Chapter 39

Therapeutic Effect of Nanoparticles as Anti-inflammatory, Antibacterial and Anti-parasitic

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ABSTRACT

Nanotechnology is currently being widely used in a number of scientific fields. In particular, nanoparticles (NPs) are used in both *in-vitro* and *in-vivo* studies on parasites and bacteria which can be used as anti-parasitic and anti-bacterial drugs. Particles created in various forms and sizes, ranging roughly from 1 to 100 nanometers, are called nanoparticles (NPs). Antimicrobial resistance (AMR), which posed a threat to the prevention and treatment of an increasing number of infections caused by bacteria, parasites, viruses, and fungi that no longer respond to the standard treatments that have been used to treat them, is one of the important risk factors of the twenty-first century. To effectively treat infectious disorders, it is strategically advantageous to use nano size metals, metal oxides, (NPs), and nanocomposites. NPs which have antibacterial action against a number of bacteria species including *E. faecium*, *St. aureus*, *K. pneumoniae*, *A. baumannii, P. aeruginosa,* and *Enterobacter* species comprise of NPs containing Silver, Gold, Yttrium, Cadmium, Aluminum, Selenium, Zinc, Copper, Titanium, Magnesium, Nickel, Cerium, or Iron. Utilizing nanoparticles made of metals and their oxides is highly significant. Nanoparticles are also effective against the parasitic infection. There are commonly used nanoparticles against parasites such as Zinc, Silver, Cu and Mg nanoparticles. Various substances, such as oxidized metals, silver, chitosan, and gold nanoparticles, can inhibit the growth of various parasites, such as *Giardia*, *Leishmania, Plasmodium*, and *Toxoplasma*, as well as helminthes, such as *Echinococcus multilocularis, Trichinella spiralis*, and *Fasciola hepatica*. NPs can be used either alone or in conjunction with existing medications to treat parasites. NPs are recommended as more potent medications with less adverse effects for the prevention and management of parasites. Over the past ten years, significant progress has been made in the field of Nano medicine for the control of parasites.

KEYWORDS
Nanoparticles, Anti-inflammatory, Antibacterial and Anti-parasitic

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INTRODUCTION

Nanoparticles as Anti-inflammatory and Antibacterial

Antibiotics have proven essential in achieving substantial medical and surgical improvements in addition to saving patients' lives (Gould and Bal, 2013). They have been successful in preventing or treating infections that may occur in patients who have been undergoing chemotherapy, the ones with persistent illnesses like diabetes, kidney diseases, or

arthritis, or the patients who have undergone complex surgeries (Rossolini et al., 2014). Antibiotics have also increased longevity by modifying the course of bacterial infections (Piddock, 2012). The use of antibiotics has been beneficial everywhere in the world. In developing countries with still poor sanitation, the use of antibiotics lowers. The number of cases and fatalities resulting from food-borne and other diseases associated with poverty (Rossolini et al., 2014).

Antimicrobial resistance (AMR), which posed a threat to the prevention and treatment of an increasing number of infections caused by bacteria, parasites, viruses, and fungi that no longer respond to the standard treatments that have been used to treat them, is one of the important risk factors of the twenty-first century (Prestinaci et al., 2015).

The World Health Organization has long recognized the need for a robust and very well coordinated international effort to avoid AMR (WHO). The WHO Global Strategy for Containment of Antimicrobial Resistance presented a framework of measures in 2001 to prevent the establishment and spread of antimicrobial-resistant microorganisms. (Organization, 2001). In its 2012 report, The Evolving Threat of Antimicrobial Resistance - Options for Action, the World Health Organization (WHO) made a number of recommendations for interventions, including strengthening health systems and encouraging the development of new drugs and vaccines (Organization, 2012). The World Health Organization its report on antimicrobial resistance in 2014, from both domestic and international sources (Organization, 2014). Antibiotics have revolutionized the treatment and saved countless lives, but there has been a sharp increase of bacteria that are resistant to them all around the world (Golkar et al., 2014). Infections produced by bacteria are now again a serious threat decades after the first patients got antibiotic therapy (Spellberg and Gilbert, 2014). The problem of antibiotic resistance has been linked to the unwanted use and exploitation of antibiotics, along with challenges within the biopharmaceutical industry. These challenges include reduced financial incentives and burdensome regulatory requirements, which have hindered drug discovery and development in this field (Viswanathan, 2014).

Decades before humans began to manufacture antibiotics in large quantities to prevent and cure infections, many bacterial species had already developed the capacity to resist them (Bhullar et al., 2012). Modifications in a bacterium's genome can result in antibiotic resistance. In humans or animals treated with antibiotics, mutations easily happen and become fixed. There are fewer instances of such a significant selection pressure on pathogens elsewhere (Larsson and Flach, 2022). Furthermore, the process is unaffected by other species' genetic reserves. Therefore, external factors are frequently less likely to significantly contribute to the mutation-based establishment of resistance for the vast majority of illnesses. When considering the emergence of new resistance factors, it's important to acknowledge that water, soil, and other environments characterized by highly diverse ecological niches offer an unparalleled source of genetic diversity. This diversity surpasses that found within the microbiota of humans and domesticated animals (Schulz et al., 2017).

In England in 1961, the term "methicillin-resistant Staph. aureus" was initially adopted shortly after methicillin was used in medicine (Jevons, 1961). Methicillin is no longer available for human consumption. Safer penicillins have taken its place (Dzintars and Grayson, 2018). The terminology ‘Methicillin-resistant S. aureus’ is still in use. MRSA healthcare-associated MRSA (HA-MRSA) in many regions worldwide after its original recognition (Chambers and DeLeo, 2009). When MRSA was discovered in patients who had never had any prior medical contact (also known as community-associated MRSA, or CA-MRSA), a significant shift in MRSA prevalence was evident (Faoagali et al., 1992). It has additionally been attributed to contact with livestock since the twenty-first century (livestock-associated MRSA) (Lee et al., 2018).

The use of antibiotics in modern medicine to treat bacterial infections has revolutionized the field. Nevertheless, throughout time, the indiscriminate, improper, and frequently abusive use of antibiotics has accelerated the establishment of pathogenic bacteria AMR. These bacterial strains are resistant to common therapeutic approaches. Realizing that the emergence of AMR has outrun the introduction of new antibiotics is disappointing (Chakraborty et al., 2022). The main source of nanoscale confinement of materials combined with multivalent interactions and high surface-to-volume ratio is the therapeutic impact of nanomaterials. To effectively treat infectious disorders, it is strategically advantageous to use nano size metals, metal oxides, (NPs), and nanocomposites. (Chakraborty et al., 2022).

Pathogenic microorganisms' cell membranes can be penetrated by nanoparticles (NPs), which then create special antimicrobial mechanisms by interfering with crucial biochemical processes. NPs have shown synergy when used with the strongest antibiotics, and they may help to control the universal challenge of growing resistance to antibiotics (Lee et al., 2019).

