

Type of the Paper (Review)

## Comparative study of Green and Chemical synthesized Zinc Oxide Nanoparticles for Antibacterial and Anticancer Activity

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**Abstract:** In the past, nanotechnology has made major advances, and it is still one of the primary methods for producing materials with intended properties. By using nanotechnology for the manufacture of metal oxides, novel materials with distinct properties in nanoscale sizes have been made possible. As one of the recent classes of substances used in the pharmaceutical industry and other fields, metal oxide nanoparticles are becoming more and more significant. The ZnO nanoparticles are presently the subject of extensive research with special emphasis on their therapeutic uses because of their biocompatibility and non-hazardous nature; they play a positive role in biological functioning, according to the analysis presented in this review. As the review assembled the various review articles from a variety of additional resources. According to the research, compared to physical and chemical synthesis methods, the green route is comparatively advantageous and harmless to the environment to produce NPs to meet the increased demand for them. Intriguingly, the natural synthesis methods are appropriate due to their many health, medical, and financial benefits. Due to the strong ability of zinc oxide NPs to produce excessive amounts of reactive oxygen species (ROS), discharge Zn ions, and cause cellular death, ZnO NPs have shown immense potential in biomedicine, particularly in the areas of anticancer, antiviral, and antibacterial fields. Zinc is also renowned for maintaining the structural integrity of insulin as well; so, it is also been successfully developed as a diabetic medication agent. As a result, the nanoparticles of zinc oxide have also shown promise as a useful tool for sensing perspective and medication delivery. There is currently also a need to search for other options that have both financial and environmental benefits.

### Academic Editor:

Dr. Mudassir Hassan

**Citation:** Amjad, I., Asif, M., Ali, S., Fakhar-e-Alam, M., & Saadullah, M. (Year). Comparative study of green and chemical synthesized zinc oxide nanoparticles for antibacterial and anticancer activity. *Annals of Applied Sciences and Technology*, 1(1), 29–47.

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**Keywords:** Nanoparticles; anticancer; zinc oxide; ROS; Antimicrobial

### 1. Introduction

Metal oxide nanoparticles play a very important part in the field of nanoscience research and development [1]. Metal oxides are involved in the manufacture of electrochemical base sensors and fluorescent-based biosensing materials. The surface of metal oxides is an important element in their ability to interact effectively with target molecules. (Lallo da Silva, Abuçafy et al. 2019). The fast growth of metal- and metal oxide-based enzymes over the last decade has been attributed to their outstanding physicochemical features, as well as their low cost, great stability, and ease of storage.

Nanoparticles (NPs), which are tiny substances that act as a particular unit in conditions of transportation and property, are second-hand in nanotechnology, which is defined as the use of NPs. Researchers may discover novel methods to

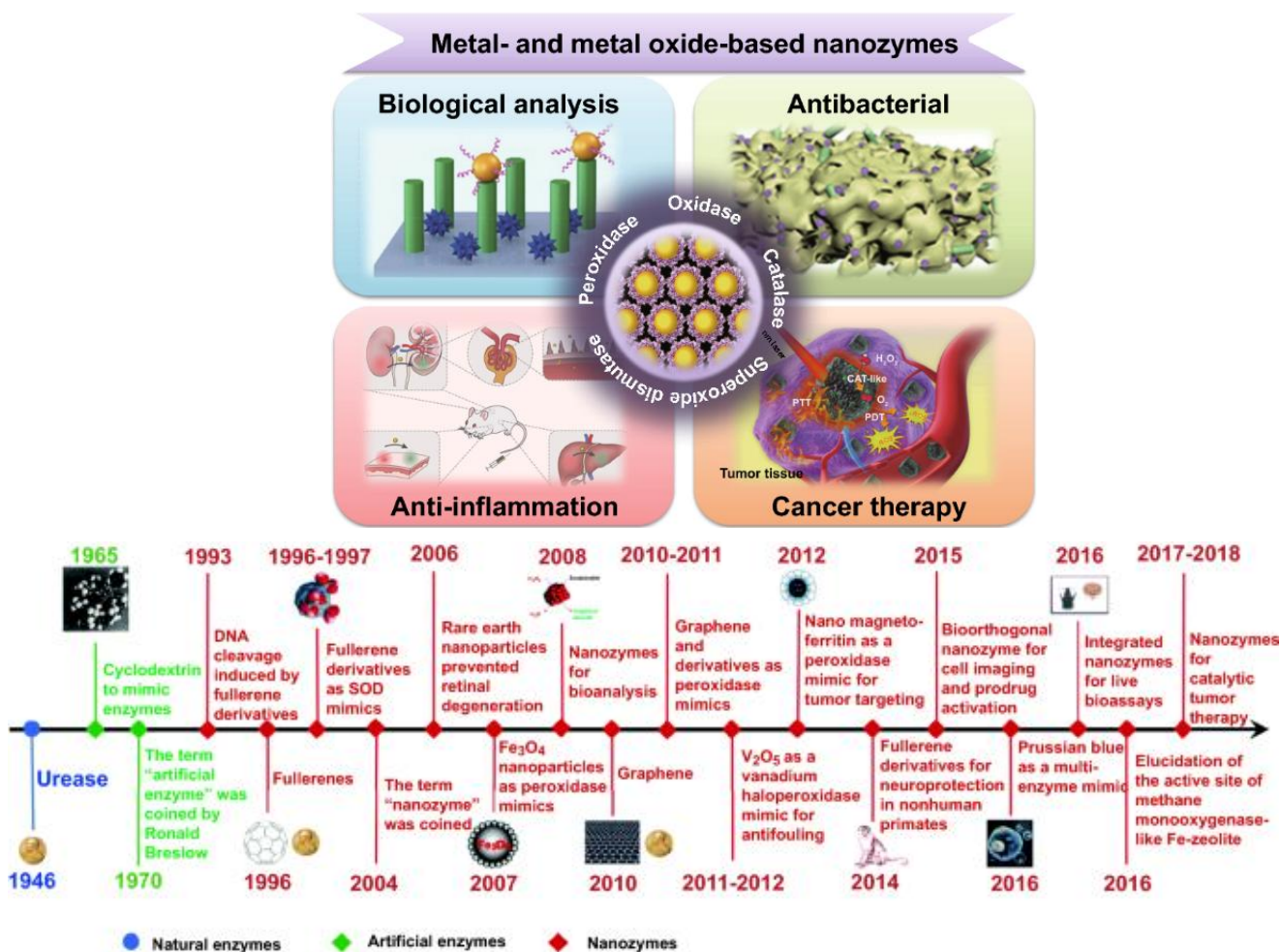
incorporate NPs into plants via nanotechnology; these methods might enhance already-existing functionalities in addition to introducing brand-new ones (Chatterjee, Bandyopadhyay et al. 2011). Depending on the qualities of NPs, their interaction with plants results in a variety of morphological and physiological alterations. NPs' efficiency is governed by various characteristics, including their compound composition, size, outer surface coverage, reactivity, and, most crucially, their effectiveness (Singh, Singh et al. 2018).

The traditional chemical reduction method uses a variety of hazardous chemicals to synthesize NPs, which can afterward cause a variety of physical condition concerns because to its toxicity, but the green synthesis process employs an ecologically friendly method benign way to manufacture NPs. Because the green synthesized procedure is free of charge of pollutants, it is

ideal for biological applications where purity is important. (Hussain, Singh et al. 2017).

It is common knowledge that a thorough understanding of catalytic activities and their mechanisms has a significant impact on the uses of enzymes. These enzymes made of metal and metal oxides place special emphasis on their catalytic mechanism and contemporary uses in biological analysis, inflammatory relief, antibacterial treatment, and cancer

therapy (Hussain, Singh et al. 2017). Zinc is a necessary element for our bodies, and it can be found in a variety of main organs such as the brain, muscle, and bone. (Vinardell and Mitjans 2015). It also has antioxidant properties and aids in protein digestion, blood coagulation, and bone metabolism (Jiang, Pi et al. 2018).



**Figure 1:** Timeline depicting the development of natural enzymes, artificial enzymes, and nanozymes from 1946 to 2018. Key milestones include the discovery of urease (1946), introduction of artificial enzymes (1965–1970), fullerene-based SOD mimics (1996–1997),  $Fe_3O_4$  nanozymes (2007), graphene-based peroxidase mimics (2010–2011), and recent advancements in tumor-targeting nanozymes and catalytic therapies (2012–2018).

### Metal oxides:

The creation of many sophisticated functional materials and smart gadgets depends heavily on metal oxides (Asif, Fakhar-e-Alam et al. 2025).

