead to

both physical and chemical modifications in their properties when compared to the majority of particles that have the same chemical composition. This has caused a lot of excitement in the scientific community [3].

Silver oxide nanoparticles (Ag_2O NPs) have garnered the most interest among these nanoparticles because of their fascinating properties and wide variety of biological activities. Silver oxide nanoparticles (Ag_2O NPs) have recently received substantial attention across a wide variety of areas owing to the unique physico-chemical qualities that they possess as well as the extensive number of applications that they may be used for. It has been known for centuries that silver had antibacterial characteristics; nevertheless, the capacity to manufacture it and control it on a nanoscale has substantially expanded the range of applications that are potentially applicable to silver. These nanoparticles have an increased surface area in comparison to their volume, which results in improved catalytic, optical, and electrical capabilities. In addition to this, they have found widespread use in the fields of catalysis, optoelectronics, and electronics. However, the use of silver and silver oxide nanoparticles in the area of biomedicine is where their promise has been most clearly shown [4]. Nanoparticles of silver oxide, more precisely Ag_2O NPs, have certain fascinating features that make them useful in a wide variety of contexts. The synthesis of Ag_2O NPs may be accomplished using a variety of processes, some of which are physical, such as vapor deposition and laser ablation, while others are chemical, such as chemical reduction and sol-gel procedures. When it comes to controlling the size, shape, and surface qualities of the particles, each technique has a number of benefits to offer. After being produced, Ag_2O NPs exhibit a wide variety of biological activities, which has drawn the interest of researchers. Because of their antimicrobial activity, for example, which has shown strong bactericidal and antifungal effects, these compounds are intriguing prospects for the treatment of microbial illnesses. In addition, Ag_2O NPs have anticancer features, such as cytotoxic effects and the ability to induce apoptosis, which indicate that they have significant potential for use in cancer treatment. These nanoparticles have also shown anti-inflammatory activity, wound healing characteristics, and immunomodulatory effects, which broadens the range of applications that are possible for them in biomedical disciplines. The processes that are responsible for the biological activities of Ag_2O NPs are complex and include complicated interactions with the biological systems that are being

studied. It has been shown that the production of reactive oxygen species (ROS), interactions with cell membranes, and processes of DNA damage and repair are crucial mechanisms that contribute to their antibacterial, anticancer, and anti-inflammatory activities [5,6]. When these processes are understood, useful insights into their mode of action may be gained, which in turn helps in the creation of applications that are more specifically targeted. However, in addition to the intriguing biological activities that Ag_2O NPs possess, it is very necessary to evaluate the possible toxicological concerns that are linked with them. It is very necessary to do exhaustive research assessing their cytotoxicity, genotoxicity, and possible repercussions on the environment in order to guarantee their safe usage and reduce the likelihood of any unintended consequences. In spite of the difficulties and factors to take into account, there is a wide range of potential uses for Ag_2O NPs. In the realm of biomedicine, they show promise in the development of drug delivery systems, coatings that inhibit the growth of bacteria, tissue engineering, and other areas. Additionally, the prospective uses of these materials extend into environmental fields, such as the purification of water and the filtering of air [7].

This review will explore the synthesis techniques, biological properties, mechanisms of action, toxicological considerations, and prospective uses of Ag_2O nanoparticles. Through an examination of synthesis methodologies, comprehension of their biological properties, and resolution of associated obstacles, the complete potential of Ag_2O nanoparticles can be realized, leading to pioneering progress in diverse domains.

The synthesis methods of Ag_2O NPs

There are numerous techniques that can be used to produce silver oxide nanoparticles. Either a "Top down" or a "Bottom up" technique can typically be used for the synthesis of Ag_2O NPs. Using physical processes to size-reduce bulk materials, the top-down approach produces nanoparticles. Silver Oxide NPs are produced via chemical and biological processes in the bottom-up strategy, which is shown in figure 1 [8].

Physical approaches

Evaporation-condensation method

Physical processes such as evaporation-condensation, which can be performed in a tube furnace under air pressure, are generally utilized for producing Ag_2O NPs. A carrier gas is created by the

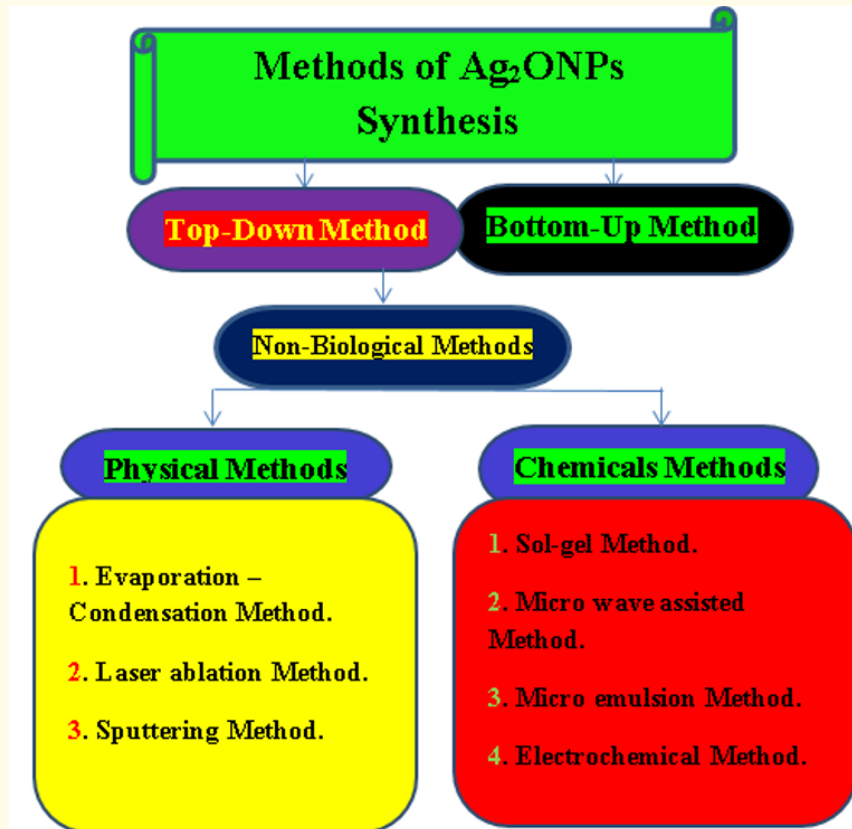


Figure 1: Methods of Ag₂ONP Synthesis.b.

evaporation of the material source inside a boat-shaped furnace. Recently, the Evaporation-Condensation method has been utilized for producing nanoparticles made of a variety of materials, including Ag and Au. However, there are several drawbacks to producing Ag₂ONPs in a tube furnace since it takes up lots of room, consumes lots of energy even after raising the temperature around the source material, requires longer time for thermal stability. To achieve a consistent working temperature, a typical tube boiler must consume many kilowatts of power and pre-heat for many minutes [9].