Antimicrobial Resistance and Wound Healing

Antimicrobial-resistant microorganisms from an infected wound could affect the patient's overall well-being and raise medical expenses (Filius and Gyssens, 2002). The process of cutaneous wound recovery is extremely intricate and regulated. If the wound healing process does not go quickly and efficiently, an extended cutaneous wound may form (Han and Ceilley, 2017). One of the main obstacles to wound healing is bioburden (Rhoads et al., 2012). Pathogens' colonization of the wound site significantly increases the persistence of the wound (Rahim et al., 2017). Besides being susceptible to basic skin infections, prior research has demonstrated that surgical site infections (SSIs), wounds brought on by diabetes, hypertension, venous disorders, and surgery are more prone to harbor harmful bacteria (Călina et al., 2017). Among these, SSIs account for 15% of the total nosocomial infections and are very challenging to treat as a result of their drug resistance (Dulon et al., 2011). S. aureus, E. faecalis, P. aeruginosa, and P. mirabilis have been identified as the most common bacteria in persistent wounds based on a number of sources (Kirketerp-Møller et al., 2008). Microbial infection is the most common challenge to wound healing. A wound is considered infected if the bacteria exceeds a threshold of 10^5 per gram of wound

tissue (Stojadinovic et al., 2008). The majority of pathogenic microorganisms that commonly colonize chronic wounds are more prone to produce biofilms, which directly contribute to a slower recovery (Wu et al., 2019). S. aureus, P. aeruginosa, and E. coli are bacteria that frequently populate wounds. Typically, these bacterial species have a negative impact on the rate at which wounds heal (Serra et al., 2015). The emergence of antibiotic resistance has urged the careful application of systemic antimicrobials, particularly in the treatment of local diseases such cutaneous wounds. Topical antimicrobials are crucial for managing chronic wounds because they help stop bacterial biofilm formation and wound infection. Topical antibiotics such polymyxin B and silver sulfadiazine are suggested for systemic antibiotic therapy for infected wounds; after the wound is healed, antibiotic usage should be stopped. (Tang et al., 2022). The management of wounds is vital because wound recovery is a difficult problem. Nanotechnology enables a wide range of contemporary regenerative medicine approaches. Many biocompatible self-assembling nanoparticles (NPs) have recently been created (Thapa et al., 2020). NPs enhance delayed wound healing and injury care. In addition to having low in vivo toxicity, metal nanoparticles (NPs) have shown promising features (Mirzahosseinipour et al., 2020). Three potential explanations for their antimicrobial activity have been established: (1) the alteration of microbial membrane perviousness due to NP accumulation will release proteins, LPs, and biomolecules; (2) the release of reactive oxygen species via nanoparticles, inducing oxidative damage to cells; and (3) NPs undergo metabolism by the microbes, resulting in a decline of intracellular NP concentration (Rowe et al., 2020).

Table 1: List of nanoparticles with different biomedical activities.

Sr. no	Nanoparticles	Effect	References
1	ZnO-Nps	Antibacterial	(Asif et al., 2023)
		Anti-inflammatory	(Zahoor et al., 2023)
		Antioxidant	(Vera et al., 2023)
2	Cu-Nps	Antibacterial	(Ma et al., 2022)
		Anti-inflammatory	(Ma et al., 2022)
		Antioxidant	(Ssekatawa et al., 2022)
3	MgO-Nps	Antibacterial	(Rodríguez-Hernández et al., 2023)
		Anti-inflammatory	(Behera et al., 2021)
		Antioxidant	(Shahid et al., 2022)
4	Ag-Nps	Antibacterial	(Palau et al., 2023)
		Anti-inflammatory	(Xu et al., 2023)
		Antioxidant	(Zhang et al., 2022)

Nanoparticles as Antimicrobial Agents

NPs have antimicrobial capabilities that can go through typical resistance mechanisms, such enzyme inactivation, reduced cell permeability, alteration of target sites/enzymes, and enhanced efflux by overexpression of efflux pumps (Baptista et al., 2018). Additionally, Antibiotics and NPs have been used in combination to combat MDROs and have synergistic effects against bacteria that result in the production of biofilms (Pelgrift and Friedman, 2013). Complex antibacterial mechanisms are provided by the combinations of NPs and antibiotic compounds to combat antibiotic resistance (Gupta et al., 2017).

Therefore, NPs are thought of as next-generation antibiotics. NPs, primarily metallic, have demonstrated effectiveness against bacteria in investigations conducted both in vitro and in vivo (Zazo et al., 2016).

NPs which have antibacterial action against a number of bacteria species including E. faecium, St. aureus, K. pneumoniae, A. baumannii, P. aeruginosa, and Enterobacter species (Beyth et al., 2015) comprise of NPs containing Silver, Gold, Yttrium, Cadmium, Aluminum, Selenium, Zinc, Copper, Titanium, Magnesium, Nickel, Cerium, or Iron (Hemeg, 2017). Cell membrane structure can be adversely affected by nanoparticles, resulting in changes to permeability and surface loading. Reactive oxygen species (ROS) generation is most likely the most prevalent way that nanoparticles affect bacteria (Karwowska, 2017). The following figure provides a summary of the molecular pathways underlying the antibacterial action of nanomaterials (Fig: 1).

Zinc oxide Nanoparticles

Utilizing nanoparticles made of metals and their oxides is highly significant. Both zinc (Zn) and zinc oxide (ZnO), two thoroughly studied metals, have an effect on living things. Zinc is an active element because it has strong reduction properties. Zinc oxide is easily produced when it is oxidized. The human body needs zinc since it is one of the important trace elements (Maret, 2011). Zinc is present in all human body tissues, although myocytes contain the most of it (85% of the body's total zinc concentration) (Król et al., 2017). It has been proven that zinc is required for the correct operation of a considerable number of biomolecules and coenzyme. As a result, zinc finger structures offer a special framework that enables protein domains to interact with DNA or other proteins (Klug and Rhodes, 1987). Zinc is necessary for the normal operation of metalloproteins. Even while it is generally accepted that free zinc ions are not hazardous, there is growing evidence to suggest that these ions may be harmful to cells. Usually, animal cell cultures are used to assess a test chemical's in vitro toxicity. Nerve cells are thought to be the cells most susceptible to outside influences (Timashev et al., 2016). Neuronal degradation is an evident side effect that is seen in individuals that have been exposed to zinc ions

(Sindhu et al., 2022). Zinc cations are attached to bioactive ligands (such as proteins) and zinc NPs are produced in order to reduce the cytotoxic impact of zinc ions. Nanostructured ZnO can have a wide range of morphological characteristics. There are numerous uses for ZnO in both engineering and medicine (Beek et al., 2004). ZnO is a biosafe substance with a variety of uses, such as photo-oxidizing and photocatalysis effects on biological and chemical species (Khater et al., 2020). Numerous studies have demonstrated that zinc oxide nanoparticles (ZnONPs) work against both gram positive and negative bacteria with their antimicrobial properties. ZnONPs are also thought to be excellent candidates for transporting pharmaceutically active compounds (Abebe et al., 2020). Cell migration, angiogenesis and re-epithelization can all be induced by ZnO NPs. These qualities are all very important for wound healing (Khan et al., 2021). ZnO nanoparticles exerts antibacterial effect by producing reactive oxygen species (ROS) like H2O2 or by producing Zinc ion (Zn^{2+}) or by the direct contact of nanoparticles with the bacterial cell membrane (Fig:1) (Ijaz et al., 2020).