## 2. Silicon Dioxide metal oxide:

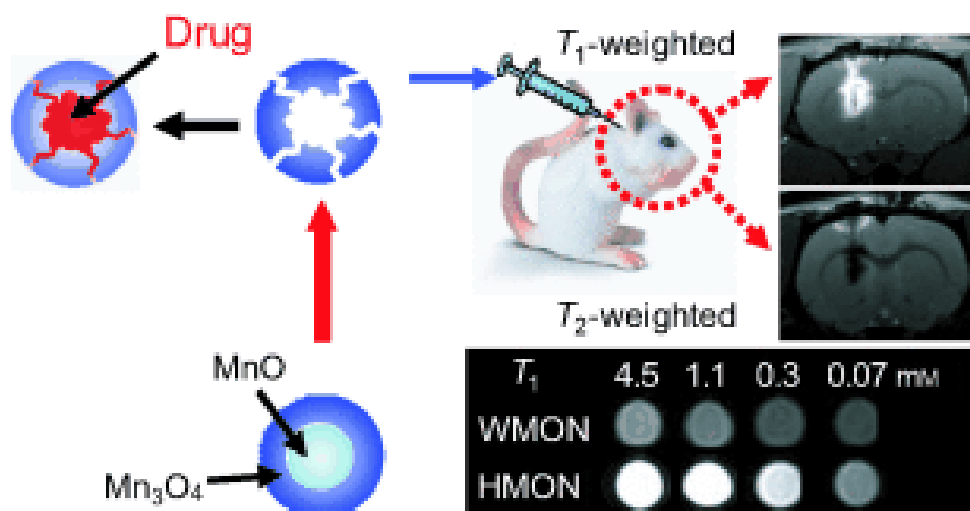
### 2.1 Importance

The electrocatalytic activity of the Blue, Green, and Tan-SiC-dots/SiO<sub>2</sub> was quite potent for the oxygen reduction process. Blue, Green, and tan-SiC-dots/SiO<sub>2</sub> nanocomposites are stable, low-toxic, and inexpensive, and they have a lot of economic potential. Light-emitting diodes, photo-shining windows, and fuel cells are examples of applications. Because of their inimitable PL

and electrical property (Liu, Zhang et al. 2021). Because the polarity of the molecule is zero, silica dioxide is not a very reactive chemical. It is soluble in hydrofluoric acid and inexplicable in acid and water. Its band gap is 8.4 to 11 eV. The melting and boiling points of silica dioxide are 1713° C and 2950° C.

### 2.2 Manganese dioxide:

When compared to solid manganese oxide nanoparticles, vacant manganese oxide nanoparticles (HMON) have much



**Figure 2:** Schematic representation of MnO/Mn<sub>3</sub>O<sub>4</sub>-based nanoformulations for drug loading and dual-mode MRI imaging. The illustration highlights T<sub>1</sub>- and T<sub>2</sub>-weighted imaging in mice, demonstrating concentration-dependent signal changes in WMON and HMON nanostructures for enhanced diagnostic applications.

### 2.3 Silver dioxide:

Using free quince leaves and green chemistry, which is an environmentally benign process, silver ions are reduced into silver metal particles. The phenolic compound is one of the bioactive phytochemicals present in quince leaves. Which have a great deal of conjugated double bonds? The quince leaves were harvested from the pure water, plants were washed. The leaves dried at room temperature for seven days before being protected from the sun. The quince leaves' original coloring was removed. At 80 °C, 4 g of quince leaves were added to 400 mL of distilled water. After that, the combination was kept at a steady temperature and out of direct sunlight.

### 2.4 Scandium oxide:

The possibility of the use of high-power pulsed UV lasers in laser communication and inertial confinement fusion systems has generated interest in thin-film UV coating damage resistance (Aziz, Marif et al. 2019). Because of the High-power UV lasers might be used as an ignition source, and

higher relativities and drug-loading capabilities (WMON). Their high cellular (uptake) application shows that they have the potential to be a medical device with dual functions that combine diagnostic imaging and targeted therapy (Shih, Chen et al. 2015). When utilized the use of colloidal particles having a huge surface area that are nanoscale in size as MRI contrast agents has various advantages (Shih, Chen et al. 2015). The manganese dioxide band gap is 1.3 eV. Its melting point is 535° C (995° F).

innovative high-refractive-index materials could be used as optical device components (such as high reactive mirrors, debris shields, protective layers, polarizers, and so on) have been developed so on) (Rainer, Lowdermilk et al. 1982). By thermally oxidizing freshly evaporated 8% scandium, scandium oxide thin films were created. Numerous studies were carried out to discover more about the substance and substantial characteristics of the generated scandium oxide films. Ellipsometry measurements have been made on concurrently produced scandium oxide films (Grosso and Sermon 2000). The scandium oxide band gap is 6.8 eV. (Pike 1972).

### 2.5 Titanium oxide:

Titanium dioxide (TiO<sub>2</sub>) is a pigment that has long been used in toothpaste, sunscreen, paint, and ointments. The preparation procedure is used to classify TiO<sub>2</sub> nanomaterials such as nanoparticles, nanorods, nanowires, and nanotubes. The sol-gel technique was utilized to generate TiO<sub>2</sub> nanoparticles from titanium hydrolysis precursor. TiO<sub>2</sub> nanoparticles differ in size, shape, and crystal structure, which affects not only the stability

of the surface but also how the material changes states under pressure or heat (Yuan, Chen et al. 2005).

In a different experiment, Titanium alkoxide nanoparticles were created by a hydrothermal reaction in an acidic ethanol-water solution (Yuan, Chen et al. 2005).

### 2.6 Iron oxide:

Iron oxides are the most prevalent metallic oxides in soil (which include oxides, oxyhydroxides, and hydrated oxides). They can be found in one or more of their mineral forms as very small particles. In most soils from various climatic zones, and at varying concentrations (Chae, Park et al. 2003). In soil solutions, the concentration of Fe<sup>2+</sup> ions are frequently substantially larger than that of Fe (III) ions (Neuberger, Schöpf et al. 2005). In addition to these names, magnetite is sometimes referred to as Hercules stone, loadstone, ferrous ferrite, and black iron oxide. It has the greatest magnetic properties among all transition metal oxides. In the inverse spinel structure of magnetite (Schwertmann and Taylor 1989), Fe (III) ions are randomly distributed between octahedral and tetrahedral sites, whereas Fe (II) ions are located in octahedral sites (Schwertmann 2007) Magnetite loses susceptibility with time and is ferromagnetic at normal temperatures. However, it becomes unstable at high temperatures (Klotz, Steinle-Neumann et al. 2008). At ambient temperature, magnetite particles smaller than 10 nm are superparamagnetic (Sun 2002) The use of magnetite in eye surgery to restore injured retinas has also been considered (Asif, Iqbal et al. 2024).

### 2.7 Tungsten oxide:

In the inverse spinel structure of magnetite (Yazdani, Sayadi et al. 2018), Fe (III) ions are dispersed at random between octahedral and tetrahedral sites, whereas Fe (II) ions are only found in octahedral sites, which is relevant to the development of "smart windows" technology. Other uses for tungsten oxide include photocatalysts for solar energy harvesting, air purification, and the manufacture of fuel, which may provide answers to the world's energy and environmental challenges (Asif, Fakhar-e-Alam et al. 2025). Because of the quantum confinement (QC) effect, the bandgap of WO<sub>3</sub> fluctuates with size (Zheng, Ou et al. 2011). The wide-bandgap semiconductor tungsten oxide has a steep valence-band edge and a relatively narrow bandgap (i.e., 2.6 eV), allowing it to absorb visible light (Asif, Fakhar-e-Alam et al. 2025). By heating tungsten in various forms, tungsten oxide nanowires have been created (plates, wires, and powders) (Watanabe, Fujikata et al. 2013). The wavelength

range of near-infrared (NIR) irradiation is 780 to 2,500 nanometers. The heat produced by the conversion of light to heat can be exploited in a diversity of applications; including photothermal therapy (29) photocatalysis (30) water evaporation (Wang, Wang et al. 2017). electrochromic devices (Wang, Hao et al. 2018) energy applications (Asif, Fakhar-e-Alam et al. 2024) NIR shielding (Liu, Sheng et al. 2018).

### 2.8 Palladium oxide:

Palladium is single of the most extensively utilized transition metals for both homogeneous and heterogeneous catalysis of chemical processes due to its optimum combination of activity and selectivity (Yazdani, Sayadi et al. 2018), (Blaser, Indolese et al. 2001). A transition metal called palladium (Pd), is mostly used in the environmental and material science fields. It may be used for a variety of things, including coating materials, fuel cells, dental crowns, and catalytic converters (Li, Wu et al. 2016) Chemical, physical, and biological processes are frequently used to produce metal nanoparticles, although they are more expensive and need high pressure. One of those processes frequently results in the production of hazardous compounds that are damaging to the environment (Yazdani, Sayadi et al. 2018). A biological technique, on the other hand, offers several advantages, including being non-toxic, cost-effective, ecologically friendly, and requiring minimal equipment and chemical components. (Anarkali, Raj et al. 2012). Dictyota indicia seaweed extract was used to examine the green production of palladium oxide nanoparticles. Dictyotales are a vast order of brown algae belonging to the Phaeophyceae family (Yazdani, Sayadi et al. 2018).

