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Article review

Inclusive review of Zinc Oxide Nanoparticles and Silver Nanoparticles: Properties and Applications

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Abstract:

Here, we discuss numerous valuable properties and functions of Zinc Oxide (ZnO) and Silver (Ag) nanoparticles, giving the readers a chance to understand the importance of the nanoparticles in activities including antifungal, antiviral, antimicrobial, and as antioxidants. ZnO nano-particulates, which are considered dual function materials because of their semiconducting and piezoelectric characteristics, have also been utilized in many fields, for example cosmetics, water purification and textiles due to their ability to kill microorganism and UV blocking attributions. Silver nanoparticles, due to their unique optical properties and having very high antibacterial efficacy utilization in medical applications like other drug delivery systems and potent agents in the removal of cancer cells has been known for a long time. Just as one nanoparticle is synthesized through green chemistry while the other goes through the clean, and green manufacturing process, showing sustainability and eco-friendliness through chemistry. Having overviewed the biomedical uses of nanoparticles generally they are being applied in drug delivery system, tissue engineering, and cancer diagnosis and treatment. In addition, the nanoparticles' antibacterial, antifungal, and antiviral mechanisms of action are analyzed and their potential antioxidant effects which pave the way towards therapeutic interventions of diseases connected with oxidative stress are examined as well.

Keywords: ZnONPs, AgNPs, Antibacterial, Antifungal, Antiviral, Antioxidant

1. Introduction:

ZnO and silver nanoparticles have been the focus of much attention recently due to their unique and special properties in comparison with their parent materials. Zinc oxide is a unique material that exhibits semiconducting and piezoelectric dual polarity properties, which have resulted in widespread use in various applications such as transducer elements, surge arrestors, and various sensing applications (Ehsan et al.2022). Due to

recent advances in nanoscience and technology, the utilization of ZnO at the nanometre level has become a reality. It can be easily seen that the form of ZnO nanoparticles widely used in products such as transparent sunscreen, makeup, packaging of food products, protective coating of wood and tiles, finishing for preserving wood, textiles and outdoor furniture is currently very popular (Xie et al., 2023). Also, as a ZnO antimicrobial, it functions as a nanoparticle to act against bacteria. This have been used in different implants or polymers and also in textiles to prevent bacterial growth. This same method can as well put into use the silver nanoparticles, therefore giving it an edge over the other nanoparticles which make them perfect choice for the antibacterial applications (Xie et al., 2023). Conduction electrons can achieve a collective oscillation and absorb the light by wavelength resonance which is how silver nanoparticles receive their luminousness characteristic that is distinctive and unique (Irfan et al., 2021). The larger the surface plasmon resonance effect the higher is light absorptions over the visible spectrum. This is an effect that is of course influenced by the size and shape of the nanoparticle. Such functionality of material may be very beneficial for silver nanoparticles tagging and cell imaging purposes especially. Silver's extremely toxic nature towards the cell has been proven a promising approach by which plasmon surface can be used as a photo mediated therapy implement the cancer destruction using silver nanoparticles (Campos et al., 2019). Silver nanoparticles have emerged as great candidates too for the purposes of fighting infectious agents, so many infections that are hard to deal with and that can be caused by some microorganisms, as well as antibiotic resistant, when compared to the bulk silver and antimicrobial agents which are frequently used in medicine. This has multiplied the possibilities of silver nanoparticles as a promising medical invention, and dental work, prosthetic materials, catheters, and many other applications can be added to the list of applicable medical uses (Bruna et al., 2021).

2. Green Synthesis

Silver and ZnO nanoparticles can be synthesized using green technology through plant-mediated synthesis. This eco-friendly approach is cost-effective and energy-saving. Jacaranda plant leaf extract was used in a study to produce ZnO and Ag nanoparticles, with the extract acting as a reducing and stabilizing agent. Proteins from the extract were responsible for reducing Ag ions to nanoparticles. These biosynthesized nanoparticles had effective antibacterial activity (Khan el al., 2022). Geranium leaf extract was also used to synthesize ZnO nanoparticles, which proved to be more environmentally friendly than the chemical method. The extract acted as a chelating and capping agent, and the particle size reached a minimum at 32 nm. UV-vis spectra indicated completion of the reaction within 72 hours (Hernández-Díaz et al., 2021).

2.1. Plant Extracts

Plants require no energy for metal ion acquisition, making this method a cost-effective way to synthesize stable NPs. Advantages include eco-friendliness, lack of hazardous substances, biological coating by plant metabolites, and potential NP recovery through chelation. Disadvantages include limited NP production, especially in hyperaccumulator plants, and difficulty controlling NP size and shape, slowing phytomining progress. (Madani et al., 2022)

What sets plant-mediated synthesis apart from other green synthesis methods is the combination of the biological system and chemical reduction agent. Plants can absorb metal ions from the soil and store them in cells and spaces between cells. This process involves metal movement, translocation, and accumulation. Once metals have accumulated at the desired site(s), they undergo reduction and bio-activation through enzymatic or non-enzymatic processes, triggering various metabolic activities. The versatility and adaptability of plant metabolic pathways in stressful situations, such as metal overexposure, is truly intriguing. (Gavrilescu, 2022)

2.2. Microorganisms

Microorganisms are an easy and controllable method for synthesizing nanoparticles. Bacteria, fungi, and actinomycetes are commonly used. Silver nanoparticles are commonly formed and can be bioactive. Bacteria are the best choice due to genetic knowledge and familiarity. There is still much to discover about optimizing nanoparticle synthesis (Dhaka et al., 2023).

2.3. Physical Methods

ZnO-NPs synthesized by sol-gel method using zinc diethyl and water as precursor. Precursor vaporized into ZnO particles from oxidation in range 300–400°C. Drawback: powdery BTE byproduct with uncontrollable particle size. Another method: ZnO-NP synthesis with thermal decomposition using zinc acetylacetonate. This process yielded high-grade ZnO nanoparticles with size below 10 nm. (Islam et al., 2022)

The other advantages of physical methods: synthesizing in the air/at room temperature, obtaining pure product without interaction with chemical reactants. Physical methods include evaporation, sol-gel methods, radiolysis, thermal decomposition, and vacuum flame. Evaporation method: synthesizing high purity AgNPs by evaporating high purity Ag with O2 and N2 at 500°C. Suitable for pure medical quality AgNP synthesis. (Zhou et al., 2023).

Physical methods for synthesizing AgNPs and ZnO-NPs are generally quicker, simpler, and more cost-effective compared to other methods. Small-scale producers can benefit from these methods. While the chemical method is still superior for kilogram quantity production, physical methods are more eco-friendly with no residual chemicals or large energy consumption. (Borehalli et al.2023).