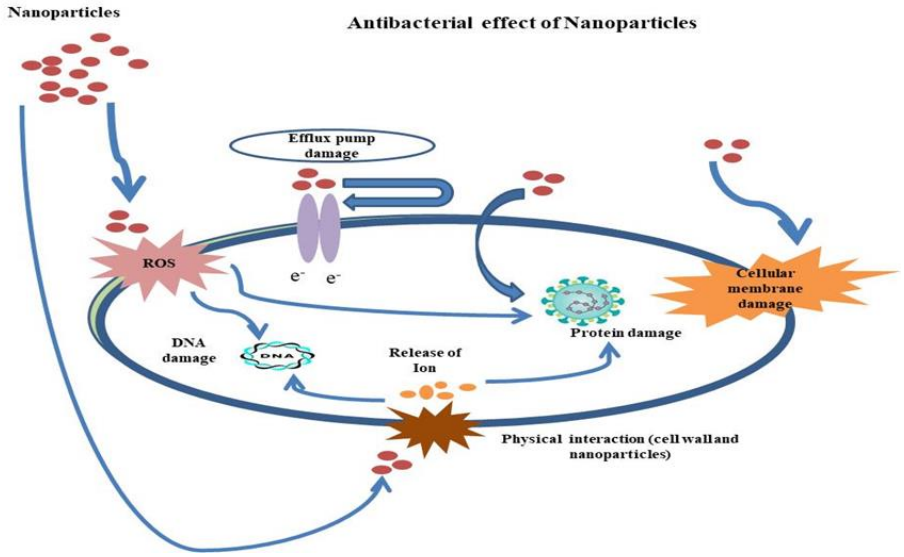

Fig. 1: Mechanism of action of antibacterial effect of nanoparticles

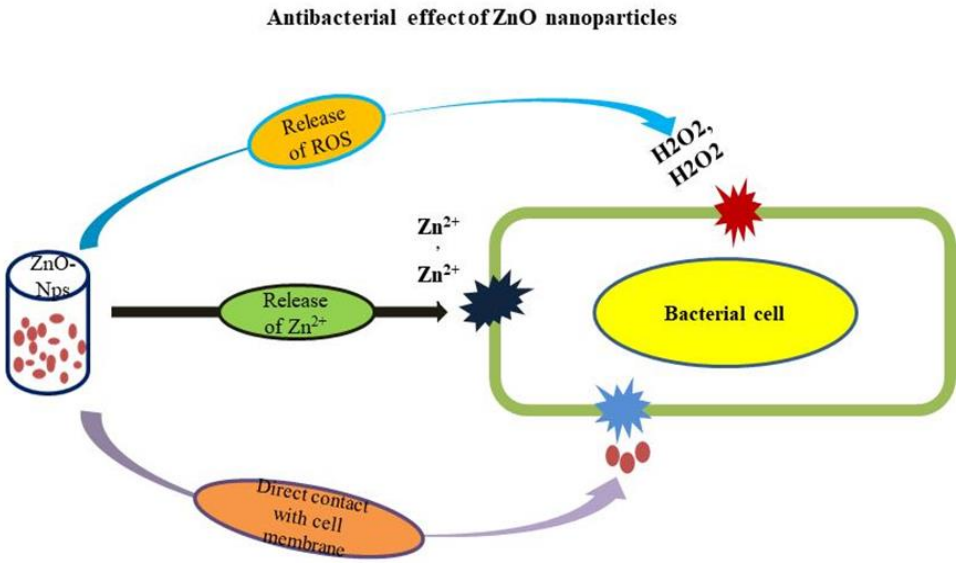

Fig. 2: Antibacterial effect of ZnO nanoparticles (ZnO-Nps)

Sliver Nanoparticles

Silver is employed in medical applications more frequently than other metals including gold, copper, iron, titanium, and zinc because of its inherent antibacterial properties. There is proof that plant-derived silver nanoparticles, which are typically present in secondary metabolites, have an innate capacity to inhibit antibiotic-resistant bacteria and foodborne pathogens (Jain and Mehata, 2017). (Morones et al., 2005) recommended that the changes made by the silver nanoparticles to the bacteria's membrane shape may have contributed to the amount of AgNPs found on and inside the bacteria. Phosphorus and Sulphur are components of the machinery found in bacterial cells. Acidic silver encourages the collapse of the pathogen's respiratory and replication framework, resulting in cell death, by forming sulphydryl groups (S-H), which are found in bacterial proteins and DNA in the cellular matrix. Proteomic analysis of silver-regulated membrane proteins in P. aeruginosa exposed to silver nitrate and silver NPs revealed that the silver binding proteins for silver NPs and Silver ions had a similar pattern, but in cells exposed to silver NPs, it was discovered that the bio-uptake of silver ions and the formation of reactive oxygen species were both increased (Chinnasamy et al., 2021). Previous research have

demonstrated that silver has pro-healing qualities that not only serve as an antibacterial agent but also hasten healing process and recovery (Seo et al., 2017). Studies show that silver nanoparticles can speed up the wound healing process by lowering inflammation and reducing the presence of scars (Liu et al., 2010). The mechanical function of the skin that has been treated with silver nanoparticles is found to be similar to that of regular skin (Kwan et al., 2011).

CU Nanoparticles

Traditional inorganic antibacterial substances include copper-containing compounds like CuSO4 and Cu(OH)2 (Hughes and Poole, 1989). Because there are more carboxylic groups than necessary in the lipoproteins at the bacterial surface, when these groups dissociate, the bacterial surface becomes negatively charged, giving bacteria a general negative charge at biological pH levels (Stoimenov et al., 2002). Due to their opposite charges, electrostatic forces are thought to be the cause of the adherence and bioactivity between bacteria and the copper ions created by nanoparticles. Peptidoglycans, which are negatively charged molecules, bind the Cu2+ ions that copper nanoparticles discharge into the liquid growth medium. Gram-negative bacteria, such as E. coli, may let more Cu2+ ions to permeate the plasma membrane as opposed to Gram-positive bacteria, although these latter are often believed to be comparatively sensitive to antibiotics (Koch, 1990). The antibacterial action of copper nanoparticles has been linked to Cu2+ ions that are released from copper nanoparticles and taken up by bacteria at high concentrations. Copper ions, which affect the cell membrane by altering protein structure or altering enzyme function, are exposed to the bacterial cell surface (Dan et al., 2005). Due to its angiogenesis, regeneration, and antibacterial capabilities, wound dressings containing copper oxide accelerate wound healing. (Salvo and Sandoval, 2022). Copper (Cu), one of the bioactive NPs, has a complicated role in a variety of cells, affects a number of cytokines' and growth factors' modes of action, and is fundamentally engaged in every stage of the healing process. (Kornblatt et al., 2016).