### 2.9 Mercury oxide:

One of the persistent contaminants in wastewater is mercury, which is also a serious threat to the environment and public health. As a result, mercury treatment is now required (Vélez, Campillo et al. 2016). Mercury poisoning in soil and water is now a danger to both human health and environmental quality (Gong, Huang et al. 2019). It is used in a variety of industrial processes, including manufacturing. Mercury is a significant hazard to all living beings. Long-term exposure to mercury causes a range of symptoms, including tremors, hearing and vision loss, and significant neurological damage, including loss of feeling (Hsiao, Ullrich et al. 2011). The World Health Organization suggested a maximum inorganic Hg content of 6 g/L for drinking water (Organization 2004). The quantity of inorganic Hg allowed by the US Environmental Protection Agency is limited. That can be present as a pollutant to 2 g/L. (Organization 2004). Ion

exchange is one of the Hg therapy methods now available (Organization 2004) Chemical precipitation (Blue, Jana et al. 2010) cementation (Asif, Fakhar-e-Alam et al. 2024) and bioremediation (Ma, Di et al. 2009).

**2.10 Gold oxide:**

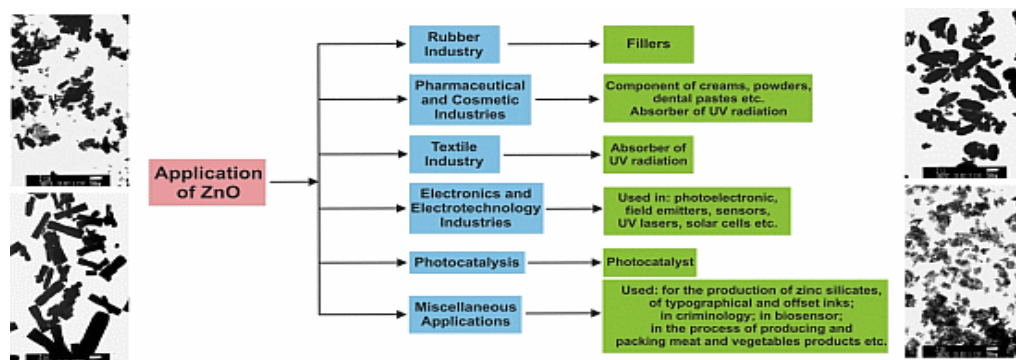
Gold nanoparticles (GNPs) have become a popularly used innovative material that has been used to build various kinds of biosensors and change a variety of electrodes. (50) Gold and nanoparticle-metal oxide are two brand-new vital materials being produced for use in scientific and medical endeavors. Our study's objectives were to examine the effects of gold (Au) and iron oxide (Fe<sub>3</sub>O<sub>4</sub>) nanoparticles on cellular growth in Escherichia coli (E. coli) and to try to interpret the results by functionalizing the Au nanoparticle for possible biological uses. (51)

**3. ZnO nanoparticles (NPs)**

They picked ZnO nanoparticles (NPs) because of the active laser medium, fluorescent bulb luminescence, and antibacterial properties. The visual transparency of ZnO NP is great, and it has good light-trapping properties. It also offers several other benefits, including featuring excellent photocatalysis, abundance in nature, and non-toxicity. By suppressing immune cells, the ZnO NP contributes significantly to toxicity processes.

These ZnO NPs were among the less costly n-type semiconductors, other than the scientific community is interested in them since they are UV light resistant.

At room temperature, ZnO nanoparticles have a high excitonic binding energy (60 meV) and a direct wide bandgap (3.3 eV) in the near-UV spectrum.



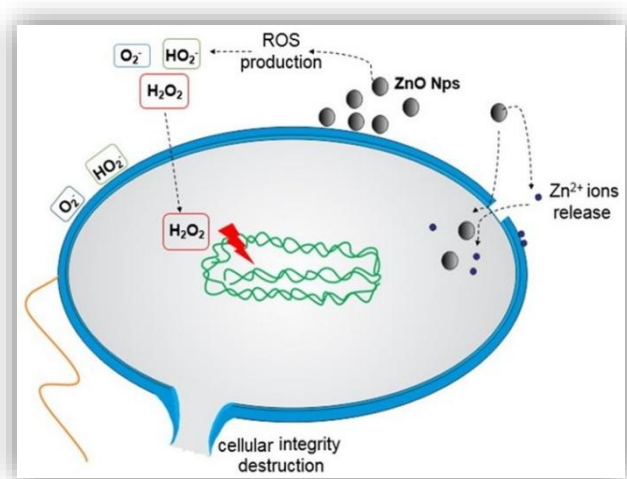
**Figure 3:** Applications of ZnO nanoparticles across multiple industries, including rubber (fillers), pharmaceuticals and cosmetics (UV protection, creams, powders), textiles (UV absorbers), electronics (sensors, lasers, solar cells), photocatalysis, and miscellaneous uses such as biosensors and criminology. Representative TEM images show the morphology of ZnO nanostructures.

ZnO offers more advantages than titanium dioxide since of all inorganic photocatalytic materials, it is more biocompatible and has the highest photocatalytic efficiency. ZnO also offers better heat resistance, durability, and selectivity. As ZnO particle size shrinks, its electrical, optical, and chemical characteristics change. Some authors contend that the quantum confinement surface is what causes these changes, opening up new possibilities for use (Viter and Iatsunskyi 2019). Rainfall, the movement of vapor, and the hydrothermal process are all chemical ways to make ZnO NPs. (Ahmed, Chaudhry et al. 2017).

ZnO NPs have a high surface area-to-volume ratio when compared to bulk material, which leads to a considerable improvement in UV-blocking efficacy. (Xie, He et al. 2011).

There are several benefits of using zinc oxide (ZnO) nanoparticles. optoelectrical, physical, and antibacterial capabilities, which means they have a lot of promise for increasing agricultural output. (Yadav, Prasad et al. 2006). ZnO NPs have the potential to boost food crop output and growth. It has been proposed that ZnO NPs be used as a Zn fertilizer in top soil as well as a foliar fertilizer (Singh, Singh et al. 2018).

Zinc oxide has a large bandgap and belongs to the II-IV semiconductor group, with binding energies of 3.2 eV and 60 meV, correspondingly. Zinc oxide nanoparticles have antibacterial, anti-cancer, and wound-healing characteristics, as well as the ability to block UV radiation. (Mishra, Mishra et al. 2017).



**Figure 4:** Proposed antibacterial mechanism of zinc oxide nanoparticles (ZnO NPs). ZnO NPs attach to the bacterial cell wall, releasing Zn<sup>2+</sup> ions and stimulating the production of reactive oxygen species (ROS) such as superoxide radicals (O<sub>2</sub><sup>-</sup>), hydroxyl radicals (HO<sub>2</sub><sup>-</sup>), and hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>). These ROS penetrate the cell, damaging nucleic acids and leading to loss of cellular integrity and eventual cell death.

### 3.1 Antimicrobial activity of synthesized Zinc Oxide NPs:

Antibacterial activities of ZnO-NPs are effective against several human ailments. Silver, titanium dioxide, and zinc oxide are used in a variety of applications (ZnO) to inhibit the growth of germs. Because inorganic antibacterial drugs have a non-specific activity, zinc oxide nanoparticles are used. (ZnO NPs) to maximize the fight against microbial resistance has attracted a lot of interest. (Madhumitha, Elango et al. 2016). The antibacterial properties of several hazardous bacteria, including *E. coli*, *Pseudomonas aeruginosa*, and *Campylobacter jejuni*, are vulnerable to ZnO NPs. (Hussain, Singh et al. 2017)