Laser ablation method

By using laser ablation, the laser’s radiation is employed to reduce the particle size to the nanoscale. The solid target material is positioned behind a thin layer and then exposed to pulsed laser light. When materials are exposed to laser light, the solid substance is broken up into tiny NPs, which stay in the liquid that surrounds

the target and also produce colloidal solution. The amount of ablated atoms and Ag₂ONPs produced depends on the length of the laser pulse and its energy [10].

Sputtering method

Sputtering entails pounding a hard surface with high-energy gas-like particle bombardments in order to produce Ag₂ONPs. Approaches for sputtering are believed to be effective for producing thin films of nanomaterials. An evacuated chamber is given the sputtering gas to begin the sputtering process. Then a high voltage is delivered to the cathode that is the target, making free electrons to clash with the gas as they go there, producing gas ions. The cathode target is struck repeatedly by powerfully accelerated positively charged ions in electric fields, causing an atom discharge on the target’s surface. The sputtered Ag₂ONPs composition is identical

to the target material having less impurities, making the sputtering technique attractive. It is also cheaper than electron beam lithography [11].

Chemical approach

Sol gel method

The sol gel approach makes use of a wide range of superior nanomaterials based on Ag₂ONPs. The current procedure is called as a “sol-gel method” for the reason that an aqueous precursor is converted to a sol during the manufacture of Ag₂ONPs, and the sol is then transformed into a network structure called as gel. Particle size can be checked by varying the precursor concentration, temperature, and pH values. It takes a mature stage to allow the evolution of solid mass; it can take a few days for the solvent to evaporate and phase shifts to take place. Ag₂ONPs are produced by separating the unstable ingredients [12].

Micro-wave assisted method

Nanotechnology as well as biological pathways are two areas where microwave assisted technique is frequently employed. Compared to conventional convective heat treatments, chemical reactions frequently occur faster, with higher yields, and with fewer byproducts. Microwave reactors are effective at controlling the reaction mixture, can resist high temperatures as well as pressures, and can produce predictable reaction responses. The utilization of microwave-assisted methodologies enables enhanced engineering regulation of the separation between the nucleation and growth stages during the formation of silver oxide nanoparticles when the reaction is started at ambient temperature. It's possible that microwave-assisted heating is to blame for part of the sensitivity in stimulating precursor materials for nanomaterials, which is essential for scalability. In order to prepare silver oxide nanoparticles, The process of microwave-assisted preparation possesses the ability to differentially heat either the solvent or the catalyst molecules [13].

Micro-emulsion method

The micro emulsion approach promises to be the flexible methods of preparation that enables the formation of particle attributes such as geometry, surface characteristics, homogeneity, surface characteristics as well as mechanisms for controlling particle size.

The micro emulsion approach is widely used in both chemical and biological fields [14].

Electrochemical method

Chemical fluctuations are caused by the passage and conduction of an electronic flow through an electrolytic solution. Two metal electrodes, the anode as well as the cathode, are submerged in electrolytic solutions that include metal salts and a stabilizing agent while also having an electric voltage applied across them in an electrochemical process. This process involves a constant electric current flowing into the electrolytic cells, which ionizes the metal salt solution and causes it to dissociate. The metal sheet is dissolved, the anode goes through oxidation, and the cathode goes through intermediate salt reduction. Dropped metal from the anode terminal onto the cathode plates. M molecules in the form of NPs are painstakingly collected from the cathode terminal toward the end of electrolysis [15].

Characterization of Ag₂ONPs

Characterizing silver oxide nanoparticles, also known as Ag₂O NPs, is essential to gaining a knowledge of the size, shape, structure, composition, and physicochemical characteristics of these particles. The following is a list of some of the more prevalent approaches for characterizing these nanoparticles shown in figure 2.

UV-visible spectroscopy

The optical absorbance as well as bandgap of the Ag₂ONPs are determined using UV-Vis absorption spectroscopy. Based on their absorption, this method is used to identify and explain metal-based nanomaterials. While the size range for characterization of Ag₂ONPs by UV-Vis absorption spectroscopy is 2-100 nm, the nanoparticle size level varies from different metals. Ag₂ONPs have a wave length range between 200 and 800 nm, and a UV-Vis spectrophotometer can detect them. Under specific salt-synthesis conditions, metallic nanoparticles exhibit significant absorption to produce a point spectrum in the detectable region. Earlier research findings shown that the absorption of wavelengths 200–800 was suitable for classifying nanoparticles with sizes between 2–100 nm [16,17].

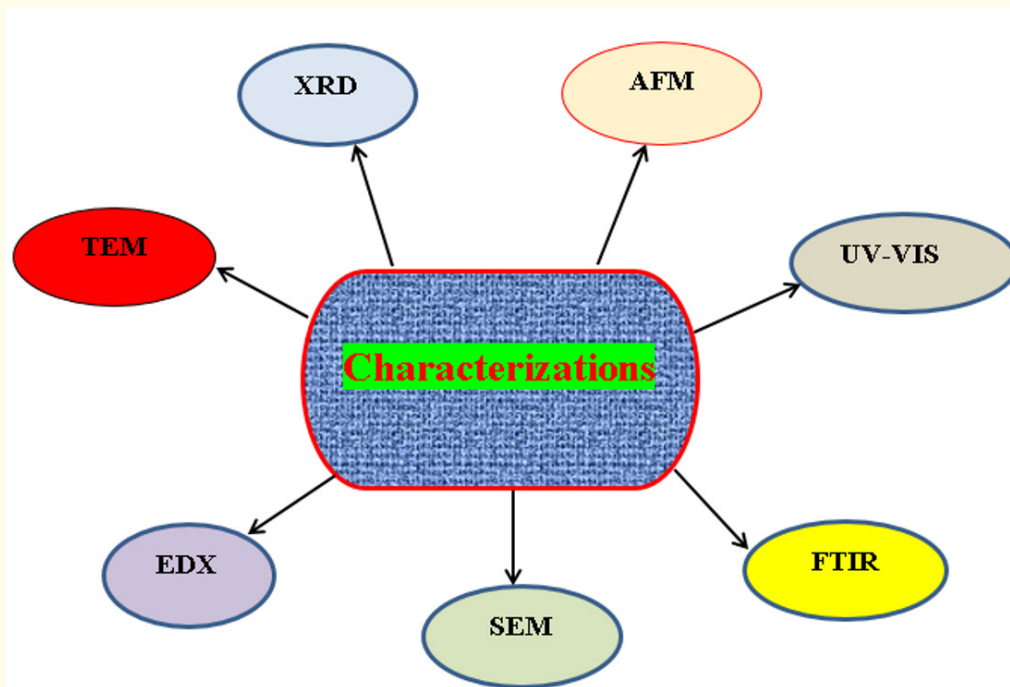


Figure 2: Various Characterization Techniques.