Mg Nanoparticles

Increasing research has been done on a novel class of antimicrobial agents called metal oxide nanoparticles, such as MgO, for its potential use in food, the environment, and medicine. (Dizaj et al., 2014). The impact of metal oxide nanoparticles on bacteria involves a complex and incompletely understood process. Reactive oxygen species (ROS), which lead to bacterial lipid peroxidation, are said to be responsible for the antibacterial activities of MgO nanoparticles (Scallan et al., 2011). MgO nanoparticles, however, also exhibited non-ROS driven bacterial toxicity, indicating that oxidative stress may not be the main cause of cell death. (Leung et al., 2014). Due to its promising mechanical and biological qualities, magnesium and magnesium alloys have received more and more attention as bioresorbable metals for orthopedic applications in recent years. (Cipriano et al., 2017). Mg is biodegradable and biocompatible (Trumbo et al., 2002). Mg-based implants do not demand further procedures for implant removal, in contrast to typical nondegradable metals. (Song et al., 2019). For load-bearing implants, magnesium and magnesium alloys are preferable over ceramics due to their higher elastic modulus, strength, and fracture toughness (Geetha et al., 2009). Escherichia coli and Staphylococcus aureus were only two of the bacteria that magnesium oxide (MgO) nanoparticles shown antibacterial capabilities against in vitro *(Nguyen et al., 2018)*.

Nanoparticles as Anti-parasitic Drugs

Nanotechnology is currently being widely used in a number of scientific fields. In particular, nanoparticles (NPs) are used in both *in-vitro* and *in-vivo* studies on parasites and used as anti-parasitic drugs (H. U. R. Bajwa et al., 2022). Particles created in various forms and sizes, ranging roughly from 1 to 100 nanometers, are called nanoparticles (NPs). The use of materials and systems at the atomic scale in nanotechnology is expected to create new avenues for the control and destruction of germs. Nanotechnology is an emerging field. Millions of individuals are afflicted with parasitic infections globally, particularly in developing nations, and there are numerous treatment options that are restricted. Drug resistance has recently been shown by several parasites, which has raised the need for safer, more effective treatments or for developing new medications to prevent parasitic infections. Chemotherapy is currently the basis of control because there is no vaccination available to prevent many parasite diseases. Since current anti-parasitic medications have some negative effects and their usefulness is still being investigated, NPs have drawn the most attention as anti-parasitic drugs in the last few decades. Nevertheless, the application of derivatives of nanoparticles as an anti-parasitic medication has received minimal attention. Antiparasitic effects of nanoparticles are given id fallowing table (Table: 2).

Table 2: Antiparasitic effect of different nanoparticles

Sr. no	Nanoparticles	Effect	References
1	ZnO-Nps	Anti-Parasitic against Protozoon (*Giardiasis*)	(Anah et al., 2022)
		Leishmaniosis	(Norouzi, 2017)
		Toxoplasmosis	
2	Au-Nps	*Leishmaniosis*	
		Echinococcus multilocularis	(Raj et al., 2022)
		Trichinella spiralis	
3	Antimony sulfide	*Leishmaniosis*	

		Giardiasis	(Mohtasebi et al., 2019)
4	Ag-Nps	*Cryptosporidiosis*	
		Toxoplasmosis	(Zhang et al., 2023)
		Flukes	

Different Types of Nanoparticles against Different Parasitic Diseases

As Research has shown that various substances, such as oxidized metals, silver, chitosan, and gold nanoparticles, can inhibit the growth of various parasites, such as Giardia, Leishmania, Plasmodium, and Toxoplasma, as well as helminthes, such as Echinococcus multilocularis, Trichinella spiralis, and Fasciola hepatica. NPs can be used either alone or in conjunction with existing medications to treat parasites. As a result, NPs are recommended as more potent medications with less adverse effects for the prevention and management of parasites (Norouzi, 2017). Generally nanoparticles works in different ways, that include damaging the parasite membrane, DNA (Deoxyribonucleic acid) disruption, protein synthesis inhibition and free-radical formation (Fig: 3) (H. U. Bajwa et al., 2022).

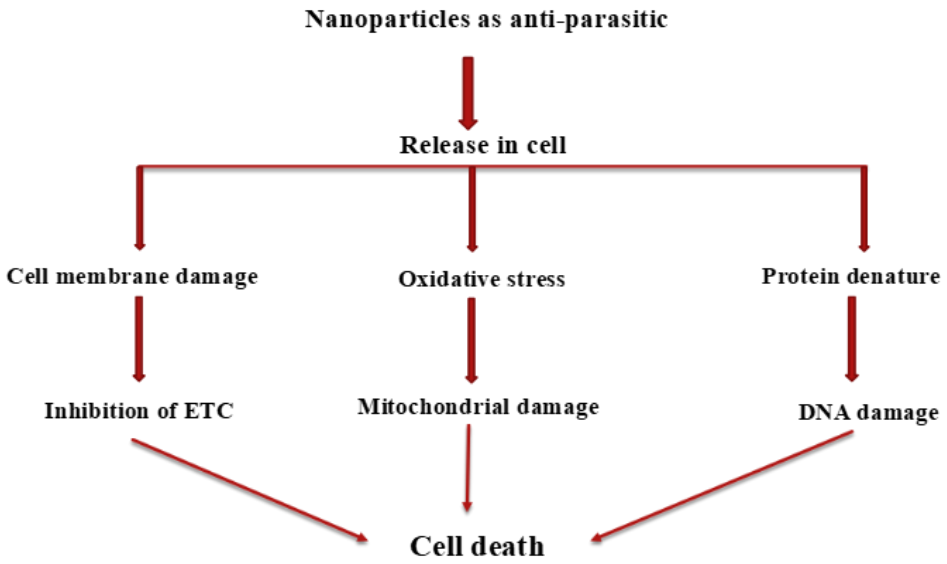

Fig. 3: Antiparasitic effect of nanoparticles

Helminths, ectoparasites, and protozoa are the three primary types of parasites found across the world. These days, anti-helminthic, anti-ectoparasitic, and chemotherapeutic antiprotozoal drugs are utilized to treat these parasites; however, the side effects of these drugs have caused drug resistance over time. In this regard, it is demonstrated that the use of nanoparticles has significantly improved the diagnosis, treatment, and management of parasite diseases. Over the past ten years, significant progress has been made in the field of Nano medicine for the control of parasites. When using gold and silver nanoparticles to treat various parasitic infections, promising results have been seen. Numerous traditional and molecular technologies are used to produce these incredibly powerful nanoparticles. They tear down the parasite membrane, interfere with the synthesis of proteins, damage DNA (deoxyribonucleic acid), and produce free radicals, among other things. These compounds are also effective against parasites that live inside cells. Other nanoparticles, such as those composed of iron, nickel, zinc, and platinum, have also shown promise in the management and treatment of parasitic illnesses. It is anticipated that research in this field will progress the creation of modern drugs (H. U. R. Bajwa et al., 2022).