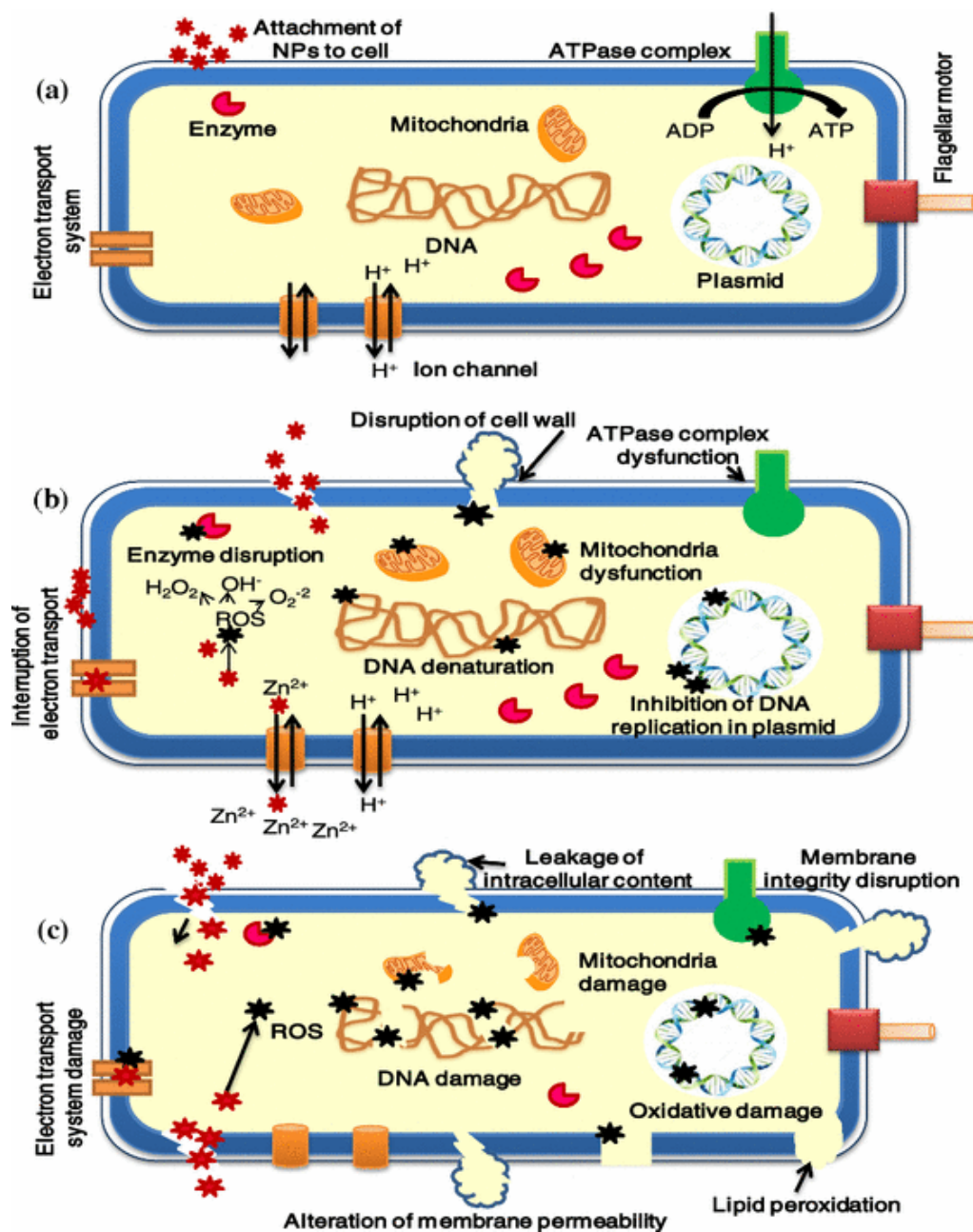
ZnO has been investigated as an antibacterial substance on both the micro- and nanoscales. ZnO becomes more

antibacterial as its size is reduced to the nanoscale. This study aims to summarise the mechanisms of action reported in the literature as well as the potential effects of ZnO's physicochemical characteristics and surface modifications on its antibacterial activity. This research may thus help in finding the most desired ZnO NP characteristics to produce the optimum antibacterial effect. (Lallo da Silva, Abuçafy et al. 2019).

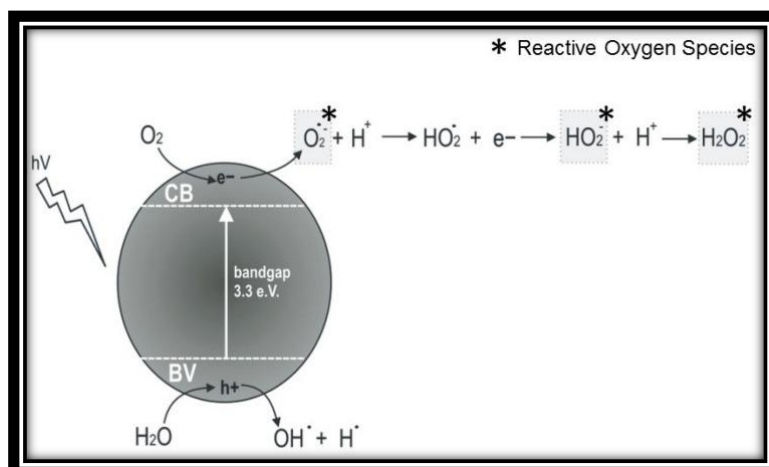
Four pathogenic bacteria the antibacterial activity of ZnO NPs generated by *B. megatherium*, *B. pumilus*, *B. cereus*, and *E. coli* was tested using *B. megatherium*, *B. pumilus*, *B. cereus*, and *E. coli*. *C. rhizoma*. In contrast to gram-positive bacteria, the generated ZnO NPs were active against the gram-negative bacterium *E. coli*, according to the data. (1) This section will go through the primary modes of action mentioned in the literature

to better understand how structural characteristics of ZnO NPs may affect their antibacterial activity (Lallo da Silva, Abuçafy et al. 2019) The picture shows a schematic illustration of how bacteria and ZnO nanoparticles interact. ZnO NPs harm and deplete the cell wall when consumed. It also inhibits DNA replication, releases metallic ions, and generates reactive oxygen species in the bacterial cell.

•ZnO NPs produced chemically are good antibacterial agents due to their capacity to absorb UV light. Gram-positive bacteria respond to ZnO NPs more readily than Gram-negative bacteria, according to several studies (Bhuyan, Mishra et al. 2015). ZnO nanoparticles' antibacterial properties include direct interactions with bacterial cells, which alter bacterial protein structure and disrupt membrane permeability (Premanathan, Karthikeyan et al. 2011). Within the bacterial cell, oxidative stress and the production of reactive oxygen species are brought on by the intake of damaging dissolved zinc ions as well as the admission of ZnO NPs brought on by the proton motive force (ROS). Because of their high reactivity and oxidizing ability, ROS are hazardous to bacteria. Reactive species like hydrogen peroxide are one example of this ( $H_2O_2$ ), OH (hydroxyl radicals), and  $O_2^{\cdot -}$  being among the reactive species (peroxide) (Kairyte, Kadys et al. 2013) These species cause harm to as Biological The integration of lipids, DNA, and proteins into the bacterial cell membrane results in the formation of these components. In addition, ZnO nanoparticles stimulate metabolic enzymes. impairing mitochondrial function and cellular metabolism as well as causing cytoplasmic contents to leak out, which prevents bacterial cell growth and/or results in bacterial cell death (Lan, Ge et al. 2020). The interaction of bacterial cells with ZnO nanoparticles is schematically depicted in Figure. The ingestion of ZnO NPs breaks the cell wall, depletes intracellular resources, and interferes with DNA replication, releasing metallic ions, among other effects, and generating reactive oxygen species in the bacterial cell. (Abbasalipourkabir, Moradi et al. 2015).



**Figure 5:** Schematic illustration of the multiple antibacterial mechanisms of nanoparticles against bacterial cells: (a) Initial attachment of nanoparticles (NPs) to the cell surface, interference with ion channels, and dysfunction of the ATPase complex. (b) Disruption of the cell wall, release of  $Zn^{2+}$  ions, ROS generation, enzyme inactivation, mitochondrial dysfunction, and DNA denaturation, leading to inhibition of plasmid replication. (c) Severe oxidative stress and electron transport system damage cause membrane permeability alteration, leakage of intracellular contents, mitochondrial damage, lipid peroxidation, and DNA damage, ultimately resulting in bacterial cell death.