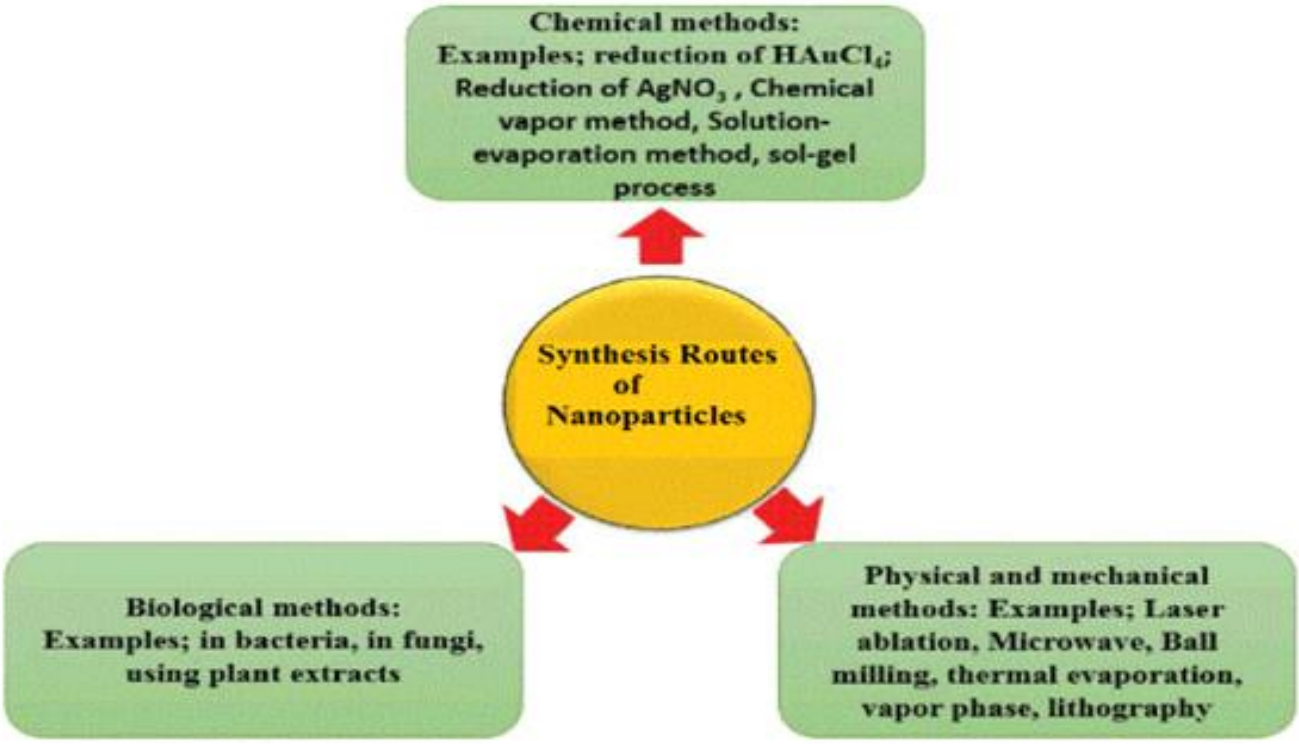

Figure 1: Different Methods of Nanoparticles synthesis (Anwar, 2018)

3. Biomedical Applications

Nanomaterials are widely used for biomedical applications. Topical drug delivery with zinc oxide nanopowder is cost-effective, safe, and improves patient compliance. It can be used as a filler for oral pills and can also be directly absorbed into the skin, eliminating the need for needle injections (Jiang et al., 2023). Zinc oxide nanoparticles can also be used for targeted drug delivery to cancer cells, enhancing radiation treatment. Within the range, silver nanoparticles suppress tumors more than albumin-stabilized nanoparticles and they can be decomposed or removed from cells at the stage of their function. Skin cancers and reconstructive and autoimmune skin diseases are all potential applications of these nanoparticles in therapeutic settings. In gene therapy, zinc oxide has application denoted by Anjum et al., 2021.

3.1. Drug Delivery Systems

Nanoparticles have emerged as crucial in pharmaceutical uses because they possess uniform size, capacity encapsulation of drugs, F specific targeting and release drug rate controlable. Smallest metallic zinc oxide (ZnO) nanoparticles have been the ones carrying and protecting insulin along the GIT for example (Halarkjotali et al., 2023). Chitosan/ZnO nanoparticle composite microspheres have also been successfully in pharmaceutical preparations as carriers for anti-ulcer drug controlled release. ZnO-coated (Mikušová et al., 2021) the drugs is likely to reach the lumen of the gastrointestinal tract. The silver nanoparticles are a topic which had been synthesized easily and operating for different pharmaceutical delivery processes. They have demonstrated efficacy in cancer therapy and possess anti-inflammatory properties. Create your Own Post! Writing Instruction: Write a well-structured essay that identifies prominent and emerging music genres of the modern era and analyzes their contribution to cultural diversity. Consider the role of technology in shaping these genres and their impact on society as a whole. It has also been demonstrated in a rat model that silver nanoparticles can actually speed up burn healing rates (Xu et al., 2020).

3.2. Tissue Engineering

Keeping biologists and engineers on a technically tight rope, tissue engineering is magnetic: it aims to generate biological tissues through engineering and life sciences. Nanoparticles may provide the cell and tissues growth that can be at the molecular level. The employment of zinc oxide nanocomposite for cell culture can act as the matrix system capable of the cell growth and on-demand release of the drug from the nanoparticles. The representation of zinc oxide particles can be found beneficial in tissue designing because of their immune-regulatory effects (Chen et al., 2022). An experimental environment that is created using zinc oxide nanoparticles is replicated the cell and tissue environment. It is simulated that these building materials can migrate to the cells and result in cell's damage and neoplasm formation. Such a technique can be usable both in tissue engineering (Wiesmann et al., 2021; Singh et al., 2021).

3.3. Cancer Treatment

In the recent times, experimentation with metal oxide and silver nanoparticle treatments in cancer has shown unprecedented results. Zinc oxide nano-crystals have revealed they can both stop the growth of cancer cells, and suffer damage, produced with the use of UV rays. These nano-particles, depending on the drug delivery method, may prove efficient in eradicating esophageal cancers. Likewise, silver nanoparticles can lead to inhibition of the processes of division of cancer cells. They also can interfere with due cycles. Lastly, their healing and imaging abilities can make treatment destruction-specific, as well. From the research done so far, the use of silver nanoparticles in clinical cancer therapy reveals that it holds a great potential (Takáč et al., 2023).

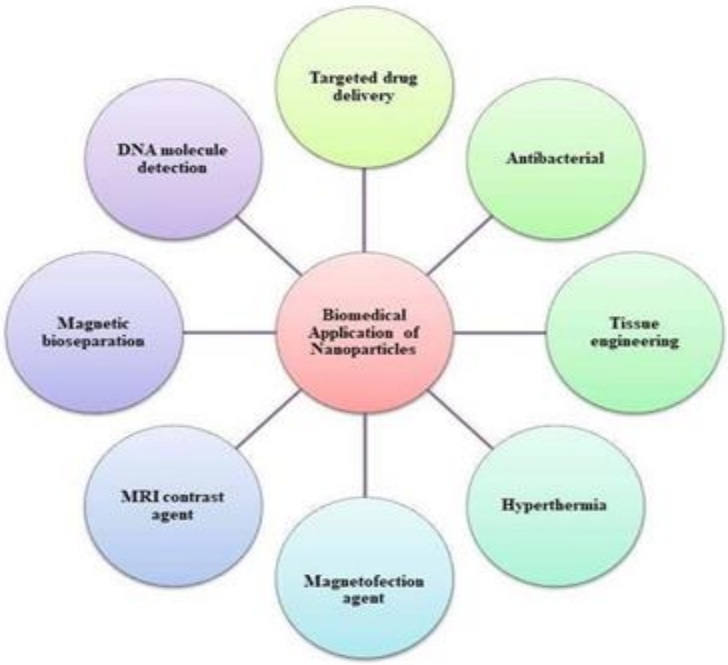

Figure 3: The biomedical application of nanoparticles (Alsuraifi , 2020)