Atomic force microscopy (AFM)

Atomic force microscopy (AFM) spectroscopy is a powerful tool for imaging, probing, and manipulating materials at the nanoscale. When it comes to silver oxide nanoparticles, AFM spectroscopy can provide significant insights into their structure, properties, and behavior. AFM classified as well as confirmed the size, shape, outside the region of produced Ag_2ONPs [18].

Energy-dispersive X-ray spectroscopy (EDX)

EDX analysis, short for Energy-Dispersive X-ray Spectroscopy analysis, is an approach used to determine the sample's elemental composition. EDX analysis offers qualitative as well as semi-quantitative information about the elemental composition of the sample. It can identify the presence of elements such as silver, oxygen, and any other elements that may be present as impurities or additives. The analysis can be used to verify the composition of the nanoparticles and ensure that they are consistent with the intended silver oxide formulation [19].

Scanning electron microscopy (SEM)

SEM is capable of characterizing Ag_2ONPs . This instrumentation study aims to characterize the distribution, size, morphology, and form of silver oxide nanoparticles. The SEM study measured how a morphological structure changed both before and after treatment. According to earlier research, observable changes in cell shape as well as nanoparticle perforations in the cell wall have been employed a sign for antibacterial effect of NPs. Ag_2ONPs produced through phytosynthesis had their surface shape determined using SEM [16,18,20].

Transmission electron microscopy (TEM)

The crystal structure as well as particle size of the material were classified and verified using transmission electron microscopy (TEM) at the nanoscale level. The morphology as well as dimensions of Ag_2ONPs were determined using transmission electronic microscopy (TEM). The sample was created by pouring the Ag_2ONPs solution onto a copper grid that had been coated with carbon and then setting it on a specimen holder. TEM images were used to verify the Ag_2ONPs ' sizes and forms [16,18].

X-ray diffraction (XRD)

XRD is able to study the atomic structures of materials. The quantitative as well as qualitative levels of materials can be determined with the use of this technology. Crystalline nanoparticle shapes and sizes were identified and verified using XRD analysis. Applying the Debye-Scherrer formula to determine the width of the Bragg reflection law according to the equation: $d = K\lambda/\beta \cos \theta$, where d is the particle size (nm), K is the Scherrer constant, λ is the X-ray wavelength, β is the full width half maximum, and θ is the diffraction angle (half of Bragg angle) that corresponds to the lattice plane, allowed for the analysis of the particle dimension of nanomaterials from XRD data. Every crystalline substance has a unique diffraction pattern that can be utilized to detect the crystalline structure and nanoparticle morphology using X-ray diffraction (XRD) [16,18,21].

Fourier transform infrared spectroscopy (FTIR)

In order to reduce, stabilize, and cap Ag_2ONPs , a functional group must be found using Fourier transform-infrared (FTIR) spectroscopy. In FTIR analysis, the sample is exposed to infrared red rays, some of which are absorbed by it, and the remainder of which pass through. The spectrum shows wavelength-dependent absorption or transmission, which describes the sample materials. A good, affordable, straightforward, and non-invasive method to identify the role of biomolecules in the reduction of Ag_2ONPs is FTIR analysis. The potassium bromide is used in the FTIR analysis in the 400–4000 cm^{-1} range to produce a fine powder [16,22].

Biological activities of silver oxide nanoparticles

Nanoscale particles called silver oxide nanoparticles (Ag_2O NPs) are made up of atoms of both silver and oxygen. Because of their unique characteristics, nanoparticles like these have recently received a lot of interest from the scientific community. It is possible to provide a brief overview of their general biological activities as follows:

Antimicrobial activity

Ag_2O NPs have been shown to possess potent antibacterial action against a broad variety of pathogens, including fungi, and bacteria. The nanoparticles' discharge of silver ions (Ag^+) interferes with the structure and function of the cell membranes of microorganisms, which has the effect of destabilizing the cells. Due to

the antibacterial properties of silver oxide nanoparticles, they have found use in a variety of applications, including wound healing, disinfection, and sterilization.

Bactericidal effects

Since ancient times, people have known that silver has antibacterial properties, and today, silver is used in a wide range of scenarios to prevent the development of germs in situations such as dental procedures, catheters, and burn injuries. In view of the possibility that they possess antibacterial characteristics, silver oxide nanoparticles have recently received a lot of interest. These nanoparticles have bactericidal properties against a broad variety of microbes, and they are made up of silver atoms that have been linked with oxygen. Silver and compounds based on silver are very poisonous to microorganisms and have been shown to have substantial biocidal effects on as many as 12 different types of bacteria, including *E. coli*. Recent research has resulted in the synthesis of silver oxide nanoparticles that demonstrate antibacterial properties. The examination of this phenomena is now becoming more important as a direct result of the rise in bacterial resistance to antibiotics that has been induced by the inappropriate use of antibiotics. The antibacterial activity of silver nanoparticles may be utilized to minimize infections and to avoid colonization on prostheses, catheters, vascular grafts, dental material, stainless steel material, and human skin. This can be accomplished by using the antibacterial activity of silver nanoparticles. Nanoparticles, which have an extremely high ratio of surface area to volume, are very effective in preventing the development of bacteria in both aqueous and solid mediums. Materials that include silver may be used for either the removal of germs from textile fibers or for the treatment of water. Both of these applications are viable options [23]. The following is an outline of some of the most important information about the bactericidal effects of silver oxide nanoparticles:

Mechanism of action

The bactericidal effects of silver oxide nanoparticles are caused by a variety of different processes, which contribute to their overall effectiveness. They are capable of releasing silver ions (Ag^+), which when they contact with the membranes of bacterial cells, may cause the membranes to become disrupted and more permeable. This causes the homeostasis and metabolic processes inside the cell to become unstable, which eventually leads to the death

of the cell. In addition, silver oxide nanoparticles are capable of producing reactive oxygen species (ROS), such as hydrogen peroxide. These ROS produce oxidative stress in bacteria, which in turn causes DNA, proteins, and other cellular components of the bacterium to get damaged.

Activity against a wide range of bacteria

Silver oxide nanoparticles have been shown to possess antibacterial activity that is effective against a wide range of bacteria, including Gram-positive and Gram-negative forms of bacteria. They have been shown to be effective against a variety of common infections, including *Salmonella enterica*, *Escherichia coli*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa*, amongst others. Due to the broad spectrum of activities that they exhibit, silver oxide nanoparticles are a potentially useful agent in the fight against bacterial infections.

Enhanced efficacy

The antibacterial activity of silver oxide nanoparticles is generally significantly improved as compared to that of bulk silver. The enhanced surface area-to-volume ratio of nanoparticles enables more contact with bacteria, which in turn facilitates the transport of silver ions and reactive oxygen species in a more effective manner. Because of this improvement in effectiveness, the needed concentrations are lower, and the toxicity is decreased as well.