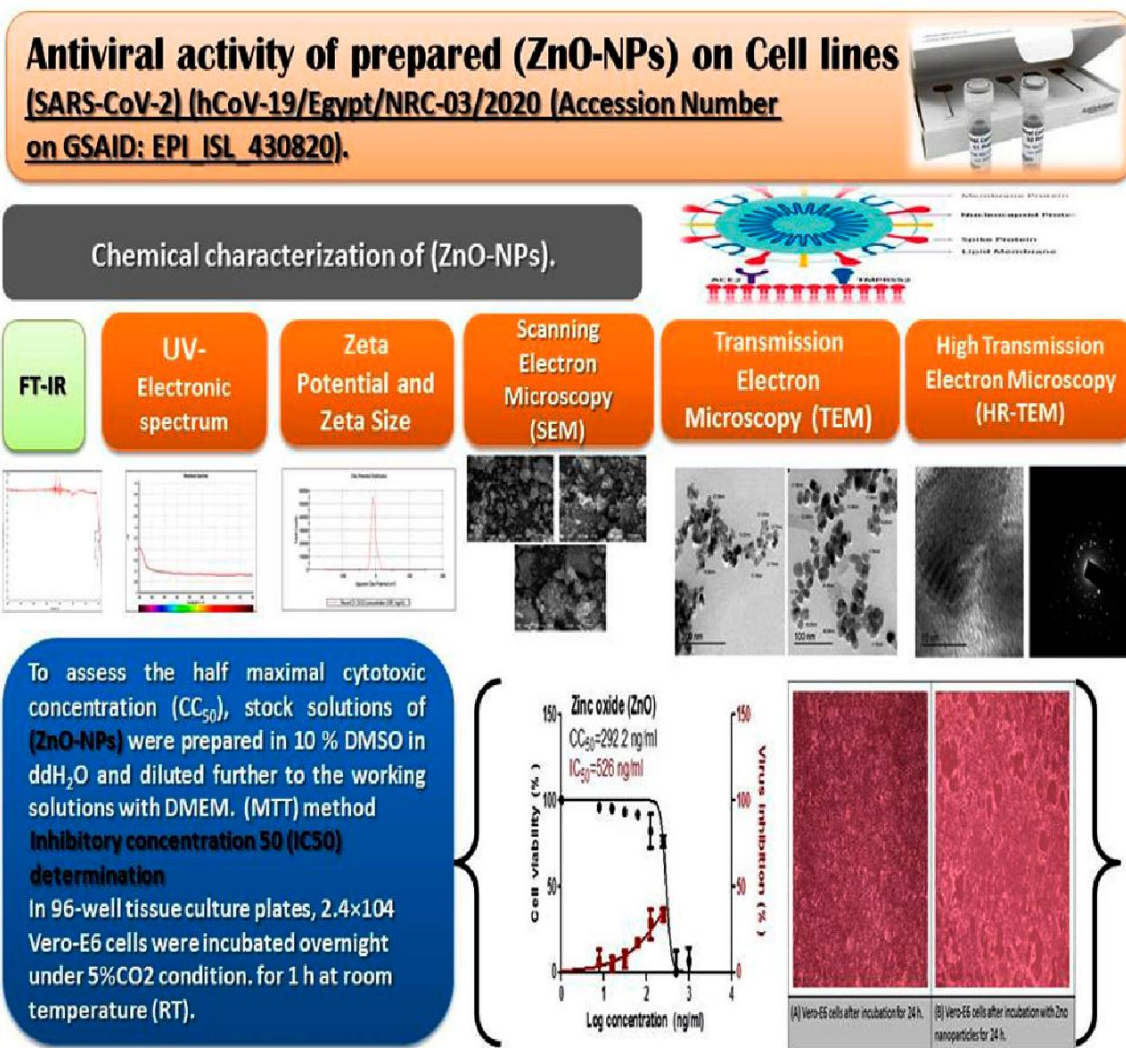


**Figure 6:** Mechanism of the act of ZnO NPs in opposition to microorganisms (Lallo da Silva, Abuçafy et al. 2019)

### 3.2 Antiviral activity:

Viruses are genetically encoded proteins that are incredibly tiny. In the container of the encapsulated virus, extra. The virus is surrounded by lipid layers, which can be transmitted in one of two ways: directly between cells or through an aqueous environment. (Perlman and Netland 2009). Coronaviruses (CoVs) are RNA viruses that are classified as such. They are a significant pathogen that causes a variety of isolated illnesses in mammals and birds (Zhang, Zhou et al. 2020). CoVs infect mammals and birds' upper respiratory tracts first. In humans, cough and fever are the most common signs of CoV infection, and SARS-CoV-2 can also cause breathing difficulties. A modified ZnO-NP surface may affect virus infection potential by neutralizing the virus rather than interfering with cellular targets. This is accomplished via H-ZNPs' electrostatic interference with the virus as opposed to the hydrophobic interaction of ZNPs. As a consequence, we think that coating ZnO-NPs in polyethylene glycol has been shown to have a substantial anti-COVID-19 action, reducing cytotoxicity and inhibiting the production of reactive oxygen by hiding ZNO-NPs (Refat, Hamza et al. 2021). Numerous human illnesses have been demonstrated to be resistant to ZnO-NPs' antibacterial capabilities, leading Later in the pathogenesis phase, viral death in host cells occurs. ZnO NPs have sparked a lot of attention among nanoparticle types ZnO-NPs in polyethylene glycol have been shown to have a substantial anti-COVID-19 action, reducing cytotoxicity. It possesses antiviral properties. (Perlman and Netland 2009). Zn has antiviral properties and could be used to treat a variety

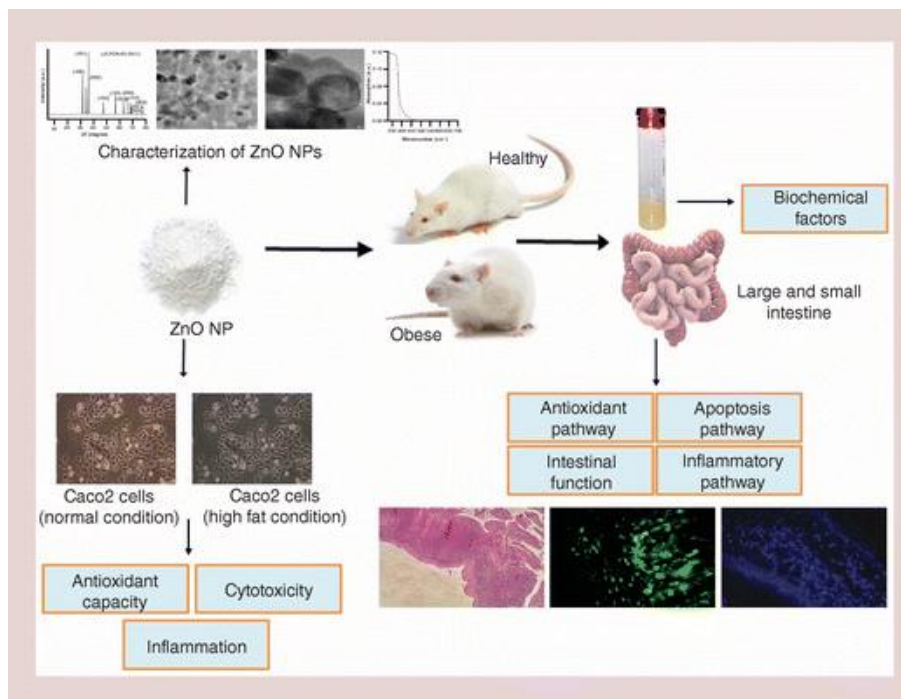
of respiratory viruses, including SARS-CoV-2. As a result, incorporating vitamins and minerals in one's diet can be utilized in conjunction with antiviral medications to treat COVID-19 disease. (Islam, Quispe et al. 2021). Zinc supplementation may improve the efficacy of other medications like hydroxychloroquine that are currently being studied (Refat, Hamza et al. 2021). The modified ZnO-NP surface may affect virus infection potential by neutralizing instead of interfering with biological objectives. This is accomplished by the electrostatic interaction of H-ZNPs with the virus rather than the hydrophobic interaction of ZNPs. As a consequence, we believe that encapsulating ZnO-NPs in polyethylene glycol has a significant anti-COVID-19 effect. impact while also reducing cytotoxicity. and inhibiting the production of reactive oxygen by hiding ZNO-NPs (Refat, Hamza et al. 2021). Numerous human illnesses have been demonstrated to be resistant to ZnO-NPs' antibacterial capabilities. (Abbasi-Oshaghi, Mirzaei et al. 2018).



**Figure 7:** Antiviral activity of ZnO-NPs

Using Zn (NO<sub>3</sub>)<sub>2</sub> as a powerful modified ZnO-NP surface may reduce the possibility for virus infection by neutralizing instead of interfering with biological objectives. This is achieved by the electrostatic contact of H-ZNPs with the virus rather than the hydrophobic interaction of ZNPs with the virus. As a consequence, we think that encapsulating ZnO-NPs in polyethylene glycol can significantly inhibit COVID-19 while also lowering cytotoxicity (Zheng, Ou et al. 2011). Various-sized nano crystallites were produced by annealing zinc oxide for four hours at temperatures between 100 and 650 degrees Celsius. Zinc oxide nanoparticles' size and shape were determined using SEM, TEM, and XRD.

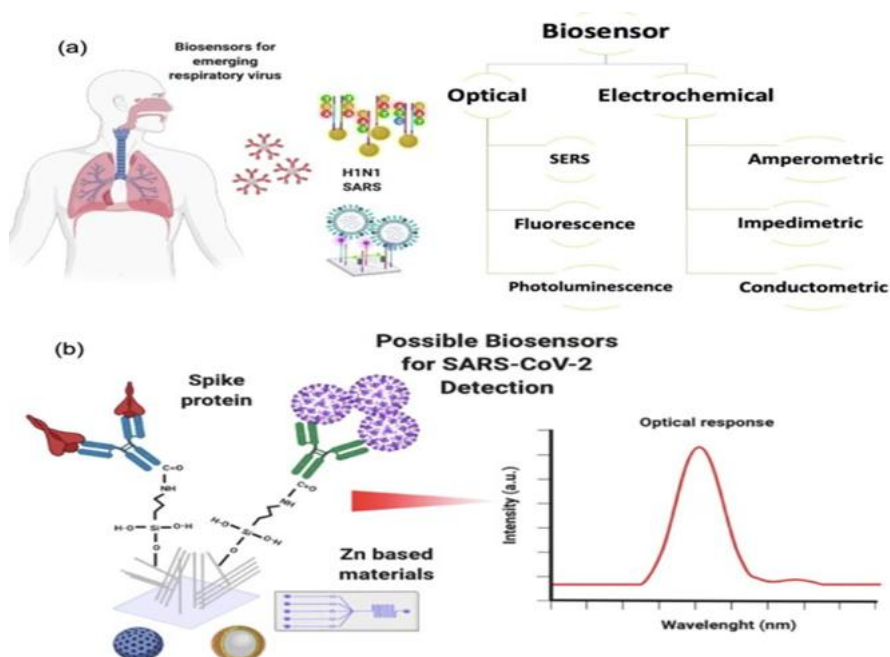
ZnO-NPs' ability to kill The MTT method was used to assess VERO-E6 cells. VERO-E6 cells were seeded in 96-well plates at a density of  $3 \times 10^5$  cells/mL and a concentration of 100 L/well. They were then incubated in CO<sub>2</sub> for 24 hours at 37 degrees Celsius (5 percent). After around 24 hours, VERO-E6 cells were given different concentrations of ZnO-NPs in triplicates and three sterile phosphate buffer saline washes were performed on the cellular monolayers. Each well received 20 L of MTT solution (5 mg/mL ZnO-NPs solution) before being incubated at 37°C for around 4 hours. The medium was then aspirated. Crystals of formazan are present in each well in good shape. (Rodelo, Salinas et al. 2022).