4. Antibacterial Uses

Zinc Oxide Nanoparticles (ZnO NPs) were experimentally proven to attach to the surface of E. coli, causing shape changes and aggregation. High concentrations of ZnO NPs decrease the survival rate and damage the cell membrane, leading to cytoplasm leakage (Mendes et al., 2022). Similar to Silver Nanoparticles (Ag NPs), Ag NPs also adhere to bacteria, penetrate the membrane, and damage the cell structure (More et al., 2023). ZnO NPs have been studied in other bacteria and consistently inhibit growth. Leaving behind the antibiotic action, they may suppress the fungal, viral, and cancerous attacks, too. In comparison to other adsorbents, ZnO NPs have the ability to take out contaminants and toxic substances from wastewater. The good thing about them is that are highly stable, not poisonous, and photocatalytic. This readily avails them for water purification (Babayevska et al., 2022). ZnO NPs hold a great promise in the fields of medical therapy, biotechnology, and environmental research, and can possibly give way to to even newer developments and techniques (Anjum et al., 2021).

Nano-ZnO NPs exhibits a pronounced antibacterial activity against a variety of bacteria particularly Streptococcus mutans. The surface of ZnO NPs has jaggedness, which thus produce holes in the carbohydrate layer of S. mutans that in due course may cause cell lysis. Lenient mechanism for nanomedicine and creation of antibacterial strategies have been demonstrated via this notion. ZnO NPs have an ability of managing dental caries, which are the sulfuric mutans. Yet, noting the account of safety and biocompatibility before extensive use is necessary. Finally, the work highlights the activity of creative ideas in nano medicine in order to fight infectious diseases and to make a person healthier (Morales et al., 2021; Hamad & Atiyea, 2021).

4.1. Against Gram-Positive Bacteria

Silver exhibits outstanding antibacterial activity for gram-positive and gram-negative bacteria. Silvers damages the membrane of these bacteria and leaks out its cell contents (Zhang et al., 2022). Nevertheless, the mechanisms of ZnO Mr. against bacteria stand apart by a huge margin. The bacteria carcinogenic effects of ZnO nanoparticles were elaborately tested on gram positive and gram negative bacteria. Studies has shown that ZnO has a remarkable inhibitory effect on gram-positive bacteria but, on the other side, it doesn't possess antimicrobial activity for gram-negative bacteria. This conclusion, therefore, was in favor of the likelihood of two bacteria types being susceptible in regards to indoor chemistry of cell walls (Mendes et al., 2022).

Gram-positive bacteria possess a thick layer of peptidoglycan, which is a polymer of amino sugars cross-linked by short polypeptides. The rigid cell wall with multilayered superposition in gram-positive bacteria imparts robustness. In contrast to the gram-positive bacteria, the outer membrane of the gram-negative bacteria hosts a thin layer of peptidoglycan containing the periplasmic space. This is between the outer layer and the plasma membrane. The firmly connected and tightly bitter peptidoglycan layer of gram-negative bacteria is conjointly related to the plasma membrane; respectively, that prevents the damage to the peptidoglycan layer or leakage of cell contents (Kong et al., 2022).

It is revealed by scientific research that ZnO particles lead to Lysis, i.e., bacterial chain cells not only become of smaller size but also detach from the cell wall and as a result, the cells become condensed. These changes shared a feature of increased cell membrane permeability, that in the last analysis, caused cell death. Additionally, ZnO particles were found to adhere to the entire bacterial cell surface and exhibit remarkable adhesiveness to bacteria. Notably, the high surface area and the presence of surface hydroxyl groups are believed to render ZnO particles highly reactive against bacteria, facilitating their bactericidal effects even on gram-positive bacteria (Kim et al., 2020).

In comparison, silver exerts its antibacterial activity by releasing silver ions, which can bind to DNA and inhibit replication and transcription. Furthermore, silver ions can bind to proteins and induce protein inactivation, leading to bacterial cell death. The mechanism of action of silver leads to a

major mismatch versus that of pure ZnO whose bacteria destroying effect comes through the direct touch (Yin et al., 2020).

Actually, contacting with ZnO crystals has been reported to cause fall out of the organizations which regulate the cell metabolism in the bacteria, and thus it buries their lives. Furthermore, the ZnO particles have been to some extent been proved that the released Zn2+ from the ZnO can also stop bacteria cell wall synthesis and protein synthesis. But, one can't deny the fact that the mechanism related to ZnO antibacterial effect are still unclear; therefore, more research should be done in this regard (Kong et al., 2022).

Whether the actual way for the sterilization of different articles is the interaction of oxygen atoms with skin microorganisms or the release of certain chemicals, ZnO provides a great chance for destroying skin germs because of its powerful anti-bacterial and disinfectant effects. Moreover, ZnO comes out with superior antibacterial performance against different types bacteria; hence, it can play key role in destroying some resistant bacteria and keeping good hygiene in many circumstances (Mendes et al., 2022).

These applications are not confined to medical use only but also used for everyday objects like tableware, clothing, etc, The household things that are played my role for this. In conclusion, the extraordinary antibacterial properties of ZnO relies upon its key characteristics which make it outstanding candidate for the prophylaxis and therapy of microbial infections (Puspasari et al., 2022).

4.2. Against Gram-Negative Bacteria

Using it in conjunction with another type of nanoparticles, such as gold nanoparticles, silver nanoparticles was capable of efficiently retarding bacteria, E. coli growth and proliferation. Therefore, the formation of these cutting-edge silver nanoparticles showed the enormous capacity in bacterial killing and replication cessation (Gouyau et al., 2021). However, it should be noted that the antibacterial potency of silver nanoparticles is affected by duration of exposure and thus prolonged usage may cause a loss of antibacterial capabilities Meanwhile, an evaluation of the antibacterial effects of nanosized zinc oxide particles demonstrated considerable difficulties in discerning any visible effect on E. coli bacteria (Bruna et al., 2021).

In general, due to the noticeable lack of any inhibitory properties, the use of zinc oxide nanoparticles seems to not be a sensible choice in the struggle to fight E. coli infections. Further inquests have traced how silver nanoparticles have the hallmark to curtail cellular ATP formation in E.coli bacteria. On the other hand, the intriguing part is the fact that, contrary to what was expected, the journal article showed that besides the staph gram-positive bacteria, ATP production is also inhibited by the mechanism. This concept highlights the fact that non-downregulation of ATP production in E. coli suggests that the latter is not associated with majority of the phenomena in the course of metabolism. As a result, to distinguish the discussions and detail the certain mechanism of the modes of action, broad and lengthy special research work is required (Yoo et al., 2021).