Resistance prevention

Silver oxide nanoparticles also show promise in preventing the evolution of resistant bacterial strains. As a result of the drug's complex mode of action, which concurrently targets several cellular components, it is very difficult for bacteria to build resistance mechanisms in response to silver oxide nanoparticles. This quality is very necessary in light of the fact that the development of antibiotic-resistant bacteria presents a substantial risk to the health of people all over the world.

Concerns about biocompatibility

Although silver oxide nanoparticles have significant antibacterial characteristics, one must also take into account the possibility that they would be cytotoxic and examine whether or not they are biocompatible. The toxicity of these nanoparticles is now the subject of a substantial amount of study that is being carried out. Their

biocompatibility may be affected by a variety of factors, including the particle size, concentration, length of exposure, and route of administration. The goal of these studies is to improve the antibacterial activity of silver oxide nanoparticles while simultaneously reducing the risk of any harmful effects that may be caused by their production or surface changes [24].

Antifungal effects

Fungi are recognized as having the capacity to act as pathogens, which means that they are capable of triggering severe health issues in human beings. In addition to the antimicrobial activity and antibacterial behavior of silver nanoparticles (Ag_2O NPs), several studies have also demonstrated the antifungal activities of Ag_2O NPs against a wide variety of fungal species. Numerous research have been conducted on the antifungal activity of silver oxide nanoparticles, and the findings have been found to be encouraging [25]. The following is an outline of some of the most important information about the antifungal effects of silver oxide nanoparticles:

Mechanism of action

Antifungal activity is shown by silver oxide nanoparticles via processes that are analogous to the ones that underlie their antibacterial properties. They are capable of releasing silver ions (Ag^+), which when they contact with the membrane of the fungal cell, may cause the membrane to become disrupted and more permeable. This causes the integrity of the fungal cell to be compromised as well as vital activities, which eventually leads to cell death. In addition, the production of reactive oxygen species (ROS) by silver oxide nanoparticles may create oxidative stress in fungus, which can damage the cellular components of the fungi and prevent the fungi from growing.

Fungicidal and fungi-static effects

It has been shown that silver oxide nanoparticles display both fungicidal (the ability to kill fungi) and fungi-static (the ability to stop the development of fungus) effects. The precise result is contingent on a number of elements including the concentration of nanoparticles, the length of exposure, and the species of the particular fungus that is being targeted.

Broad-spectrum action

Silver oxide nanoparticles, in addition to possessing antibacterial capabilities, also exhibit broad-spectrum antifungal activity

against a large variety of fungus species. It has been shown that they are effective against a variety of common fungal infections, including *Candida albicans*, *Aspergillus fumigatus*, *Trichophyton rubrum*, and *Cryptococcus neoformans*, amongst others.

Synergistic effects

Silver oxide nanoparticles, when employed in conjunction with traditional antifungal treatments, have the potential to display synergistic effects. Studies have demonstrated that mixing silver oxide nanoparticles with antifungal medications like fluconazole or amphotericin B might improve the overall antifungal effectiveness, perhaps lowering the needed drug concentrations, and limiting the development of drug resistance in the fungal infection.

Concerns with biocompatibility

It is essential, as is the case with other nanoparticles, to take into account the biocompatibility and possible cytotoxicity of silver oxide nanoparticles. The concentration, size, and surface charge of the particles, as well as the length of time they are exposed to the substance, are all crucial elements in determining their level of safety and the extent to which they have harmful effects on human cells and tissues. Extensive research is now being carried out in order to assess the biocompatibility of silver oxide nanoparticles and enhance their characteristics for the purpose of developing efficient antifungal applications [26].

Anticancer activity

An ever-increasing number of people are being diagnosed with cancer and passing away from the disease as a direct result of the widespread industrialization and changes in lifestyle that have occurred in the contemporary period. The diagnosis and treatment of cancer are now the subjects of a significant amount of study. The diagnosis, localization, and therapy of cancer are all thought to benefit enormously from the use of nanomaterials. When compared to their bulk form, nanoparticles exhibit distinct differences in their chemical, optical, mechanical, and magnetic capabilities, and these differences have begun to interfere with our daily lives. As potential instruments for the development of innovative cancer therapies, silver and nanoparticles based on silver are receiving a growing amount of research [27]. Recent research has shown that silver oxide nanoparticles have tremendous potential for use as an anticancer therapy. The amazing capacity of silver oxide nanoparticles to induce cytotoxicity in cancer cells has been the subject of a great

number of studies, which have documented the phenomenon in a variety of ways, including oxidative stress, DNA damage, cell cycle arrest, apoptosis, and necrosis. Silver oxide NPs have been shown to have strong anticancer activity in a variety of animal models, and they are also powerful sensitizers for cancer chemotherapy and radiation [28]. The following are some important details about the cancer-fighting properties of silver oxide nanoparticles:

Induction of cancer cell death

Silver oxide nanoparticles have shown the capacity, via a variety of different ways, to cause cancer cell death. The production of reactive oxygen species (ROS), which are capable of inflicting oxidative stress on cancer cells as well as causing damage to their DNA, proteins, and other biological components, is one way. This damage may cause a stop in the cell cycle as well as programmed cell death, which is known as apoptosis. In addition, silver oxide nanoparticles have the potential to alter the operation of mitochondria, which may ultimately lead to the death of cells due to a lack of energy [29].

Inhibition of the proliferation of cancer cells

It has been observed that silver oxide nanoparticles may prevent the growth of cancer cells. They are able to thwart the development and multiplication of cancer cells by interfering with certain biological processes or signaling pathways. However, more research has to be done in order to determine the precise pathways that are responsible for this inhibiting impact.

Enhanced drug delivery

The one-of-a-kind features of silver oxide nanoparticles make them suitable candidates for use as carriers for anticancer medicines, resulting in improved drug delivery. They have a huge surface area that can be functionalized to bind or encapsulate anticancer medications, which enables targeted and regulated drug delivery to cancer cells. This is made possible by the fact that they have this vast surface area. By limiting the amount of medication that is taken up by healthy cells, this strategy offers the potential to increase treatment effectiveness while simultaneously lowering the risk of adverse effects.

Inhibition of angiogenesis

The process of angiogenesis, which refers to the production of new blood vessels, is essential for the growth and spread of tu-

mors. Silver oxide nanoparticles may contain anti-angiogenic capabilities, according to the findings of several research, since they interfere with the signaling pathways that are involved in the process of angiogenesis. Because these nanoparticles hinder the creation of blood vessels, they may assist restrict the flow of nutrients and oxygen to tumors, which in turn may help to slow the growth of tumors.