**Figure 8:** Schematic diagram for Acute toxicity evaluation of ZnO-NPs

According to the study, At 50 mg/kg body weight, ZnO-NPs had no adverse effects on the liver or intestines of rats. (Li, Chen et al. 2017). After that, rats given ZnO-NPs at doses ranging from 200 to 600 mg/kg showed substantial negative effects on inflammatory indicators, liver enzymes, oxidative stress, cytochrome enzymes, hematological variables, and liver histological parameters. (Sivakumar, Lee et al. 2018).As

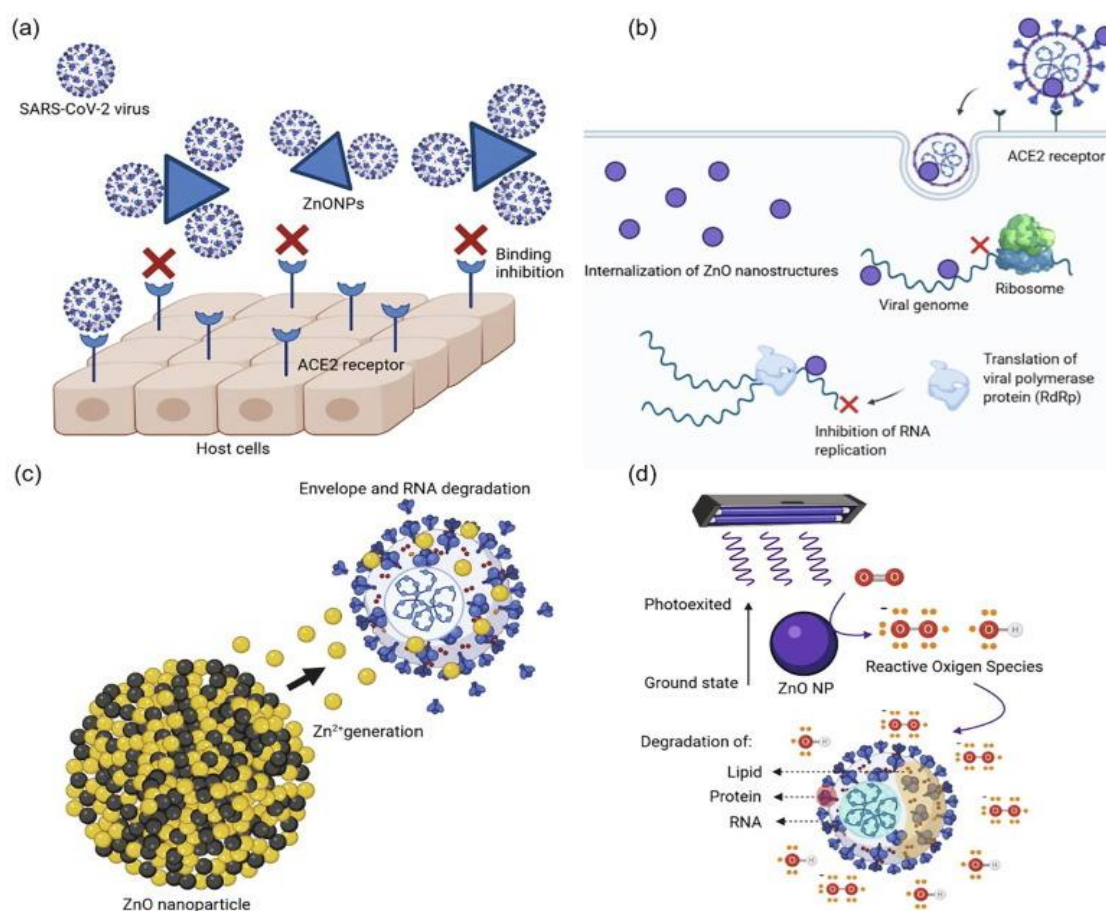
a result, a large dosage of ZnO-NPs (more than 100 mg/kg) was required may result in higher toxicity while decreasing efficiency. Oral administration of ZnO-NPs at a dose of 5 mg/kg to rats, on the other hand, displayed anti-inflammatory and antioxidant capabilities and was useful in healing colitis in a different study. They said that at this dosage, no hazardous consequences were observed. (Hong, Park et al. 2014).



**Figure 9:** Use of ZnO in biosensor formations

A retrospective on Zn-found nanoparticles and their possible use in SARS-CoV-2 discovery is opened as a result of these studies. Trials including precise antibodies aligned with the well-known point protein S1 could be developed using these promising technologies. (Rodelo, Salinas et al. 2022). Functioning electrodes (WEs) adorned with upright grown-

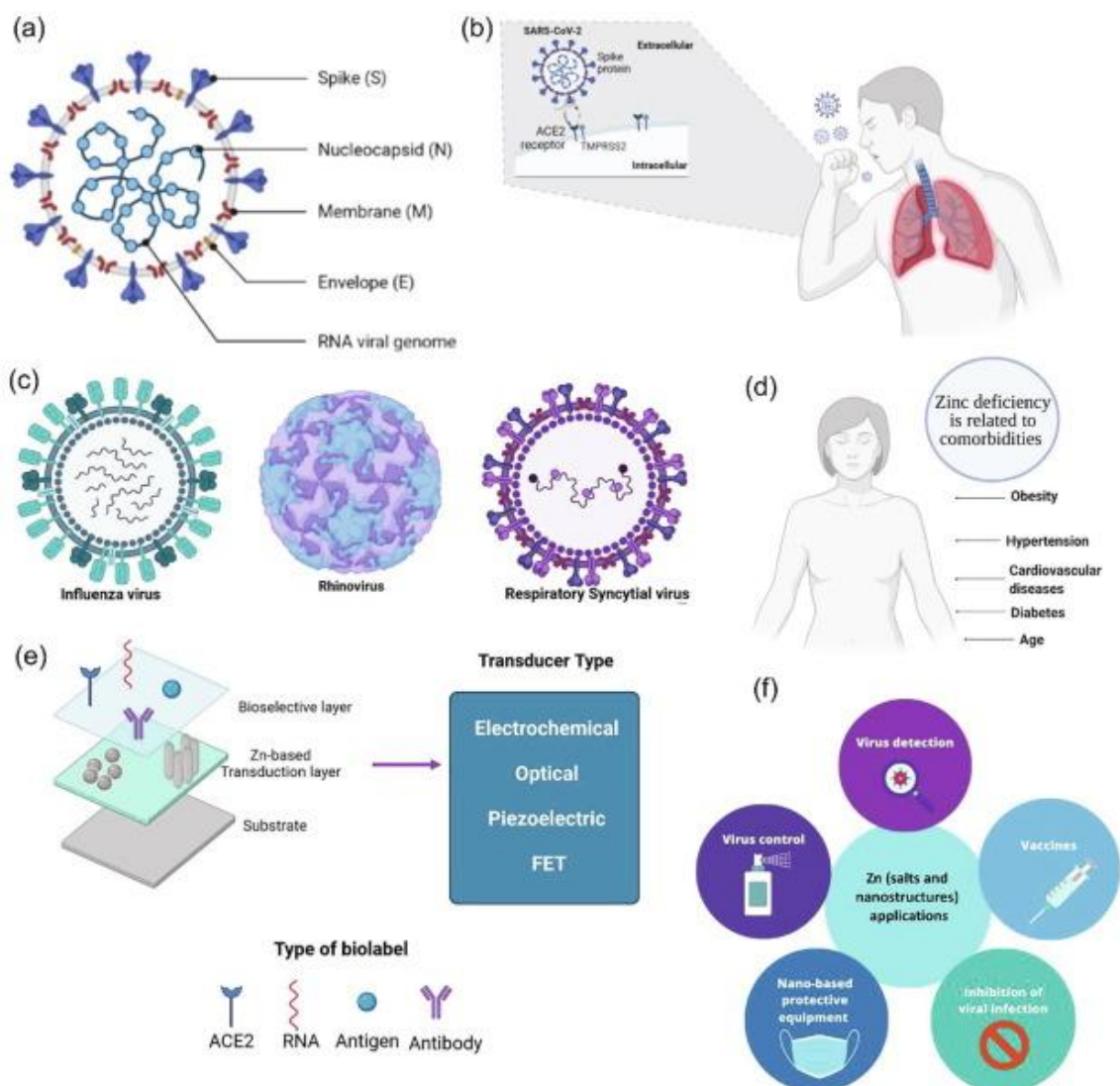
up ZnO NWs were used to improve the biosensing electrochemical impedance sensing (EIS) nano biosensor performance on paper. Different amounts of Human blood samples had IgG antibodies to SARS-CoV-2 (CR3022). may be distinguished using these nano biosensors (blank, 10 ng ml<sup>-1</sup>, 100 ng ml<sup>-1</sup>, and 1 g ml<sup>-1</sup>) (Hussain, Oves et al. 2019).