To summarize, the damage of membrane has been witnessed for the silver nanoparticles while interacting with E. coli cells. This is due to losing a large amount of the completed proteins and essential components of an intact cell membrane. In the case with the rising concentration of silver nanoparticles within the bacteria cells envelope, the cells lose their normal size and shape and the DNA within them becomes highly compact and condensed, phenomenon that mimic exactly the features of apoptosis. The discoveries achieved are revolutionary through the particularly high antibacterial activity of silver nanoparticles demonstrated in E. coli treatment as confirmed by the results presented. Nano zinc oxide in like manner does not exhibit prominent antibacterial activities when used alone, however, the opportunity to use amalgamated nanoparticle is present. As a result of this, researchers are to do an in-depth and comprehensive research to investigate and fully realize the added synergistic effects of zinc oxide nanoparticles together with other nanoparticles , for instance in the context of fighting against E. coli infections. Nevertheless, there is no room for doubt that in the present time as a result of the current researches that have been

executed, zinc oxide nanoparticles that is not toxic do not meet the specific requirements for it to be established as a single cure of E. coli infections (Gouyau et al., 2021; Bruna et al., 2021).

4.3. Synergistic Effects with Antibiotics

Testing whether or not these combined NP treatments exhibit synergistic effects with traditional pharmaceutical antibiotics is an important area of research, and represents a possible means of minimizing the likelihood of related drug resistance. A study by Ali et al. and Malawong et al. was among the first to explore this in any detail. They tested a combination of Ag NPs with the antibiotic tetracycline on Staphylococcus aureus and Escherichia coli. Based on their results, it was concluded that combined treatment of Ag NPs and tetracycline exhibited synergy on S. aureus. That is why the evaluation, by comparing measures with Ag NPs treatment and those with tetracycline alone, resulted in the inhibitory concentration (IC) of the combination of 0.3125 of that for each of the individual drugs. In other words, the when the antibiotic and the Ag NPs were combined together were more effective than either Ag NPs alone or tetracycline treatment. The most effective inhibitory factor was obtained with the highest dose given at the end of the 24th period of incubation, exceeding that of each individual component taken alone in the same conditions. It is essential that the mechanism of the added agent is identified before implementing something that we cannot achieve (Ali et al., 2021; Malawong et al., 2021). Ali et al., 2021 conducted that different amount of ZnO NPs were paired with the antibiotics penicillin and streptomycin in order to watch the effect on S. aureus. With this study, they concluded that there was no effect associated with the utilized mixture (observed through the growth curve and cell count) compared to monotherapies.

The main antimicrobial mechanism of the ZnO and silver nanoparticles involve nanotoxicity which leads to the release of Zn2+. Meanwhile, ZnO NPs were being protected from having a direct contact with bacteria by the spread and inactive antibiotic molecules beause of such diffusing and inactivating agents. The role of ZnO NPs as an antimicrobial agent includes the generation of reactive oxygen species (ROS), and therefore, one would think that a more effective healthcare medicine includes antibiotics able to initiate a breach to the bacterial membrane. Perhaps, the current studies have gone ahead with the extracting findings of synergism between combination of NP and antibiotics (Ali et al., 2021; Malawong et al., 2021).

A study for example have looked into the antimicrobial effects of the union of TiO2 NPs and the antibiotic amoxicillin in several strains of bacteria. The effects that were manifest were synergistic, as the combined treatment proved to be highly potent, exhibiting more antibacterial activity than either treatment administered on its own. The ratio of synergistic interaction was found to be very low, as the inhibitory dose of the combination had a fraction of the efficacy of each agent by itself. The Microbial population growth is largely inhibited by these properties of TiO2 NPs which display both direct as well as indirect antibacterial activity. Finally, the direct antibacterial effect occurs due to release of those reactive oxygen species when light is applied. The media indirectly affects process as it improves the accumulation of it and more cellular uptake of antibiotic (Younis et al., 2023).

5. Antibacterial Mechanism of Action

The creation of reactive oxygen species (ROS) via by ZnO nanoparticles is touted as their antimicrobial effect. Due to their high reactivity, ROS may attach to the biological macromolecules, which finally reduces cell reaction and even cell death. ROS can be generated by ZnO nanoparticle through their surface exposure and Zn2+ release. This exact mechanism is not clear yet. The study is being directed towards controlling the rate of ROS production and efficiency of zinc oxide nanoparticles. Generation of ROS is also a case for silver nanoparticles and these also have antibacterial properties. Silver impregnated dressings were tested side by side with sterile gauzes containing silver, proving reduced level of cells energy metabolism and ROS production (Mendes et al., 2022).

Both zinc oxide nanoparticles and silver nanoparticles have similar antibacterial mechanisms, although they differ in their effectiveness against different bacteria models. Both types of nanoparticles quickly kill bacteria without inducing resistance, making them desirable as antibacterial agents (Jomehzadeh et al.2021).

5.1. Reactive Oxygen Species Generation

One of the toxic effects of metal and metal oxide nanoparticles is the generation of reactive oxygen species (ROS). ZnO nanoparticles can generate both types of ROS in cell-free systems and increase intracellular ROS in bacteria. The presence of

dissolved oxygen enhances the antibacterial activity of ZnO nanoparticles. ROS cause membrane damage, but this was not investigated. Identifying ROS in bacteria using a probe has shown increased ROS generation after exposure to ZnO nanoparticles. ZnO nanoparticle cytotoxicity and genotoxicity in human cells may be attributed to high levels of ROS. Ag nanoparticle toxicity involves multiple mechanisms, including ROS generation. 10nm Ag nanoparticles induce oxidative stress in murine macrophage cells. Ag nanoparticles also cause ROS generation and inflammatory responses in rat tissue. However, there is no direct link between Ag nanoparticle antibacterial activity and ROS generation in bacteria. (Hemdan et al., 2023).

5.2. Membrane Disruption

Membrane disruption by NPs causes cell injury in bacteria. Gong et al linked E. coli inactivation by Ag NPs to cellular material leakage and increased uptake of propidium iodide. Xiu et al found that ZnO NPs increased cell membrane permeability in a time and concentration dependent manner. DNA damage also occurred from ZnO NP exposure. OH radical formation by TiO2 NPs caused E. coli inactivation, with resistance observed in non-pathogenic strains with changes to the cell envelope. Fe2O3 NPs caused E. coli cell membrane rupture due to electrostatic attraction. (Mendes et al., 2022)

5.3. DNA Damage

Mechanisms of genotoxicity relate to NP-driven oxidative stress and direct interaction of NPs with DNA. Interaction of ZnO NPs or zinc ions with DNA repair enzymes hindering repair may explain persistence of SSB and failure to maintain G2/M checkpoint integrity. DSB likely occur through an indirect oxidative mechanism. These mechanisms pose a hazard to long-term cell viability and may underpin ZnO NP carcinogenicity. More research is needed to understand the interaction of NPs with cellular and nuclear structures. Techniques like synchrotron x-ray fluorescence and nano-SIMS can be used to study intracellular NP distribution and NP localization in subcellular organelles. (Singh et al., 2020).

The main mode of genotoxicity is DNA damage, with stronger evidence supporting this claim. ZnO NPs have been extensively tested, showing clear DNA damage in multiple assays. The methodology used was comprehensive and rigorous, with NPs characterized and cells exposed properly. There was dose-dependent release of zinc ions, but the relative contribution of this and NPs to genotoxicity is unclear. Oxidative stress was not found to be a cause of DNA damage. Various assays showed DNA strand breaks, chromosomal breakage, and failure to repair. A novel assay showed ZnO NPs to be highly genotoxic. These findings are supported by other assays, indicating both lethal and sublethal consequences (Anjum et al., 2021).