The primary motivation for these studies is their potential for use in the treatment of various parasitic diseases. Utilizing microorganisms as distinct biofactories, a novel biotechnology approach has made it easier to produce targeted nanoparticles. Biofactories and Biosynthetic methods have been used to create applications such as magnetite iron oxide NPs, silver (Ag), gold (Au), selenium (Se), cadmium-sulfide and sulfoxide, due to their specific properties, rapid synthesis, and regulated toxicity, biogenic synthesized nanoparticles are considered environmentally friendly (Kandeel et al., 2022).

Nano-medicine against Parasitic Disease

The Nano-medicine effectively treats parasites and removed these barriers to the advancement of animal husbandry and health; but, due to their short half-lives and insolubility, which lowers their bioavailability, these medications need to be given often. The advantages of anti-parasitic drugs are increased when these obstacles are removed by using nano-medicines (Sun et al., 2019). Nano-medicine uses nanoparticles to control, monitor, detect, halt, and treat infectious parasitic diseases (Gutiérrez et al., 2016). Under UV light, ZnO NPs show photocatalytic activity. Their anti-parasitic efficacy can be increased by taking use of this characteristic. ZnO NPs produce reactive oxygen species (ROS) when illuminated, which cytotoxically affects parasites and increases their potential for therapeutic use.

Depending on the medication's characteristics and the stage of the illness, it may be administered intravenously, topically, orally, or by other methods. When these drugs enter the body, their delusion and disruption occur. Depending

on the medication's characteristics and the stage of the illness, it may be given intravenously, topically, orally, intra-gastrically, or by other methods. Research has shown that nano-medicine effectively treats parasites. All three types of nanoparticles—organic, inorganic, and polymer-based—show potential for both *in-vivo* and *in-vitro* applications. Numerous different types of nanoparticles are available to treat parasite illnesses.

Antimony sulfide nanoparticles effect both *in-vitro* and *in-vivo* against Leishmaniosis

Biological antimony sulfide NPs have been successfully synthesized in *S. marcescens* and have demonstrated antibacterial efficacy against Escherichia coli and Staphylococcus aureus. Furthermore, studies have demonstrated that antimony sulfide nanoparticles have cytotoxic and parasiticidal effects on protozoan parasites such as *L. infantum*. Even though the chemical synthesis of antimony sulfide NPs has been reported in literature. In recent years, there has been a lot of interest in the use of inorganic nanoparticles in various industrial and therapeutic items. Inorganic nanoparticles (NPs) have become increasingly prevalent in a wide range of commercial and medicinal products. Examples include microelectronic devices, lubricants, catalysts, and antimicrobials. To the best of the author's knowledge, no studies on *L. major* have been published that examine the effects of biogenic antimony sulfide nanoparticles both *in-vitro* and *in-vivo* (Mohtasebi et al., 2019). An increasing amount of study is being conducted on nanoparticles for anti-parasitic drugs can be made from a variety of nanoparticle types and applications. The following is a list of potential applications for nanoparticles as anti-parasitic drugs uses for anti-parasitic nanoparticles in pharmaceutical formulations. The drugs on this list minimize the application of nanoparticles as agents that fight parasites. It is possible to create nanoparticles that specifically target parasites with the least amount of harm to healthy cells. Therapy efficacy is increased and side effects are reduced by this targeted delivery. Medicines in nanoparticle form may be more bioavailable, allowing them to enter the infected area more effectively. This is particularly beneficial for parasite infections that are difficult to treat due to inadequate medication distribution.

Sustained Release

Medicines can be liberated from nanoparticles in a way that maintains therapeutic concentrations steadily over time. When treating chronic parasite infections, this is beneficial counselling.

Protection of Substance Molecules from Breakdown

Drug molecules can be protected from the body's breakdown by nanoparticles, which extends their half-life and ensures their efficacy until they reach their intended target.

Combination Counselling

Combination therapy can target multiple stages of the parasite's life cycle or target drug-resistant parasites since a variety of drugs or therapeutic ingredients can be incorporated into nanoparticles. Attacks by parasites can be fatal for both people and animals. Since parasite infections don't often have obvious signs, they can be more fatal than bacterial infections because they're harder to identify and cure. On the other hand, parasite infections could not show any obvious signs, which makes them difficult to diagnose and treat. This is due to the fact that bacterial illnesses usually exhibit unique symptoms. Trypanosomiasis, malaria, and leishmaniosis are among the infectious parasite diseases that have significant fatality rates in developing countries (Wang et al., 2017). Human malaria is caused by four different species of Plasmodium, with Plasmodium falciparum having the highest global fatality rate (Barnes and White, 2005). Twelve million people were afflicted with leishmaniosis, of which 1-2 million had cutaneous cases and 0.5 million visceral cases. Their infections have become global health concerns due to resistant parasite strains. The anti-parasitic drugs have to be administered constantly due to their short half-life and insolubility, which lowers their bioavailability. However, they are essential for the advancement of animal husbandry and the safety of animal health.

Zinc Oxide Nanoparticle as Anti-parasitic Drug

It has been demonstrated that ZnO NPs naturally contain anti-parasitic qualities. When they interact with parasites, they may damage their membranes, obstruct their metabolic activities, and finally cause them to perish. They are potential candidates to fight different parasite illnesses because of their direct activity (do Carmo Neto et al., 2022). Nanomaterials can be used to treat a wide range of illnesses that affect both human and animal health. Primarily, these materials are employed to tackle the problem of pathogenic organisms becoming resistant to conventional drugs. One thoroughly investigated example of a potential component for biomedical applications is zinc oxide (ZnO) nanoparticles (NPs). Its anti-parasitic effect is intimately associated with its capacity to generate or induce ROS that affect the pathogen's homeostasis. Prior exposure to helminths and protozoa, which are detrimental to both human health and animal productivity, resulted in this type of nanoparticle. Zinc oxide nanoparticles are effective to treat the protozoal diseases (Anah et al., 2022).

Gold Nanoparticle as Anti-parasitic Drugs

It has been demonstrated that AuNPs have anti-parasitic activity against a variety of parasites, such as helminths and protozoa. They have the potential to cause oxidative stress, damage cellular structures, and interfere with parasite metabolism, all of which can result in parasite mortality. Antibodies or ligands that specifically target receptors or antigens on the surface of parasites can be used to functionalize AuNPs. By improving AuNP accumulation at the infection site, this

focused delivery maximizes its effectiveness while reducing off-target impacts on host cells.

It has been demonstrated recently that CHY quickly neutralizes Leishmania by targeting the parasite's MAP kinase 3 enzyme. However, the use of CHY is restricted due to problems with quick excretion, limited absorption, and low bioavailability. In this work, a new CHY-gold nanoformulation with enhanced efficacy against the parasites was created and tested. Gold nanoparticles were reduced and conjugated using CHY's reducing power. In mammalian macrophages, conjugated CHY and gold nanoparticles—which are already well-known for their anti-leishmanial qualities—showed a reduced parasite load (Raj et al., 2022).