**Figure 10:** ZnO NPs efficacy against SARS COVID

The current coronavirus epidemic (COVID-19) has multiplied throughout the world. Resulting in a pandemic that has so far been predicted to have killed 5 million people, according to WHO. Although there is no cure, the epidemic is regrettably still expanding. In addition, additional hospitalization and mortality records have been produced as a result of the fast spread of novel viral strains like the so-called Delta variety (Lan, Ge et al. 2020). Coronavirus 2 from COVID-19 is caused by (ACE2) and the S protein sense organ triggers viral recognition, which is followed by

endocytosis and viral multiplication. (Li, Qin et al. 2021). Approaches based on nanotechnology to tackle SARS-CoV-2. (a) SARS-CoV-2 structural diagram. (b) To link to the host cell, Severe Acute Respiratory Syndrome causes COVID-19 (SARS-CoV-2). The virus's capsid, which houses the single-stranded RNA genome, is surrounded by a second layer of glycoproteins. Detection utilizing Zn-based nanostructures is accomplished using a variety of biosensing approaches. Potential applications of zinc (salts and nanostructures) to battle the present epidemic. (Milani, McLaughlin et al. 2012).

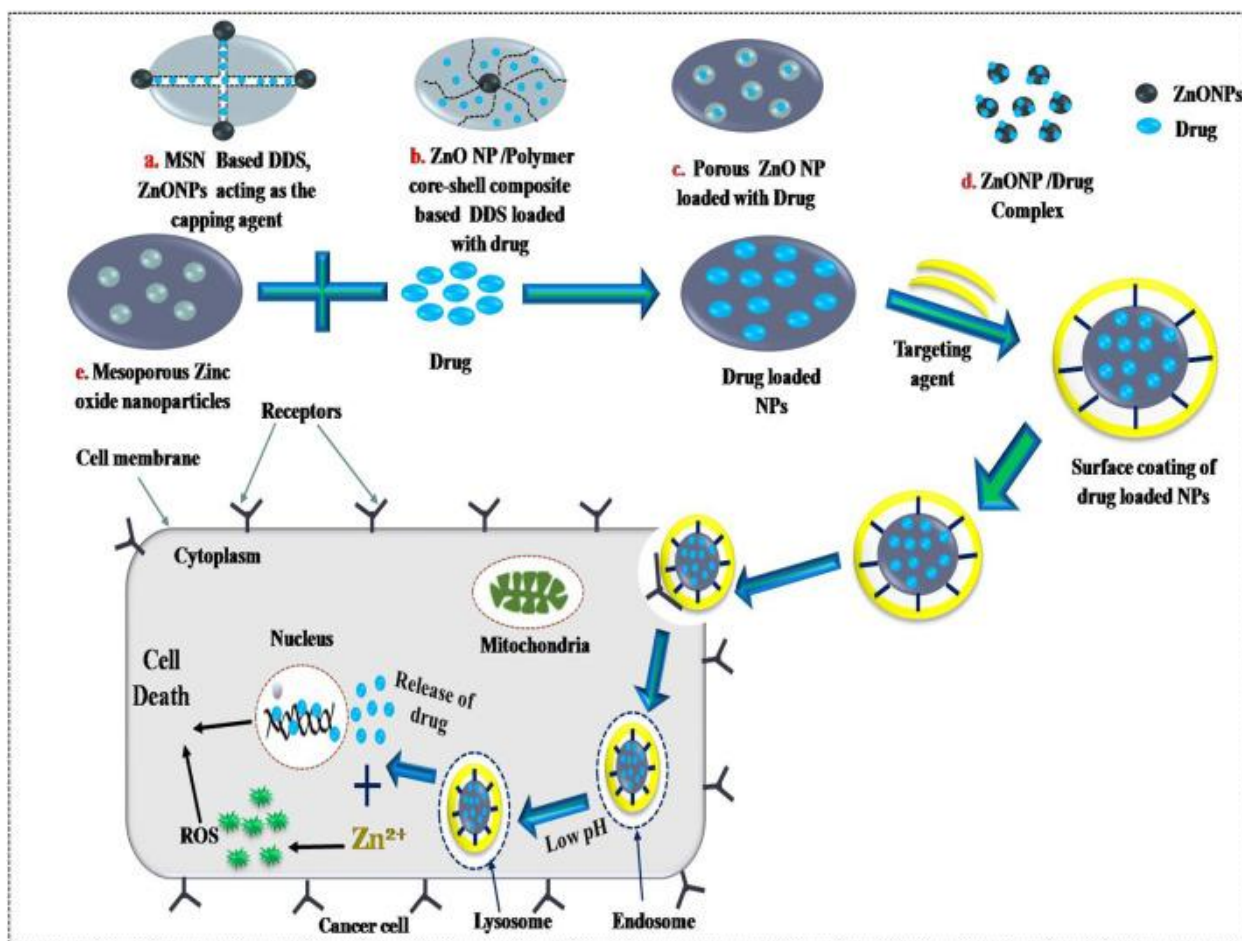


**Figure 11:** Complication associated with the Zn deficiency in humans

### 3.3 Anti-cancer activity:

Cancer is individually of the most important causes of passing away internationally among noninfectious diseases. (Jiang, Pi et al. 2018). The current cancer treatment, which includes alkylating chemicals and antimetabolites, has numerous side effects and is known to cause systemic toxicity. As a consequence, tailored therapy is critical in the treatment of cancer (Skrajnowska and Bobrowska-Korczak 2019). Metallic compounds Antibacterial and anticancer characteristics are found in metals such as gold, silver, copper, copper oxide, titanium dioxide (TiO<sub>2</sub>), and zinc oxide (ZnO). Reports on the possible use of ZnO as an anticancer drug, on the other hand, agree that ROS, together with apoptosis and necrosis, are the principal cell death processes (Kumar,

Venkateswarlu et al. 2013). An independent investigation found that spherical ZnO NPS had dual activity against germs and cancer cells. The key cell-killing pathways include ROS production, apoptosis, necrosis, and cell membrane rupture. (spherical, hexagonal, and rod-like) bacteria, as well as HeLa carcinoma cells, were produced and tested. In this study. Although ZnO NPS has been demonstrated to have anti-cancer and antibacterial properties, the function of morphological characteristics has not been established. (Such as size and shape) has yet to be determined. As a result, three distinct morphologies of ZnO NPS (Structures of various shapes (spherical, hexagonal, and rod-like) were developed and tested against *E. coli*, *S. aureus* bacteria, and HeLa cancer cells in this study. (Vinardell and Mitjans 2015).



**Figure 12:** Drug loaded Zn nanoparticles enhanced efficacy against cancer treatment.

### ZnO NPs as a channel for the delivery of anticancer drugs;

- Acid-sensitive ZnO NPs are used as pore-blocking agents in DDS based on mesoporous silica nanoparticles;
- Drug loading in a ZnO/polymer core-shell nanocomposite's hydrophobic shell;
- Drugs are put into the pores of porous ZnO NPs;
- As a result of the intracellular synthesis of highly hazardous  $Zn^{2+}$  ions in a mildly acidic environment microenvironment, ZnO NPs have a synergistic anticancer impact. (Eker, Duman et al. 2024).