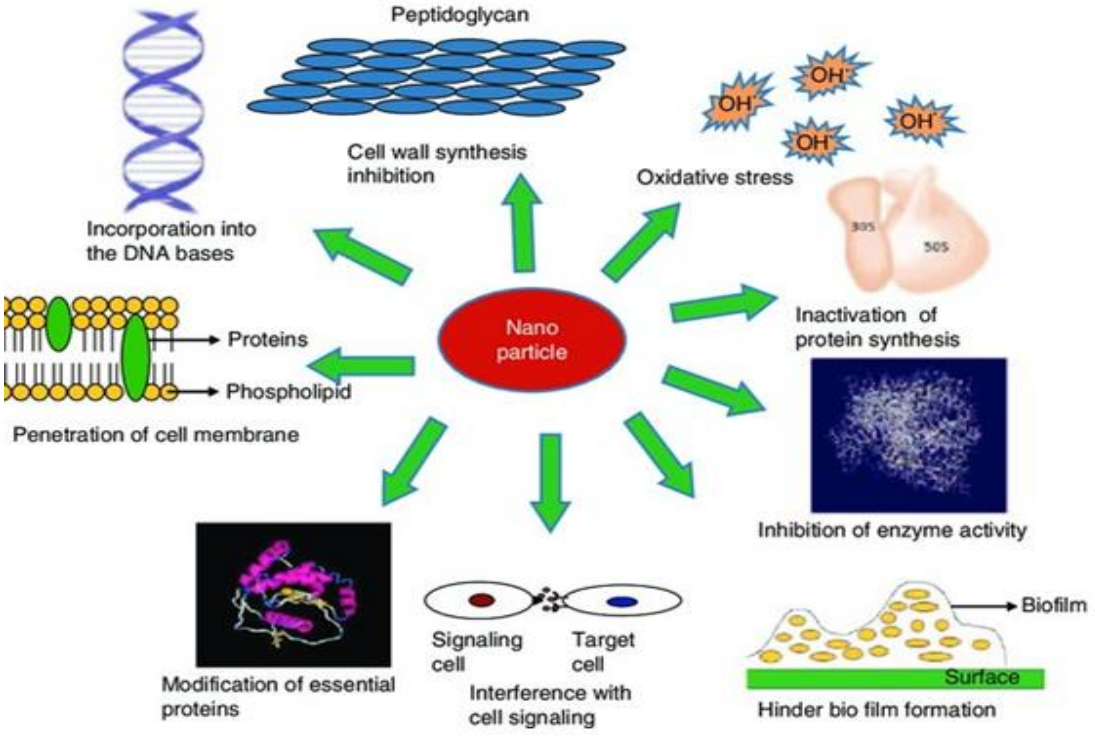

Figure 3: The mechanisms of action of nanoparticles toward bacteria (Singh et al., 2014)

6. Antifungal Uses

Ag NPs have shown inhibitory activity against Candida species, including resistant isolates. Minimum inhibitory concentrations ranged from 1.9 to 15.5 μg/ml. Ag NPs also inhibit biofilm formation and damage the cell wall of C. albicans. There is no literature on in vivo effects, but in vitro data suggests Ag NPs could be used to treat Candida infections. (Zhou et al.2021).

6.1. Against Candida Species

The observed ZnO nanoparticle (NP) mechanisms contrast to those proposed for zinc salts, which were shown to inhibit Candida albicans germ tube formation and phosphomannose isomerase activity (Zhou et al.2021). Despite the positive in vitro anti-candida activity of ZnO2+ ions and NAC-ZNP1, a Zn-porphyrin complex, poor solubility will limit their potential as antifungal agents. It is well documented that silver has antifungal properties, and this is no different for Ag NPs, which have strong anti-candida activity (Mare et al.2021). Recently, it was found that Ag NPs greatly enhanced the activity of two azole antifungals against C. albicans, and this increased susceptibility resulted in reduced ATP levels in the fungi (Ahamad et al., 2022). High-resolution TEM imaging has revealed that agglomerated Ag NPs on the cell membrane is taken up and rapidly disintegrate into smaller particles, which penetrate the cell, causing damage to the organelles and eventual cell death. Collectively, these findings suggest that zinc metal and oxide materials would be highly effective against Candida species, and the emergence of silver-based technologies may further increase the potency of such antifungal agents. Therefore, the utilization of ZnO NPs and Ag NPs as antifungal agents holds significant promise for the treatment of Candida infections. Additionally, the investigating of the design of new types of multifunctional nanoparticles that use different mechanisms for enhancing the antifungal activity of these nanoparticles may contribute to the establishment of more sophisticated and effective ways to treat Candida species (Malik et al.2022).

ZnO NPs from the study described in the article were shown to be remarkably efficient against three types of Candida belonging to a group of fungi which contribute to the development of human diseases such as tropical candidiasis and vaginal candidiasis. It illustrated that a commercially existing antifungal compartment used together with ZnO NPs greatly increased the elimination speed of fungi. The most interesting part was that although the NPS showed better antibacterial activity when used in small concentrations, they showed much lower activity when used in bigger quantities than the commercial drug, which showed the huge power that they had. This part of the ZnO NPs anti-candida activity manifests itself through the influence of NPS on the cell wall, which leads towards disintegrative damages with the ensuing non-specific cell death mechanisms (Tan et al., 2022). This is supported as the findings reveal the exposure of phosphatidylserine and show rapid progress of DNA fragmentation occurrence. Surprisingly, the fungi cells were dedifferentiated and instead became have amoeba-like shape while congregating, unique findings that substitute both the budding and filamentation process that commonly at lead to apoptosis. Aside from that, the nano-size ZnO (NPs) demonstrate a strong H+ ATPase-inhibitory activity especially in the C. albicans, consequently causing its intracellular acidity increase and the ion homeostasis disturbance. The disturbance of membranes thereby enhances the overall antibacterial effect of ZnO NPs and patents the multi-implication of that mode of action, pointing to the niche applications of this novel therapy. (Joshi et al., 2022; Fayed et al., 2021).

6.2. Against Dermatophytes

Out of all the fungal organisms, those related to the diseases of skin, hair, and nails have resisted credible therapy. The infections by these dermatophytes are enormously common and often persistent (Kruithoff et al., 2023). Silver salts and compounds, renowned for their medicinal properties throughout the ages, have been widely used as external treatments in antiseptics, astringents, and as agents to precipitate protein. It is worth mentioning that silver nitrate, a pioneering

antifungal compound, was the first to be applied to the treatment of superficial infections, ranging from cutaneous mycoses to yeast infections of the skin and mucous membranes, including candidiasis. Despite its relatively frequent use, there is a paucity of controlled trials that extensively explore the efficacy of silver nitrate or any other silver compounds (Żyro et al., 2023). on the other hand, zinc pyrithione, which is widely acknowledged as a well-known antimicrobial and antifungal agent, it is predominantly employed in shampoos to combat seborrheic dermatitis and dandruff caused by the fungi Malassezia. Additionally, it has been proven effective in the treatment of psoriasis (Mangion et al., 2021). Remarkably, while the effectiveness of pyrithione has been extensively studied, little attention has been paid to the role of the zinc ion. It is important to note that zinc pyrithione is lipophilic and exhibits strong adhesion to the skin, thereby facilitating the gradual release of pyrithione over an extended period. The ability to penetrate the protective outer layer of fungi is a major advantage of silymarin as this allows it to be used as an effective topical antifungal treatment (Reeder et al., 2011). In the mentioned study, two modes of treatment were studied in order to compare the effectiveness of a 1% zinc pyrithione vaginal cream with a three-day miconazole regimen for treating acute vulvovaginal candidiasis. This study has demonstrated extremely high curative effect, with the miconazole group revealing an outstanding 85% cure rates and zinc pyrithione group enjoying a commendable 77% cure rate. The efficacy of zinc pyrithione as an antifungal could be said with persuasion. It may be as a remedy of superficial fungal infections by the way of Reeder et al. article (Reeder et al., 2011).