Considerations about biocompatibility and possible toxicity

It is essential that silver oxide nanoparticles' biocompatibility and potential toxicity be exhaustively investigated prior to using them in cancer treatments in order to ensure that they do not pose a risk to patients. Their biocompatibility and the possible adverse effects are impacted by a variety of factors, including nanoparticle size and concentration, as well as surface changes and the method of administration. The characteristics of silver oxide nanoparticles are now being studied in an effort to improve them so that their anticancer activity may be increased while at the same time reducing the cytotoxicity they cause to healthy cells [30].

Anti-inflammatory activity

Nanoparticles made of silver and silver oxide have been the subject of substantial investigation due to the unique qualities they possess and the potential uses they might have in a variety of sectors, including medicine. One of these areas of study is the anti-inflammatory effect that silver oxide nanoparticles have on the body. Inflammation is a biological reaction that is generated by the immune system of the body in order to guard against harmful stimuli such as infections, damaged cells, or irritants. Inflammation may also occur as a result of injury to cells. On the other hand, inflammation that is severe or persistent may be hazardous and is linked to a number of disorders, including arthritis, cardiovascular diseases, and cancer. As a result, treating inflammation effectively is a primary objective in the treatment of a wide variety of health disorders [25,31]. The precise process by which silver oxide nanoparticles exert their anti-inflammatory effect is still the subject of active research, however the following are some of the postulated mechanisms:

Inhibition of inflammatory cytokines

The synthesis of inflammatory cytokines may be inhibited by silver nanoparticles, according to the findings of certain research. Inflammatory cytokines include substances such as interferon, in-

terleukin, and tumor necrosis factor; all of which have a role in the development of inflammation.

Modulation of reactive oxygen species (ROS)

Silver nanoparticles may have anti-inflammatory effects because of their ability to modulate the formation of ROS. If an excessive amount of these chemically reactive molecules are created, they may lead to oxidative stress and inflammation, despite the fact that they are necessary for cell communication and homeostasis.

Inhibition of cell signaling pathways involved in inflammation

Silver nanoparticles may interfere with cell signaling pathways involved in inflammation, such as the nuclear factor-kappaB (NF- κ B) pathway, which plays a vital role in controlling the immunological response to infection. This may lead to an increase in the severity of inflammation.

Wound healing properties

Based on their ability to kill microbes, silver oxide nanoparticles have been the subject of a great deal of research. These features make them of substantial interest in the field of wound healing. Dressings made of silver and nanoparticles of silver have both been shown to reduce the risk of infection in wounds, and there is also some evidence that they may hasten the healing process.

Antibacterial property

Silver has been used for centuries because of the antibacterial characteristics it has. The presence of bacterial infection in wounds is one of the primary contributors to a prolonged healing process. Silver nanoparticles, when included into wound dressings, may aid to control bacterial infection in wounds.

Anti-inflammatory effects

While inflammation is a normal reaction to injury, it should be avoided for as long as possible since it might slow down the healing process. It has been observed that silver oxide nanoparticles possess anti-inflammatory capabilities, which have the ability to regulate inflammation in wounds and help the healing process.

Stimulating granulation and re-epithelialization

There is some evidence to indicate that silver nanoparticles may enhance the proliferation of fibroblasts and keratinocytes, both of which are essential to the production of granulation tissue and the

process of re-epithelialization during the process of wound healing.

Safety and biocompatibility

It has been shown that silver nanoparticles, at specific concentrations, are biocompatible with human cells and do not cause any damage to them. Because of this, they are an excellent choice for use in wound care [32].

However, it is essential to highlight that despite the fact that there are encouraging indicators of the advantages of silver oxide nanoparticles for wound healing, further study is required to fully understand the processes and optimize the use of these nanoparticles in a clinical environment. This is true despite the fact that there are promising signs of the benefits.

Immunomodulatory effects

In view of their well-established antibacterial capabilities, Ag₂O NPs are attracting a lot of attention for potential applications in the medical field, food preservation, and the textile industry. It has not yet been determined whether or whether silver nanoparticles are biocompatible with the cells of the immune system, despite the fact that their usage is very prevalent. Despite this, a number of investigations have shown that nano silver compounds may have potentially immunotoxic and/or immunomodulatory properties. It has been shown that nanoparticles of silver oxide exhibit immunomodulatory properties, which means they may have an influence on the immune system and the reactions it produces. The interactions that silver oxide nanoparticles have with various parts of the immune system are primarily responsible for their immunomodulatory effects. The following are some of the potential mechanisms:

Interaction with immune cells

Silver nanoparticles are known to have the ability to interact with a wide variety of immune cells, including lymphocytes, macrophages, and neutrophils. They have the ability to influence the activity of these cells, which may have an effect on processes such as phagocytosis (a process in which certain cells consume and kill germs) and the production of cytokines (small proteins that are essential in cell communication during immune responses).

Modulation of cytokine release

It has been discovered that silver nanoparticles may influence the release of cytokines. It has been shown in a number of studies that they have the ability to inhibit the production of pro-inflammatory cytokines like interleukin-1 beta (IL-1 beta), tumor necrosis factor alpha (TNF-alpha), and interferons, while simultaneously encouraging the release of anti-inflammatory cytokines like interleukin-10 (IL-10). Inflammation and immunological responses may be brought under better control as a result.

Formation of reactive oxygen species (ROS)

The presence of silver nanoparticles in immune cells has been shown to stimulate the formation of reactive oxygen species. While excessive amounts of reactive oxygen species (ROS) may harm cells, levels of ROS that are more moderate serve critical functions in immunological responses, including the elimination of pathogens and the transmission of cell signals.

Toxic effects on cells

Silver nanoparticles, when present in larger quantities, may have a toxic effect on immunological cells, ultimately leading to the death of such cells. However, when present in lower amounts, they have the potential to trigger apoptosis, a sort of programmed cell death that is a natural component of immune responses.

Modulation of immune gene expression

Several studies have shown that silver nanoparticles have the ability to change the expression of genes relevant to the immune system, which in turn may have an effect on immunological responses [33].

Mechanisms of action of silver oxide nanoparticles

Nanoparticles of silver oxide have their own set of characteristics that make them particularly valuable in a variety of circumstances. Their mechanism of action is complicated and is to a considerable extent depends on the setting in which they are used. The following is a shortened version of a more detailed description of how these nanoparticles may function via the production of reactive oxygen species (ROS) and interactions with cell membranes:

The reactive oxygen species (ROS)

It is possible for nanoparticles made of silver or silver oxide to stimulate the creation of reactive oxygen species if they are put into a biological system. ROS are reactive oxygen species, which are molecules that include oxygen and are chemically reactive. Examples of ROS include peroxides, superoxide, hydroxyl radical, and singlet oxygen. Within the biological system, the nanoparticles have the potential to engage in interactions with molecular oxygen or water, therefore encouraging processes that create ROS. ROS may produce oxidative stress, which is a process that can cause severe damage to the structures of cells when present in high enough concentrations. The antibacterial effect of silver nanoparticles relies heavily on this ROS-based mechanism. Damage to the bacterial cell wall, disruption of essential physiological functions (such as breathing), and damage to the DNA may all be caused by ROS, which ultimately results in the death of the bacterial cells [34,35].