Silver Nanoparticle as Anti-parasitic Drugs

The potential of nanoparticles of silver (AgNPs) as anti-parasitic medicines attracts attention owing to their particular features and methods of action. AgNPs have been effective against a variety of parasites, such as helminths, ectoparasites, and protozoa. They have the ability to interfere with several phases of the parasite life cycle, such as metabolism, growth, and replication. AgNPs have the ability to interact with parasite cell membranes, causing permeabilization and structural damage. This damage weakens the integrity of the membrane, which allows cell contents to seep out and ultimately results in cell death.

AgNPs, or silver nanoparticles, are extremely small silver particles that range in size from one to one hundred nanometers. They have distinct chemical and physical characteristics, in contrast to bulk silver. AgNPs have been demonstrated in numerous studies to have positive biological effects on a range of disorders, including antioxidant, antibacterial, anti-inflammatory, and antiparasitic ones. AgNPs are a promising contender for antibacterial drugs because to their tremendous ability to eradicate germs that are resistant to several drugs. This is one of their most well-known uses in the field of antibacterial applications. In comparison to conventional antiparasitic medications, AgNPs produced from plant extracts have demonstrated exceptional antiparasitic activities, including a reduced half-life and improved capacity to impede parasite multiplication. The types, traits, and mode of action of AgNPs in anti-parasitism, with a particular emphasis on their impact on *leishmaniasis, flukes*, *cryptosporidiosis*, *toxoplasmosis*, *Haemonchus*, *Blastocystis hominis*, and *Strongylides*. The purpose is to offer a resource for the use of AgNPs in the management and prevention of parasitic infections (Zhang et al., 2023).

REFERENCES

Abebe, B., Zereffa, E. A., Tadesse, A., and Murthy, H. A. (2020). A review on enhancing the antibacterial activity of ZnO: Mechanisms and microscopic investigation. *Nanoscale Research Letters*, *15*, 1-19.

Anah, S. A., Anah, S. A., and Al-Khalidy, K. A. H. J. K. J. V. R. (2022). Anti-parasitic activity of zinc oxide nanoparticles against Eimeria tenella in broilers experimentally infected. *62*(4), e30.

Asif, M., Chaudhry, A. S., Ashar, A., Rashid, H. B., Saleem, M. H., Aslam, H. B., and Aziz, A. (2023). Zinc oxide nanoparticles accelerate the healing of methicillin-resistant Staphylococcus aureus (MRSA)-infected wounds in rabbits. *Asian Pacific Journal of Tropical Biomedicine*, *13*(11), 488-496. https://doi.org/10.4103/2221-1691.389574

Bajwa, H. U., Khan, M. K., Abbas, Z., Riaz, R., Rehman, T. U., Abbas, R. Z., Aleem, M. T., Abbas, A., Almutairi, M. M., Alshammari, F. A., Alraey, Y., and Alouffi, A. (2022). Nanoparticles: Synthesis and Their Role as Potential Drug Candidates for the Treatment of Parasitic Diseases. *Life*, *12*(5).

Bajwa, H. U. R., Khan, M. K., Abbas, Z., Riaz, R., Rehman, T. u., Abbas, R. Z., Aleem, M. T., Abbas, A., Almutairi, M. M., and Alshammari, F. A. J. L. (2022). Nanoparticles: Synthesis and their role as potential drug candidates for the treatment of parasitic diseases. *12*(5), 750.

Baptista, P. V., McCusker, M. P., Carvalho, A., Ferreira, D. A., Mohan, N. M., Martins, M., and Fernandes, A. R. (2018). Nano-strategies to fight multidrug resistant bacteria—"A Battle of the Titans". *Frontiers in Microbiology*, *9*, 1441.

Barnes, K. I., and White, N. J. J. A. t. (2005). Population biology and antimalarial resistance: The transmission of antimalarial drug resistance in Plasmodium falciparum. *94*(3), 230-240.

Beek, W. J., Wienk, M. M., and Janssen, R. A. (2004). Efficient hybrid solar cells from zinc oxide nanoparticles and a conjugated polymer. *Advanced Materials*, *16*(12), 1009-1013.

Behera, K., Nasim, I., and Rajesh Kumar, S. (2021). Antioxidant and anti inflammatory activity of magnesium oxide nanoparticles-an in vitro study. *International Journal Dent Oral Science*, *8*(5), 2913-2917.

Beyth, N., Houri-Haddad, Y., Domb, A., Khan, W., and Hazan, R. (2015). Alternative antimicrobial approach: nano-antimicrobial materials. *Evidence-based Complementary and Alternative Medicine*, *2015*.

Bhullar, K., Waglechner, N., Pawlowski, A., Koteva, K., Banks, E. D., Johnston, M. D., Barton, H. A., and Wright, G. D. (2012). Antibiotic resistance is prevalent in an isolated cave microbiome. *PLoS One*, *7*(4), e34953.

Călina, D., Docea, A. O., Rosu, L., Zlatian, O., Rosu, A. F., Anghelina, F., Rogoveanu, O., Arsene, A. L., Nicolae, A. C., and Drăgoi, C. M. (2017). Antimicrobial resistance development following surgical site infections. *Molecular Medicine Reports*, *15*(2), 681-688.

Chakraborty, N., Jha, D., Roy, I., Kumar, P., Gaurav, S. S., Marimuthu, K., Ng, O.-T., Lakshminarayanan, R., Verma, N. K., and Gautam, H. K. (2022). Nanobiotics against antimicrobial resistance: harnessing the power of nanoscale materials and technologies. *Journal of Nanobiotechnology*, *20*(1), 375. https://doi.org/10.1186/s12951-022-01573-9

Chambers, H. F., and DeLeo, F. R. (2009). Waves of resistance: Staphylococcus aureus in the antibiotic era. *Nature Reviews Microbiology*, *7*(9), 629-641.

Chinnasamy, G., Chandrasekharan, S., Koh, T. W., and Bhatnagar, S. (2021). Synthesis, characterization, antibacterial and wound healing efficacy of silver nanoparticles from Azadirachta indica. *Frontiers in Microbiology*, *12*, 611560.

Cipriano, A. F., Lin, J., Lin, A., Sallee, A., Le, B., Cortez Alcaraz, M. C., Guan, R.-G., Botimer, G., Inceoğlu, S., and Liu, H. (2017). Degradation of bioresorbable Mg–4Zn–1Sr intramedullary pins and associated biological responses in vitro and in vivo. *ACS Applied Materials and Interfaces*, *9*(51), 44332-44355.

Dan, Z., Ni, H., Xu, B., Xiong, J., and Xiong, P. (2005). Microstructure and antibacterial properties of AISI 420 stainless steel implanted by copper ions. *Thin Solid Films*, *492*(1-2), 93-100.