6.3. Combination Therapies

Two studies combined metal nanoparticles with antifungal drugs. Ag NPs with chloroquine showed synergy, reducing C. albicans survival to 0%. Chloroquine's toxicity to mammalian cells decreased when combined with Ag NPs (Moorthy et al., 2023). ZnO Particles/Amphotericin (B) system also created synergy effect with low concentration /No Inhibition was observed. The results of these experiments suggest that metals release could be used for better therapeutics against fungal infections Abo-(Shama et al., 2020). The basic building blocks of metal nanoparticles have the unique ability to become multifaceted, diagnosing fungus, and successfully treating resistant microbial strains. They could also be used in various fields such as antibacterial and antiviral medications (Wahab et al., 2023). On the other hand, concerned issue is safety, because it should be verified in more reliable testing. While facing challenges, the inclusion of metal nanoparticles into the antifungal therapeutic framework is an excellent promise for the improvement in patients' results and progress in medicine (Wahab et al., 2023).

7. Antifungal Mechanisms

Although the killing mechanism of silver nanoparticles against microbial cells is not yet clearly yet, it is most probably done through the generation of reactive oxygen species (ROS) (Rohde et al., 2021). Up till very recent past, the proteins were believed to be un-specifically modified by the silver ions, and it was purported to have happened. However, the modern research says that the cell membrane is disrupted which leads to cell death and cell contents leakage. Mutant strains deprived of the specific membrane proteins showed resistance to the silver ions, evidencing a membrane influence behind their antimicrobial effect. Alternately, silver ions must affect synthesis of fatty acids and phospholipids. These act as major structural and functional components of molecular membranes, which is important for cellular health (Li et al., 2021). Whereas, the action of silver and zinc oxide nanoparticles on the fungal cell membrane is the same denaturation of the physiology and serious damage to the intraorganellar structures (Varghese et al., 2024).

7.1. Cell Wall Disruption

Zinc and silver ions inhibit a wide range of fungi, suggesting that nanoparticulate forms of these metals could also have an inhibitory effect. Metal ions impede fungal growth through protein denaturation, disrupted metabolism, and

interference with nucleic acid synthesis (Li et al., 2024; Alhujaily et al., 2022). However, the mechanism of ion release from nanoparticles and its impact on fungal enzymes, energy production, and nucleic acid synthesis is still debated. Understanding this phenomenon requires marking nanoparticles to trace their locations and measuring the site-specific impact of ion release (Frei et al., 2023). Zinc and silver ions can competitively inhibit enzymes, thus disrupting their function. If nanoparticles can disrupt enzymes at their localized site, ion release might have a similar inhibitory effect (Li et al., 2024; Alhujaily et al., 2022).

7.2. Membrane Permeabilization

ZnO and Ag have antifungal effects by damaging fungal cell membranes. Nanoparticles are in direct contact with cells, causing absorption on the cell surface. ZnO QDs are visualized on C. albicans, while AgNPs are seen in contact with Mucor. The nanoparticles alter the cell wall and membrane structure, leading to further studies on their effects. AgNO3 inhibits C. albicans growth by affecting cell wall and membrane processes (Alavi & Nokhodchi, 2021; Jian et al., 2022).

7.3. Inhibition of Enzymes

Enzymes lower the energy required for biological reactions by binding to a specific site. Enzyme inhibition occurs when a molecule decreases enzyme activity (Cooper, 2000). Silver nanoparticles have been shown to inhibit the activity of certain enzymes, including maltase and sucrase. Ag(+) ions also competitively inhibit maltase activity. This inhibition is significant for disrupting Candida's maltose catabolic pathway and potentially inhibiting fungal growth. Citrate-stabilized silver nanoparticles have been found to irreversibly inhibit glycolytic enzymes in Saccharomyces cerevisiae. The nanoparticles disrupt disulfide bridges on the enzyme proteins, suggesting their potential as antifungal agents. The inhibition of enzyme activity is not due to NAD+ depletion or metal release. Silver nanoparticles could be used to selectively inhibit fungal enzymes with minimal side effects, unlike current antifungal drugs that have general toxicity (SUTJARITVORAKUL et al., 2023; Madasamy et al., 2023).

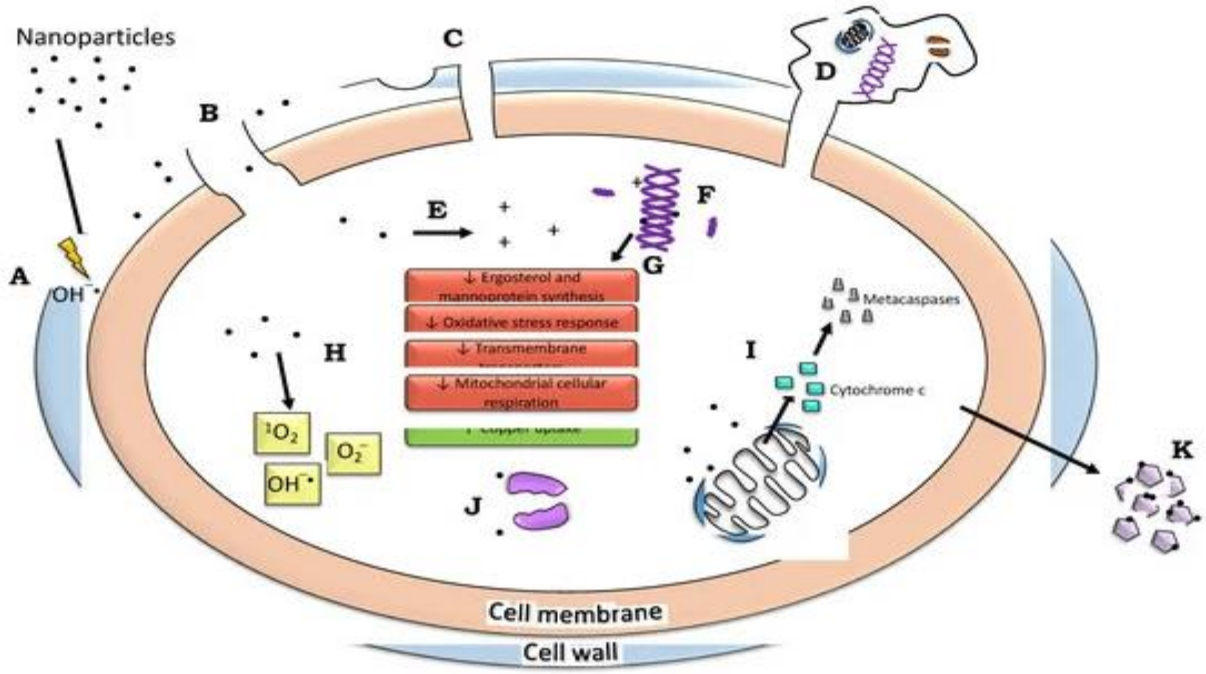

Figure 4: The antifungal mechanisms of action: (A) Inducing lipid peroxidation via ROS, (B) embedment adsorption and rupture of cell membrane and wall, (C) quarry and hole creation, (D) outflow, liberating DNA and organelles as of the cell, (E) liberating of ion, (F) DNA embolism, triggering compression and division, (G) deviations of gene expression, (H) generation of ROS, (I) liberating of Mitochondrial cytochrome C into the cytoplasm, growing meta-caspase levels, foremost to apoptosis cascade, (J) de-polymerization of ribosome, and (K) adsorption on extra polysaccharide, preventing biofilm development (Slavin, 2022).