Interactions with the membranes of cells

It is also possible for nanoparticles made of silver and silver oxide to have direct interactions with the cell membranes of bacteria. Because of their tiny size, they are readily able to attach themselves to the cell membrane and interfere with its function. Once connected, these nanoparticles have the power to bring about physical changes in the membrane, such as enhanced permeability, or they have the capability of completely penetrating the cell. Once they are inside, they are able to interact with the many different cellular components and disturb the essential functions. For example, the silver ions that are produced from the nanoparticles may attach to proteins and DNA, which can impair normal cell activity and ultimately lead to the death of the cells. The antibacterial actions of Ag₂O NPs are also partially due to this process, which is another important component [36,37].

It is essential to keep in mind, with regard to both pathways, that even if they have the potential to be useful for certain applications (like antibacterial purposes), they also have the possibility of being damaging to human cells. The reactive oxygen species (ROS) that are produced have the potential to harm human cells, and the resulting breakdown of cell membranes may have cytotoxic consequences. Therefore, when utilizing nanoparticles containing silver or silver oxide in any biological setting, considerable attention and investigation are required.

Toxicological considerations of silver oxide nanoparticles

Since the unique qualities that they possess, nanoparticles of silver oxide, like other nanomaterials, provide certain advantages but also carry the potential for some drawbacks. The following are some things to keep in mind with relation to their toxicology.

Cytotoxicity and the viability of the cells

Cytotoxicity is the state of being harmful to cell growth and reproduction. It has been shown via research that nanoparticles composed of silver oxide may be harmful to both bacterial cells and human cells. The formation of reactive oxygen species (ROS) and direct contact with cell membranes are the two processes that are often to blame for the toxicity of the substance in question. The nanoparticles have the ability to produce ROS, which may then cause oxidative stress, which in turn can damage biological components including proteins, lipids, and DNA, and may even result in the death of cells. In a similar manner, their contact with cell membranes may disrupt normal cell function. This can happen either because their connection causes physical changes in the membrane or because their engagement with the cell allows them to penetrate the cell and interfere with the cell's internal components. In addition, silver nanoparticles are capable of releasing silver ions, which are equally hazardous to cells due to their cytotoxic properties. They are capable of binding to biological components, which may result in dysfunction of the cell and ultimately cell death. The cytotoxic effects may be contingent on a variety of parameters, such as the concentration of nanoparticles, the size of the nanoparticles, and the form of the nanoparticles and the kind of cells that they are interacting with. Silver nanoparticles may not be detrimental to certain cells when present in low quantities; nevertheless, when present at larger concentrations, they may have a major cytotoxic impact [38,39].

Environmental Impact

Nanoparticles made of silver oxide may be harmful to the natural environment. They may enter the environment through a variety of channels, such as trash from industrial processes, items containing silver nanoparticles that are abandoned, and even medicinal uses. These nanoparticles, if released into the environment, have the potential to cause toxicity in a variety of creatures. For instance, research has revealed that they may be poisonous

to aquatic species, which can have an impact on the organisms' ability to grow, reproduce, and even survive. In addition, silver nanoparticles have the ability to undergo transformations in the environment, such as the release of silver ions or the creation of aggregates; these changes may have an effect on the toxicity of the nanoparticles. They may also get bio accumulated in some species, which might result in effects that last for a longer period of time. In adding, the environmental effect of silver nanoparticles is not merely a problem for wild animals to be concerned about. It is possible for these nanoparticles to go into the food chain and eventually be swallowed by people; the ramifications of this are currently unclear [40-42].

In general, silver oxide nanoparticles have features that show promise for a variety of applications; nonetheless, it is important not to discount the possibility that they may have hazardous effects on cells and the environment. It is necessary to do more study in order to have a complete understanding of these hazards and to design methods for reducing them.

Applications of silver oxide nanoparticles

Due to their exclusive physical, chemical, and biological features, nanoparticles made of silver oxide have a broad variety of uses in a variety of different sectors. The following are some applications that may be found in the fields of biomedicine, the environment, and other areas.

Applications in the biomedical field

Antimicrobial agents

Incorporating Ag₂O NPs into wound dressings serves two purposes: first, to protect the wound from being infected by germs; second, to hasten the process of wound healing. They do this by interfering with the bacteria's cellular metabolism and damaging the cell walls, which ultimately results in the bacteria's death. In order to avoid infections that are related with medical devices, they are also used in the coatings of catheters and other types of medical implants [43].

Drug delivery

Ag₂O NPs may have therapeutic medications loaded onto them and then be targeted to specific parts of the body. Because of their diminutive size, nanoparticles are able to travel the circulatory system and transport medications to particular tissues, even those

that are often difficult to access, such as cancers. The nanoparticle coating has the potential to prevent the medicine from being broken down in the body, which would result in increased bioavailability as well as efficacy of the medication [44,45].

Cancer treatment

Ag₂O NPs may be made to seek out cancer cells and transport chemotherapeutic medications directly to tumors, causing the least amount of damage possible to healthy cells in the process. They are also capable of causing oxidative stress in cancer cells, which may lead to the induction of apoptosis (also known as programmed cell death), which is beneficial in the treatment of cancer [46].

Tools for diagnosis

Ag₂O NPs, because of their high interaction with light, are used in imaging methods such as Surface Enhanced Raman Spectroscopy (SERS), which are used to diagnose diseases in their earliest stages. They improve the Raman signal of trace biomolecules, which helps in the early diagnosis of illnesses in their earliest stages [47].

Environmental applications

Water Treatment Ag₂O NPs have the ability to remove pollutants from water, hence making the water more pure. They have a high surface area that may bind to and precipitate out specific contaminants, and their antimicrobial effect can help kill waterborne microorganisms, making the water safe to drink and reducing the risk of becoming sick from consuming contaminated water.

Antifouling agents

Biofouling, also known as the undesired buildup of microbes, plants, algae, and tiny animals on wetted surfaces, may have major implications on the operation and maintenance of maritime vessels and structures. Antifouling agents are designed to prevent this accumulation. The development of these organisms may be inhibited by including silver nanoparticles into paints and coatings, which in turn reduces the amount of times they need to be cleaned and the costs associated with such cleanings [48].

Some other applications

Textiles

Ag₂O NPs are used in the textile sector because of the antibacterial qualities that they possess. They have the ability to prevent the

development of germs and fungus when they are woven into textiles, which keeps the cloth smelling clean and fresh. They are also able to prevent the breakdown of fibers caused by bacteria, which results in an increase in the lifetime of the textile.