Dizaj, S. M., Lotfipour, F., Barzegar-Jalali, M., Zarrintan, M. H., and Adibkia, K. (2014). Antimicrobial activity of the metals and metal oxide nanoparticles. *Materials Science and Engineering: C*, *44*, 278-284.

do Carmo Neto, J. R., Guerra, R. O., Machado, J. R., Silva, A. C., and da Silva, M. V. J. C. M. C. (2022). Antiprotozoal and anthelmintic activity of zinc oxide Nanoparticles. *29*(12), 2127-2141.

Dulon, M., Haamann, F., Peters, C., Schablon, A., and Nienhaus, A. (2011). MRSA prevalence in European healthcare settings: a review. *BMC Infectious Diseases*, *11*, 1-13.

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Faoagali, J., Thong, M., and Grant, D. (1992). Ten years' experience with methicillin-resistant Staphylococcus aureus in a large Australian hospital. *Journal of Hospital Infection*, *20*(2), 113-119.

Filius, P. M. G., and Gyssens, I. C. (2002). Impact of Increasing Antimicrobial Resistance on Wound Management. *American Journal of Clinical Dermatology*, *3*(1), 1-7. https://doi.org/10.2165/00128071-200203010-00001

Geetha, M., Singh, A. K., Asokamani, R., and Gogia, A. K. (2009). Ti based biomaterials, the ultimate choice for orthopaedic implants–A review. *Progress in Materials Science*, *54*(3), 397-425.

Golkar, Z., Bagasra, O., and Pace, D. G. (2014). Bacteriophage therapy: a potential solution for the antibiotic resistance crisis. *The Journal of Infection in Developing Countries*, *8*(02), 129-136.

Gould, I. M., and Bal, A. M. (2013). New antibiotic agents in the pipeline and how they can help overcome microbial resistance. *Virulence*, *4*(2), 185-191.

Gupta, A., Saleh, N. M., Das, R., Landis, R. F., Bigdeli, A., Motamedchaboki, K., Campos, A. R., Pomeroy, K., Mahmoudi, M., and Rotello, V. M. (2017). Synergistic antimicrobial therapy using nanoparticles and antibiotics for the treatment of multidrug-resistant bacterial infection. *Nano Futures*, *1*(1), 015004.

Gutiérrez, V., Seabra, A. B., Reguera, R. M., Khandare, J., and Calderón, M. J. C. S. R. (2016). New approaches from nanomedicine for treating leishmaniasis. *45*(1), 152-168.

Han, G., and Ceilley, R. (2017). Chronic wound healing: a review of current management and treatments. *Advances in Therapy*, *34*, 599-610.

Hemeg, H. A. (2017). Nanomaterials for alternative antibacterial therapy. *International Journal of Nanomedicine*, 8211-8225.

Hughes, M. N., and Poole, R. K. (1989). Metals and Micro-organisms.

Ijaz, M., Zafar, M., Islam, A., Afsheen, S., and Iqbal, T. (2020). A review on antibacterial properties of biologically synthesized zinc oxide nanostructures. *Journal of Inorganic and Organometallic Polymers and Materials*, *30*, 2815-2826.

Jain, S., and Mehata, M. S. (2017). Medicinal plant leaf extract and pure flavonoid mediated green synthesis of silver nanoparticles and their enhanced antibacterial property. *Scientific Reports*, *7*(1), 15867.

Jevons, M. P. (1961). "Celbenin"-resistant staphylococci. *British medical journal*, *1*(5219), 124.

Kandeel, M., Akhtar, T., Zaheer, T., Ahmad, S., Ashraf, U., and Omar, M. J. P. V. J. (2022). Anti-parasitic Applications of Nanoparticles: A Review. *42*(2).

Karwowska, E. (2017). Antibacterial potential of nanocomposite-based materials – a short review. *Nanotechnology Reviews*, *6*(2), 243-254. https://doi.org/doi:10.1515/ntrev-2016-0046

Khan, A. u. R., Huang, K., Jinzhong, Z., Zhu, T., Morsi, Y., Aldalbahi, A., El-Newehy, M., Yan, X., and Mo, X. (2021). Exploration of the antibacterial and wound healing potential of a PLGA/silk fibroin based electrospun membrane loaded with zinc oxide nanoparticles [10.1039/D0TB02822C]. *Journal of Materials Chemistry B*, *9*(5), 1452-1465. https://doi.org/10.1039/D0TB02822C

Khater, M., Khater, S. S., Gholap, H., Patil, R., and Kulkarni, G. (2020). Comparative studies on measurement of membrane potential of bacterial cells treated with ZnO nanoparticles by spectrofluorometry, fluorescence microscopy and flowcytometry. *Journal of Microbiological Methods*, *173*, 105920.

Kirketerp-Møller, K., Jensen, P. Ø., Fazli, M., Madsen, K. G., Pedersen, J., Moser, C., Tolker-Nielsen, T., Høiby, N., Givskov, M., and Bjarnsholt, T. (2008). Distribution, organization, and ecology of bacteria in chronic wounds. *Journal of Clinical Microbiology*, *46*(8), 2717-2722.

Klug, A., and Rhodes, D. (1987). Zinc fingers: a novel protein fold for nucleic acid recognition. Cold Spring Harbor symposia on quantitative biology,

Koch, A. L. (1990). Growth and form of the bacterial cell wall. *American Scientist*, *78*(4), 327-341.

Kornblatt, A. P., Nicoletti, V. G., and Travaglia, A. (2016). The neglected role of copper ions in wound healing. *Journal of Inorganic Biochemistry*, *161*, 1-8.

Król, A., Pomastowski, P., Rafińska, K., Railean-Plugaru, V., and Buszewski, B. (2017). Zinc oxide nanoparticles: Synthesis,

antiseptic activity and toxicity mechanism. *Advances in Colloid and Interface Science*, *249*, 37-52.

Kwan, K. H., Liu, X., To, M. K., Yeung, K. W., Ho, C.-m., and Wong, K. K. (2011). Modulation of collagen alignment by silver nanoparticles results in better mechanical properties in wound healing. *Nanomedicine: Nanotechnology, Biology and Medicine*, *7*(4), 497-504.

Larsson, D. G. J., and Flach, C.-F. (2022). Antibiotic resistance in the environment. *Nature Reviews Microbiology*, *20*(5), 257-269. https://doi.org/10.1038/s41579-021-00649-x

Lee, A. S., de Lencastre, H., Garau, J., Kluytmans, J., Malhotra-Kumar, S., Peschel, A., and Harbarth, S. (2018). Methicillin-resistant Staphylococcus aureus. *Nature Reviews Disease Primers*, *4*(1), 18033. https://doi.org/10.1038/nrdp.2018.33

Lee, N.-Y., Ko, W.-C., and Hsueh, P.-R. (2019). Nanoparticles in the treatment of infections caused by multidrug-resistant organisms. *Frontiers in Pharmacology*, *10*, 1153.