8. Antiviral Uses

In recent years, concerns have grown over new viruses and mutated strains. Many viruses have become resistant to antiviral medication, and some medications may even enhance virus survival. This resistance may be due to the similarity in the way current medications disrupt viruses (Vere Hodge & Field, 2011). Zinc oxide nanoparticles are being studied as they can kill viruses in multiple ways, potentially preventing resistance. Zinc ions can induce cell death, inhibiting viral replication. In an in vitro study, zinc ions completely inactivated a virus (Rodelo et al., 2022). Silver ions also inactivate cells and cause membrane loss, preventing viral replication. Furthermore, silver nanoparticles inhibit cell wall and membrane synthesis (Luceri et al., 2023). Both zinc oxide and silver nanoparticles have antiviral effects, primarily due to their ions (Rodelo et al., 2022; Luceri et al., 2023).

8.1. Against Enveloped Viruses

Enveloped viruses' morphologies were destroyed in studies using electron microscopy. HIV, HSV, respiratory syncytial, and dengue viruses experienced disrupted structures and decreased RNA/DNA when exposed to Ag-np. Ag-np proved effective during and after viral replication, showing it to be a favorable antiviral agent. (Hadinejad et al., 2023). Influenza viruses were among the first studied in relation to Ag-np activity against enveloped viruses. Low dose of Ag-np abolished viral infectivity, with a 4-log drop in as little as 15 minutes. Ag-np have strong antiviral effects by interacting with viral RNA to prevent replication. Early exposure to Ag-np reduced viral RNA in feline calicivirus study (Crane et al., 2021).

8.2. Against Non-Enveloped Viruses

Ag-NP and ZnO-NP have effective antiviral activity against non-enveloped viruses. Their effectiveness has been demonstrated with feline calicivirus (FCV), a surrogate for human norovirus. Norovirus is a significant global health concern, especially for vulnerable populations (Azam et al., 2022). Both Ag-NP and ZnO-NP have been found to have no adverse effects on food contact surfaces. Ag-NP damages the FCV capsid and inhibits replication, while ZnO-NP damages the capsid protein and viral RNA (Roy et al., 2022).

8.3. Viral Entry Inhibition

Zinc oxide inhibits viral entry into host cells, including HSV-1, HSV-2, adenoviruses, and vesicular stomatitis virus. It interferes with viral adsorption and penetration. Creams with zinc oxide can cause adverse events such as painful pustules and sores. When mixed with zinc white and exposed to sunlight, herpes-cold sore activation occurred in 10 out of 23 subjects (Nasrollahzadeh et al., 2022). Zinc oxide is also effective against picornaviruses and inhibits their replication. It inhibits SARS CoV polymerase through zinc ions (Merkl et al., 2021). Zinc ionophore effectively inhibits rhinoviruses and viral entry. Zinc oxide nanoparticles may have potential in preventing viral infections (AbouAitah et al., 2021).

9. Antiviral Mechanisms

Silver has a significant impact on viral replication. It interferes with the HIV-1 protease enzyme, preventing the formation of infective virus particles. Silver also affects the degradation of the HPV16 viral genome. Additionally, it inhibits the splicing of viral RNA with the help of host cell spliceosomes. (Singh et al., 2023). Zn2+ hinders RNA polymerase by inhibiting its activity and gene expression. Zn(O)2 can form stable complexes with six histidine residues, inactivating the protein and degrading RNA. (Huang et al.2021). Inhibition of viral replication has also been suggested as a mechanism of viral cytotoxicity by metal ions. Transition metals possess several properties that are capable of interfering with critical enzyme systems, including inhibition of DNA synthesis. (Guerrero-Arguero et al.2023).

9.1. Viral Capsid Disruption

When applied to HIV-1 and HSV-1 for short durations post infection, ZnO and Ag inhibit replication. A study using HSV-1 infected Vero cells found that adding ZnO and Ag sooner post infection had a greater impact on replication, indicating activity in viral replication events. ZnO disrupted viral capsid formation and prevented complete virion production (Akilesh and

Wadhwani, 2021). Similar results were seen with ZnO inhibition of picornaviruses, with a 4 log decrease in viral titer after 90 minutes of treatment. Zinc ions also prevented genome formation in hepatitis B, with potential for complete removal of virus DNA through dietary supplementation (Gupta et al., 2022). These findings are relevant for treating chronic HBV infection.

9.2. Inhibition of Viral Replication

ZnO and Ag nanoparticles inhibit viral replication differently. ZnO particles in solution inhibit Herpes Simplex Virus replication by aggregating the virus, preventing DNA replication (Abbasi et al., 2023). Silver particles prevent Hepatitis B virus replication through inhibiting reverse transcription. Limited knowledge on specific mechanisms of viral inhibition for these nanoparticles (Lu et al., 2008).

9.3. Interference with Viral Attachment

Silver nanoparticles prevent viral infections in vivo using a mice model, indicating their potential for inhibiting influenza virus infection through viral attachment and viral-induced membrane fusion (Naumenko et al., 2023). In vitro study tested silver nanoparticles on H3N2 influenza strain. MDCK cells pretreated with nanoparticles and infected with virus. After incubation, viral titer assessed with 0% infectivity at 40µg/ml. (Ayipo et al., 2022). Silver nanoparticles (1-10nm) prevented virus attachment to red blood cells in a dose-dependent manner. Electron microscopy showed disruption and deformation of viral particles and damage to haemagglutinin spikes (Owida et al., 2022). Recent avian and swine influenza are of concern due to high mortality and potential for a pandemic. Some strains are resistant to current treatments, necessitating alternative options. (Naumenko et al., 2023).

Viral attachment happens when a virion binds to a host cell via specific interactions of viral surface proteins with host cell receptors. Inhibiting viral attachment is a potent antiviral strategy, especially for nanoparticles. Preventing attachment may hinder the virus from evading the nanoparticle and developing resistance (Rios-Ibarra et al., 2024). Nanoparticles also disrupt membrane carbohydrates, such as modified glycoproteins like Sialic acids, that act as cellular receptors (Thomsen & Klok, 2021).