Electronics

Ag₂O NPs find a wide range of uses due to their high electrical conductivity, which makes them ideal for use in a number of electronic applications. They are able to be used in the formation of conductive lines in printed electronic circuits, in touchscreens, and in RFID (Radio Frequency Identification) tags, among other applications. In addition to that, you may put them to use in the manufacture of conductive adhesives, inks, and pastes.

Food packaging

It is possible to minimize the amount of microbial growth that occurs on food by putting Ag₂O NPs into food packaging. This may result in an extension of the product's shelf life. This kind of packaging may help preserve the freshness of the food, stop it from going bad, and perhaps even cut down on the amount of food that is wasted [49,50].

Even though Ag₂O NPs offer a wide range of fascinating and useful uses, it is essential that research into the possible risks they pose to human health and the natural environment be carried on. Because of their tiny size, they are able to interact with biological systems in novel ways. These interactions may have both positive and negative effects on the organisms they affect. Researchers are putting in effort to get a deeper understanding of these interactions and to devise methods that are both secure and efficient for making use of silver nanoparticles.

Conclusion and Future Perspectives

The potential applications of silver oxide nanoparticles (Ag₂O NPs) in the field of nanotechnology are significant. The broad range of synthesis methods employed, spanning from physical to chemical techniques, facilitates meticulous manipulation of the properties of the materials in issue. Silver oxide nanoparticles (Ag₂O NPs) demonstrate intriguing biological properties such as antimicrobial, anticancer, and anti-inflammatory effects, rendering them highly valuable in diverse biomedical applications. Additional investigation is required to comprehend the toxicity and ecological implications of Ag₂O NPs. However, the extensive array of potential uses in

domains such as drug administration, antibacterial coatings, and water decontamination render Ag₂O NPs a stimulating avenue for prospective exploration and advancement.

The utilization of Ag₂O nanoparticles exhibits significant promise in the field of targeted drug delivery mechanisms. The distinctive characteristics of nanoparticles, including their elevated surface area, regulated release abilities, and possibility for surface functionalization, render those appealing contenders for the encapsulation and administration of therapeutic agents to targeted locations within the human body. Subsequent investigations and advancements can concentrate on refining the structure and composition of drug delivery systems utilizing Ag₂O nanoparticles, resulting in improved effectiveness, minimized adverse reactions, and tailored medical interventions. The concept of theranostics, which involves the amalgamation of therapeutic and diagnostic capabilities within a singular entity, has garnered substantial interest in contemporary times. The potential of Ag₂O nanoparticles to demonstrate therapeutic effects and imaging capabilities makes them a promising candidate in this area. The integration of the innate antimicrobial or anticancer characteristics of Ag₂O nanoparticles with imaging techniques such as fluorescence or magnetic resonance imaging (MRI) can facilitate contemporaneous assessment of therapeutic effectiveness, nanoparticle localization, and individualized treatment approaches. Ag₂O nanoparticles exhibit antibacterial and catalytic characteristics that can be utilized in environmental remediation applications. The potential of their antimicrobial properties can be harnessed in water treatment systems to counteract bacterial pollution and guarantee potable water. Furthermore, the utilization of Ag₂O nanoparticles is viable in air filtration systems for the purpose of eliminating contaminants and enhancing the overall air purity. The investigation of the capabilities of Ag₂O nanoparticles in the treatment of soil and other environmental applications exhibits potential for mitigating pollution issues and fostering a sustainable ecosystem. Ag₂O nanoparticles possess distinctive characteristics such as elevated surface area, electrical conductivity, and catalytic activity, rendering them highly suitable for employment in nanoscale sensors and devices. The incorporation of these materials in the creation of sophisticated sensing platforms has the potential to bring about a significant transformation in various domains, including electronics, energy storage, and bio sensing. The utilization of Ag₂O nanoparticle-based sensors and devices has the potential to facilitate the detec-

tion of target analytes with high sensitivity, selectivity, and speed, thereby promoting progress in diverse industrial sectors.

Conflict of Interest

The authors declare that they have no conflict of interest.

Bibliography

1. Hamza M., *et al.* "Biologically synthesized zinc oxide nanoparticles and its effect-a review". *Acta Scientific Applied Physics* 2.9 (2022).
2. Zahoor S., *et al.* "Biosynthesis and Anti-inflammatory Activity of Zinc Oxide Nanoparticles Using Leaf Extract of *Senecio chrysanthemoides*". *BioMed Research International* (2023).
3. Jadoun S., *et al.* "Green synthesis of nanoparticles using plant extracts: A review". *Environmental Chemistry Letters* 19 (2021): 355-374.
4. Aisida SO., *et al.* "Biosynthesis of silver oxide nanoparticles using leave extract of *Telfairia Occidentalis* and its antibacterial activity". 36 (2021): 208-213.
5. Manikandan R., *et al.* "Biosynthesis of silver nanoparticles using ethanolic petals extract of *Rosa indica* and characterization of its antibacterial, anticancer and anti-inflammatory activities". 138 (2015): 120-129.
6. Velsankar K., *et al.* "Green synthesis of silver oxide nanoparticles using *Panicum miliaceum* grains extract for biological applications". *Advanced Powder Technology* 33.7 (2022): 103645.
7. Dharmaraj D., *et al.* "Antibacterial and cytotoxicity activities of biosynthesized silver oxide (Ag₂O) nanoparticles using *Bacillus paramycoides*". *Journal of Drug Delivery Science and Technology* 61 (2021): 102111.
8. Parmar S., *et al.* "Recent advances in green synthesis of Ag NPs for extenuating antimicrobial resistance". *Nanomaterials* 12.7 (2022): 1115.
9. Sakono N., *et al.* "Immobilization Method for Silver Nanoparticles Synthesized via Evaporation/Condensation onto a Glass Plate". *Chemistry Letters* 51.11 (2022): 1074-1076.
10. Hasan S., *et al.* "Antibacterial activity of silver nanoparticles created by one step nanosecond Nd: YAG laser ablation in water". *Advances in Natural Sciences: Nanoscience and Nanotechnology* 14.2 (2023): 025013.
11. Rajkumar P., *et al.* "Realization of ZnO microrods and Ag nanoparticles on glass and Si substrates by magnetron sputtering and near band edge photoluminescence enhancement from the exciton-plasmon system". *Materials Letters* 325 (2022): 132898.
12. Patel H and J Joshi. "Green and chemical approach for synthesis of Ag₂O nanoparticles and their antimicrobial activity". *Journal of Sol-Gel Science and Technology* (2023): 1-13.
13. Kaur N., *et al.* "Microwave assisted green synthesis of silver nanoparticles and its application: A review". *Journal of Inorganic and Organometallic Polymers and Materials* 33.3 (2023): 663-672.
14. Beyene HD., *et al.* "Synthesis paradigm and applications of silver nanoparticles (AgNPs), a review". *Sustainable Materials and Technologies* 13 (2017): 18-23.
15. Herrera-Marín P., *et al.* "Green synthesis of silver nanoparticles using aqueous extract of the leaves of fine aroma cocoa *Theobroma cacao* linneu (Malvaceae): Optimization by electrochemical techniques". *Electrochimica Acta* 447 (2023): 142122.
16. Said A., *et al.* "Antibacterial activity of green synthesized silver nanoparticles using lawsonia inermis against common pathogens from urinary tract infection". *Applied Biochemistry and Biotechnology* (2023): 1-14.
17. Danish MSS., *et al.* "Green synthesis of silver oxide nanoparticles for photocatalytic environmental remediation and biomedical applications". *Metals* 12.5 (2022): 769.
18. Habeeb Rahuman HB., *et al.* "Medicinal plants mediated the green synthesis of silver nanoparticles and their biomedical applications". *IET Nanobiotechnology* 16.4 (2022): 115-144.