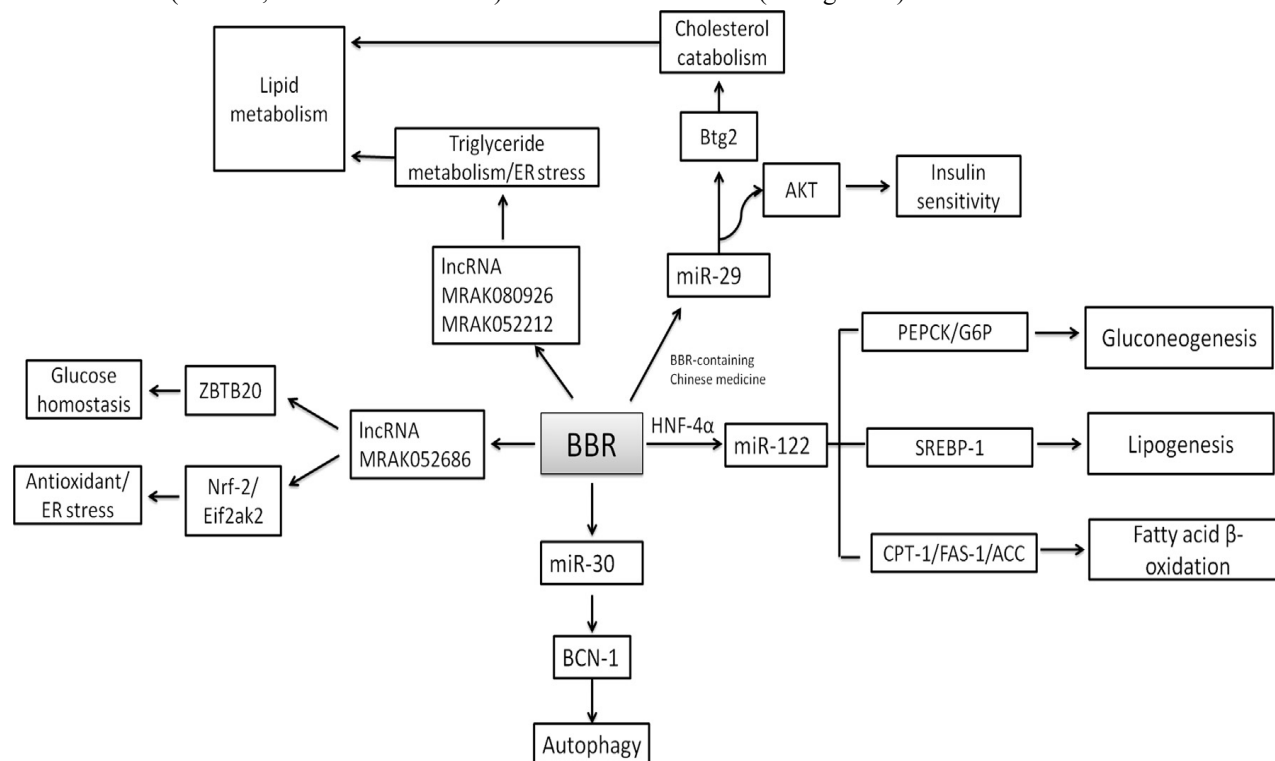
### 3.4 Antidiabetic activity:

Diabetes affected 415 million people worldwide in 2015. The figure is expected to rise to 592 million by 2035. (Reference finds). There is a hazard to the world's public health as adult-onset diabetes mellitus becomes increasingly widespread. The countries with the greatest diabetes prevalence rates by 2030 are predicted to be China, India, and the United States. (Wild, Roglic et al. 2004). Known medically as type 2 diabetes mellitus (T2DM), a multifaceted condition that

necessitates ongoing medical care and multifactor risk reduction efforts. The avoidance or delay of complications, as well as the Diabetes therapy, aims to maintain one's quality of life. Adopting a balanced diet increases physical activity while keeping a healthy body weight are the cornerstones of T2DM management. To assist regulate blood glucose levels, a variety of oral and injectable medicines are available. Metformin is a well-known diabetes medication that is also one of the most powerful. Sulfonylureas (SUs), which increase insulin secretion in type 2 diabetes, are other essential diabetic medications. In recent decades, the availability of innovative drugs, some of which belong to different therapeutic classes, has increased Diabetes management is complicated (Chu, Hsu et al. 2019). After metformin became widely used, five new classes of oral anti-diabetic drugs (OADs) emerged: alpha-glucosidase inhibitors (AGIs), thiazolidinediones (TZDs), nonsulfonylurea insulin secretagogues glinides, dipeptidyl peptidase-4 (DPP4) inhibitors, and sodium-glucose cotransporter 2 inhibitors (SGLT2) Both rapid-acting and long-acting insulin are employed because to their superior pharmacokinetic and pharmacodynamic features.

Analogues have grown in popularity. GLP-1 receptor agonists (GLP1RAs), an injectable medication, have been launched in Taiwan alongside insulin. Despite having different mechanisms of action and safety profiles, these anti-diabetic medications have similar efficacies, according to clinical research (Bennett, Maruthur et al. 2011).

Alloxan and its reduction product, dialuric acid, create an oxidative cycle as an effect of the manufacture of superoxide radicals. A considerable rise in the concentration of cytosolic calcium coincides with the dismutation of these radicals into hydrogen peroxide, which causes the rapid death of pancreatic cells. (Chang 2017)



**Figure 12:** An overview of the non-coding RNA-targeting properties of hesperidin as a diabetes treatment (Chang 2017)

Humans and many other animals employ gluconeogenesis as one of the key methods for maintaining blood glucose levels and preventing hypoglycemia. The liver, as a primary insulin-sensitive organ, is important for Homeostasis of cholesterol and glucose levels. Fatty acid metabolism and several liver diseases, such as non-alcoholic fatty liver disease, hepatocarcinogenesis, and HCV replication, have both been connected to MiR-122. (Wang, Lai et al. 2016). MiR-122 is a crucial regulator of the liver's homeostasis and has the potential to be a biomarker for metabolic disorders (Hsu, Wang et al. 2012). Insulin is found in primary cultured rat hepatocytes induced an upregulation of miR-122 expression. Additionally, miR-122 is present in considerably larger concentrations in the serum of ob/ob mice, and blocking. In a diet-induced obesity mice model, miR-122 reduced plasma cholesterol levels and liver lipogenic gene

expression. Berberine reduces gluconeogenesis, which enhances glucose metabolism in diabetic rats. (Zhang, Lv et al. 2012). It is still unclear how berberine works, though Berberine at a high dose of 160 mg/kg/d for four weeks significantly decreased miR-122 in the blood and liver of mice with high-fat diet-induced diabetes. Even at modest doses (40 mg/kg/d), berberine lowered miR-122 levels in diabetic mouse livers by 47%. (Wei, Zhang et al. 2016) Berberine treatment reduced the expression of miR-122, which reduced the expression of hepatic gluconeogenesis enzymes (such as PEPCK and G6Pase) and important proteins for lipid synthesis (such as SREBP-1, FAS1, and ACC), as well as the expression of CPT-1 in palmitic acid-treated HepG2 cells. (Asif, Fakhar-e-Alam et al. 2024).

**Table 1:** ZnO nanoparticles and its biomedical applications

Sr.no	Nanoparticles	Green synthesis/chemically	ANALYSIS	Effects	Applications	Reference
1	ZnO	<i>Costus pictus</i> leaf extract	FTIR, XRD, SEM, EDX, TEM, SEM	Biosynthesized ZnO nanoparticles were proven to be potent antibacterial and anticancer agents against bacterial and fungal phytopathogens	Anti-cancer and Antimicrobial activity	Reference 116
2	ZnO	Human cervical cancer cell line (HeLa)	Fluorescence and Confocal Laser Scanning Microscope (CLSM)	ZnO NPs reduce cell viability by 5 to 50% in HeLa cells treated for 48 hours at concentrations ranging from 0.001-0.06 mg/mL via oxidative stress and apoptosis.	Cancer treatment and therapy.	Reference 117
3	Fe-doped ZnO		Cell culturing	When compared to pure ZnO NPs, Fe-doping reduces the release of Zn <sup>2+</sup> ions and shows less toxicity in cancer cells. However, Fe-doped ZnO NPs demonstrated greater cytotoxicity in cancer cells than in normal cells. In a syngeneic preclinical animal model, 2% Fe-doped ZnO NPs demonstrated significant antitumor activity after peritumoral administrator	Anticancer Human bronchial epithelial cells (Beas-2B), HeLa cells, and mouse lung squamous carcinoma were all used in this study (KLN 205)	Reference 118
5	ZnO	Chemically synthesis	SEM, DNA separation, EMA treatment, and EMA-qPCR assay.	The bactericidal impact of ZnO nanoparticles against <i>C. jejuni</i> was very efficient, and the antibacterial activity of ZnO nanoparticles rises with a reduction in particle size.	Antibacterial activity	Reference 119
6	ZnO	Chemically synthesis	SEM, TEM, XRD, FTIR	Several fungi, viruses, and bacteria are poisonous to zinc oxide nanoparticles. followed by metal ion release and DNA damage that causes cell death.	Antimicrobial activity	Reference 120
7	ZnO	Green synthesis		Inhibiting or changing DNA replication, protein synthesis, food metabolism, and respiration are all examples of biological processes is another way	Anti-bacterial	Reference 121

**Aknowlegement:** Authors express our sincere gratitude to Allah Almighty for bestowing us with knowledge and wisdom. Authors are also deeply thankful to our honorable teachers for

their guidance, support, and invaluable mentorship, which have significantly enriched our work.

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