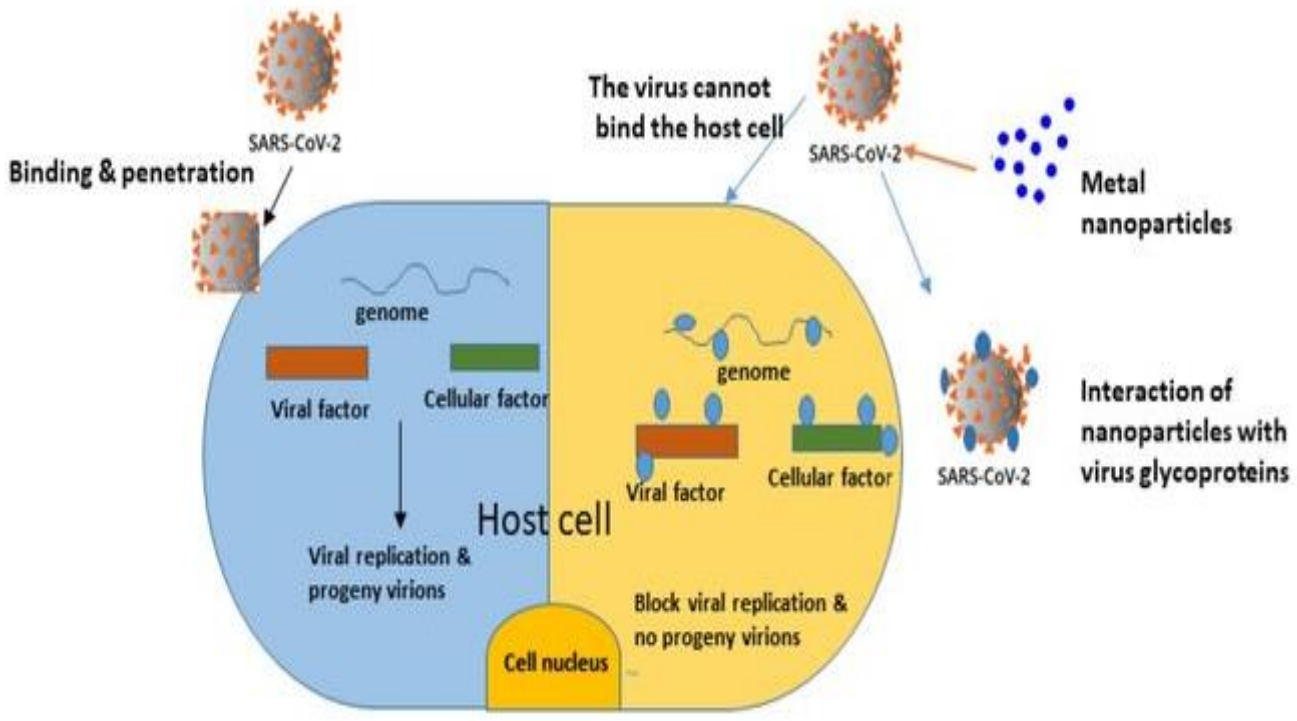

Figure 5: Antiviral mechanisms of action of nanoparticles (Serag & El-Zeftawy, 2021).

10. Potent Antioxidant Agents

Oxidative stress occurs when there is an imbalance between ROS production and antioxidant defenses. This can lead to damage of macromolecules and disease development (Pizzino et al., 2017). ZnO NPs can reduce oxidative stress and protect against DNA damage, while Ag NPs prevent cell death and protein damage from oxidative stress (Singh et al., 2020; Hou et al., 2021). Free radical quenching involves reducing chain reactions and inhibiting electron transfer. ZnO and Ag NPs lower nitric oxide levels, a toxic radical in carcinoma. Ag nanoparticles effectively adsorb nitric oxide as an N2O ligand and ammonia decomposition (Shabestarian et al., 2023). ZnO and AgNPs are effective antioxidants. ZnO NPs scavenge reactive oxygen species (ROS) like superoxide, hydroxyl radicals, and hydrogen peroxide. These ROS cause oxidative damage to biological systems. ZnO NPs inhibit the formation of hydroxyl radicals and reduce levels of superoxide and hydrogen peroxide. They also prevent iron-induced lipid peroxidation in plasma. (Li et al., 2020).

10.1. Scavenging Reactive Oxygen Species

(ZnO) NPs generate ROS under UV irradiation and can cause oxidative stress in certain cells. However, they can be beneficial as an antitumor treatment, using ROS to damage and necrose tumor cells. Additionally, ZnO nanoparticles can act as scavengers of specific ROS (Rehman et al.2023). Like them, the Ag NPs have antibacterial activity and may be considered chemical agents for cancer treatment. It is ag ions, released from Ag NPs, that are responsible for the release of ROS, and its effectiveness depends on the comparability of the redox potential of different ions (Hasan et al., 2022). Due to their reactivity formed nanoparticles can quench the harmful ROS resulting in their acting as possible antioxidants. They can chew up radical oxygen species causing damage to cells and hence preventing any mutation or cancer. This process is like an intermediary that can lead to either necrosis or apoptosis via initiating alterations of proteins, RNA or DNA (Yu et al., 2020). ROS can be from oxygen ions in different forms--like superoxide or peroxide to stable free radicals--as hydroxyl radical or highly reactive oxidizing agent- - single oxygen. ROs overbalance, and, in their turn, the organism's capability to counter oxidative stress itself, can result in oxidative stress as well as many diseases (Nakai & Tsuruta, 2021). The beneficial effects of zinc oxide and silver nanoparticles are due to their ability of ROSs free radical elimination (Sibiya et al.2022).

10.2. Free Radical Quenching

Comparison of UV absorbability of ZnO powder to ZnO nanoparticles demonstrated better protection of nanoparticle version. UV causes skin damage and oxidative stress, but ZnO nanoparticles reduced skin damage in rats subjected to UV. These findings suggest that ZnO has potential for preventing further oxidative stress in the skin (Chen et al., 2022). Free radicals cause damage to cellular components like DNA, cell membrane, and proteins. This can lead to diseases and health problems. Skin aging and skin cancer can occur due to oxidative stress on the skin (Engwa et al., 2022). Antioxidant therapy (AR) prevents DNA damage and mutations caused by free radicals. By preventing DNA damage, AR can prevent diseases. (Forman & Zhang, 2021)

10.3. Protection against Oxidative Stress

ZnO and Ag nanoparticles act as electron donors, preventing oxidation of cellular molecules and protecting against oxidative stress. Nanoparticles may have an affinity for RNA, but the mechanism is unknown. Ag nanoparticles do not cause DNA mutation or double-strand breaks and protect against UV radiation damage to DNA. This protective effect may have potential therapeutic applications in preventing skin cancer. (Al Jabri et al., 2022; Sidhu et al., 2022; Azizi-Lalabadi et al., 2021)

Conclusion:

The zinc oxide and silver nanoparticles are correspondingly a revolutionarily technological nanoscale innovation, which broaden its applications in biomedical, environmental and industrial sectors. Such distinct features are a precondition for designing newer application fields: from antimicrobial coverings and drug delivery systems to water treatment and UV-

protection. The green synthesis of these NPs is yet another example of the developing trend of environment-friendly and sustainable production cyberworks. As systemic assessments only start to reveal their potential advantages, future research is warranted in order to fully understand their mechanism of action, especially antimicrobial, antifungal, antiviral, and anti-oxidant activities. Moreover, safety aspects and the environment bringing toxicity and environmental impact into question constitute the basis for complete assessments. Zinc oxide and silver nanoparticles are herein demonstrated to be the leading effective candidates of environment and healthcare development, most of all, for their versatility, efficacy and thanks to the outstanding capabilities to eliminate the most detrimental challenges humanity is facing not less. Only further investigations will help establish conditions for full use of the real potential of nanoparticles by improving their features, search for a new destination where they may be used and ensure safe operation with them.

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