19. Ullah Z., et al. "Biogenic Synthesis of Multifunctional Silver Oxide Nanoparticles (Ag₂O NPs) Using *Parietaria alsinaefolia* Delile Aqueous Extract and Assessment of Their Diverse Biological Applications". *Microorganisms* 11.4 (2023): 1069.
20. Wu X., et al. "Biogenic silver nanoparticles-modified forward osmosis membranes with mitigated internal concentration polarization and enhanced antibacterial properties". *npj Clean Water* 5.1 (2022): 41.
21. Alaallah NJ., et al. "Eco-friendly approach for silver nanoparticles synthesis from lemon extract and their anti-oxidant, anti-bacterial, and anti-cancer activities". *Journal of the Turkish Chemical Society Section A: Chemistry* 10.1 (2023): 205-216.
22. Naganthran A., et al. "Synthesis, characterization and biomedical application of silver nanoparticles". *Materials* 15.2 (2022): 427.
23. Vithiya K., et al. "Antimicrobial activity of biosynthesized silver oxide nanoparticles". *Journal of Pure and Applied Microbiology* 4 (2014): 3263-3268.
24. Ahmad SA., et al. "Bactericidal activity of silver nanoparticles: A mechanistic review". *Materials Science for Energy Technologies* 3 (2020): 756-769.
25. Kailasa SK., et al. "Antimicrobial activity of silver nanoparticles, in Nanoparticles in pharmacotherapy". *Nanomedicine* (2019): 461-484.
26. Kim KJ., et al. "Antifungal activity and mode of action of silver nanoparticles on *Candida albicans*". 22 (2009): 235-242.
27. Karunakaran V., et al. "Optimization of biosynthesis of silver oxide nanoparticles and its anticancer activity". *International Journal of Nanoscience* 16 (2017): 1750018.
28. Lin J., et al. "Inhibition of autophagy enhances the anticancer activity of silver nanoparticles". *Autophagy* 10.11 (2014): 2006-2020.
29. Rohde MM., et al. "The mechanism of cell death induced by silver nanoparticles is distinct from silver cations". *Particle and Fibre Toxicology* 18 (2021): 1-24.
30. Kovács D., et al. "Cancer therapy by silver nanoparticles: fiction or reality?" *International Journal of Molecular Sciences* 23.2 (2022): 839.
31. Jain A., et al. "Anti inflammatory activity of Silver nanoparticles synthesised using Cumin oil". 12.6 (2019): 2790-2793.
32. Martinez-Gutierrez F., et al. "Synthesis, characterization, and evaluation of antimicrobial and cytotoxic effect of silver and titanium nanoparticles". *Nanomedicine: Nanotechnology, Biology, and Medicine* 6.5 (2010): 681-688.
33. Lappas CMJF and c toxicology. "The immunomodulatory effects of titanium dioxide and silver nanoparticles". *Food and Chemical Toxicology* 85 (2015): 78-83.
34. Alavi M., et al. "The efficiency of metal, metal oxide, and metalloid nanoparticles against cancer cells and bacterial pathogens: different mechanisms of action". 2.1 (2022): 10-21.
35. Parham S., et al. "Antimicrobial treatment of different metal oxide nanoparticles: a critical review". *Journal- Chinese Chemical Society Taipei* 63.4 (2016): 385-393.
36. Fernando S., et al. "Antimicrobial nanoparticles: applications and mechanisms of action". *Sri Lankan Journal of Infectious Diseases* (2018).
37. Maillard APF., et al. "Interaction of green silver nanoparticles with model membranes: possible role in the antibacterial activity". *Colloids and Surfaces B: Biointerfaces* 171 (2018): 320-326.
38. Bahadar H., et al. "Toxicity of nanoparticles and an overview of current experimental models". *Iranian Biomedical Journal* 20.1 (2016): 1.
39. Akter M., et al. "A systematic review on silver nanoparticles-induced cytotoxicity: Physicochemical properties and perspectives". *Journal of Advanced Research* 9 (2018): 1-16.
40. Levard C., et al. "Environmental transformations of silver nanoparticles: impact on stability and toxicity". *Environmental Science and Technology* 46.13 (2012): 6900-6914.
41. Maurer-Jones MA., et al. "Toxicity of engineered nanoparticles in the environment". *Analytical Chemistry* 85.6 (2013): 3036-3049.

42. Ong C., *et al.* "Silver nanoparticles in cancer: therapeutic efficacy and toxicity". *Current Medicinal Chemistry* 20.6 (2013): 772-781.
43. Gao A., *et al.* "The effects of titania nanotubes with embedded silver oxide nanoparticles on bacteria and osteoblasts". *Biomaterials* 35.13 (2014): 4223-4235.
44. Iqbal S., *et al.* "Application of silver oxide nanoparticles for the treatment of cancer". *Journal of Molecular Structure* 1189 (2019): 203-209.
45. Abbasi BA., *et al.* "Environmentally friendly green approach for the fabrication of silver oxide nanoparticles: Characterization and diverse biomedical applications". *Microscopy Research and Technique* 83.11 (2020): 1308-1320.
46. Miranda RR., *et al.* "Exploring silver nanoparticles for cancer therapy and diagnosis". *Colloids and Surfaces B: Biointerfaces* 210 (2022): 112254.
47. Yazdi MH., *et al.* "Metal, Metalloid, and Oxide Nanoparticles for Therapeutic and Diagnostic Oncology". 8.4 (2016).
48. Heinemann MG., *et al.* "Biogenic synthesis of gold and silver nanoparticles used in environmental applications: A review". 30 (2021): e00129.
49. Deshmukh SP., *et al.* "Silver nanoparticles as an effective disinfectant: A review". 97 (2019): 954-965.
50. Lekha DC., *et al.* "Review on silver nanoparticle synthesis method, antibacterial activity, drug delivery vehicles, and toxicity pathways: recent advances and future aspects". *Journal of Nanomaterials* 2021 (2021): 1-11.