Leung, Y. H., Ng, A. M., Xu, X., Shen, Z., Gethings, L. A., Wong, M. T., Chan, C. M., Guo, M. Y., Ng, Y. H., and Djurišić, A. B. (2014). Mechanisms of antibacterial activity of MgO: non-ROS mediated toxicity of MgO nanoparticles towards Escherichia coli. *Small*, *10*(6), 1171-1183.

Liu, X., Lee, P. y., Ho, C. m., Lui, V. C., Chen, Y., Che, C. m., Tam, P. K., and Wong, K. K. (2010). Silver nanoparticles mediate differential responses in keratinocytes and fibroblasts during skin wound healing. *ChemMedChem*, *5*(3), 468-475.

Ma, X., Zhou, S., Xu, X., and Du, Q. (2022). Copper-containing nanoparticles: Mechanism of antimicrobial effect and application in dentistry-a narrative review. *Front Surg*, *9*, 905892. https://doi.org/10.3389/fsurg.2022.905892

Maret, W. (2011). Metals on the move: zinc ions in cellular regulation and in the coordination dynamics of zinc proteins. *Biometals*, *24*, 411-418.

Mirzahosseinipour, M., Khorsandi, K., Hosseinzadeh, R., Ghazaeian, M., and Shahidi, F. K. (2020). Antimicrobial photodynamic and wound healing activity of curcumin encapsulated in silica nanoparticles. *Photodiagnosis and Photodynamic Therapy*, *29*, 101639.

Mohtasebi, S., Mohebali, M., Elikaee, S., Akhoundi, B., Foroushani, A. R., Teimouri, A., and Yarizadeh, H. J. P. r. (2019). In vitro and in vivo anti-parasitic activity of biogenic antimony sulfide nanoparticles on Leishmania major (MRHO/IR/75/ER). *118*, 2669-2678.

Morones, J. R., Elechiguerra, J. L., Camacho, A., Holt, K., Kouri, J. B., Ramírez, J. T., and Yacaman, M. J. (2005). The bactericidal effect of silver nanoparticles. *Nanotechnology*, *16*(10), 2346.

Nguyen, N.-Y. T., Grelling, N., Wetteland, C. L., Rosario, R., and Liu, H. (2018). Antimicrobial activities and mechanisms of magnesium oxide nanoparticles (nMgO) against pathogenic bacteria, yeasts, and biofilms. *Scientific Reports*, *8*(1), 16260.

Norouzi, R. J. J. B. T. s. W. (2017). A review on most nanoparticles applied against parasitic infections. *6*(10), 196-203.

Organization, W. H. (2001). *WHO global strategy for containment of antimicrobial resistance*.

Organization, W. H. (2012). *The evolving threat of antimicrobial resistance: options for action*. World Health Organization.

Organization, W. H. (2014). *Antimicrobial resistance: global report on surveillance*. World Health Organization.

Palau, M., Muñoz, E., Gusta, M. F., Larrosa, N., Gomis, X., Gilabert, J., Almirante, B., Puntes, V., Texidó, R., and Gavaldà, J. (2023). In Vitro Antibacterial Activity of Silver Nanoparticles Conjugated with Amikacin and Combined with Hyperthermia against Drug-Resistant and Biofilm-Producing Strains. *Microbiology Spectrum*, *11*(3), e00280-00223. https://doi.org/doi:10.1128/spectrum.00280-23

Pelgrift, R. Y., and Friedman, A. J. (2013). Nanotechnology as a therapeutic tool to combat microbial resistance. *Advanced Drug Delivery Reviews*, *65*(13-14), 1803-1815.

Piddock, L. J. (2012). The crisis of no new antibiotics—what is the way forward? *The Lancet infectious diseases*, *12*(3), 249-253.

Prestinaci, F., Pezzotti, P., and Pantosti, A. (2015). Antimicrobial resistance: a global multifaceted phenomenon. *Pathog Glob Health*, *109*(7), 309-318. https://doi.org/10.1179/2047773215y.0000000030

Rahim, K., Saleha, S., Zhu, X., Huo, L., Basit, A., and Franco, O. L. (2017). Bacterial contribution in chronicity of wounds. *Microbial Ecology*, *73*, 710-721.

Raj, S., Sasidharan, S., Tripathi, T., and Saudagar, P. J. I. J. o. B. M. (2022). Biofunctionalized Chrysin-conjugated gold nanoparticles neutralize Leishmania parasites with high efficacy. *205*, 211-219.

Rhoads, D. D., Wolcott, R. D., Sun, Y., and Dowd, S. E. (2012). Comparison of culture and molecular identification of bacteria in chronic wounds. *International Journal of Molecular Sciences*, *13*(3), 2535-2550.

Rodríguez-Hernández, A. P., Vega-Jiménez, A. L., Vázquez-Olmos, A. R., Ortega-Maldonado, M., and Ximenez-Fyvie, L. A. (2023). Antibacterial Properties In Vitro of Magnesium Oxide Nanoparticles for Dental Applications. *Nanomaterials (Basel)*, *13*(3). https://doi.org/10.3390/nano13030502

Rossolini, G. M., Arena, F., Pecile, P., and Pollini, S. (2014). Update on the antibiotic resistance crisis. *Current Opinion in Pharmacology*, *18*, 56-60.

Rowe, S. E., Wagner, N. J., Li, L., Beam, J. E., Wilkinson, A. D., Radlinski, L. C., Zhang, Q., Miao, E. A., and Conlon, B. P. (2020). Reactive oxygen species induce antibiotic tolerance during systemic Staphylococcus aureus infection. *Nature Microbiology*, *5*(2), 282-290.

Salvo, J., and Sandoval, C. (2022). Role of copper nanoparticles in wound healing for chronic wounds: literature review. *Burns Trauma*, *10*, tkab047. https://doi.org/10.1093/burnst/tkab047

Scallan, E., Hoekstra, R. M., Angulo, F. J., Tauxe, R. V., Widdowson, M.-A., Roy, S. L., Jones, J. L., and Griffin, P. M. (2011). Foodborne illness acquired in the United States—major pathogens. *Emerging Infectious Diseases*, *17*(1), 7.

Schulz, F., Eloe-Fadrosh, E. A., Bowers, R. M., Jarett, J., Nielsen, T., Ivanova, N. N., Kyrpides, N. C., and Woyke, T. (2017). Towards a balanced view of the bacterial tree of life. *Microbiome*, *5*, 1-6.

Seo, S. B., Dananjaya, S., Nikapitiya, C., Park, B. K., Gooneratne, R., Kim, T.-Y., Lee, J., Kim, C.-H., and De Zoysa, M. (2017). Silver nanoparticles enhance wound healing in zebrafish (Danio rerio). *Fish and Shellfish Immunology*, *68*, 536-545.

Serra, R., Grande, R., Butrico, L., Rossi, A., Settimio, U. F., Caroleo, B., Amato, B., Gallelli, L., and De Franciscis, S. (2015). Chronic wound infections: the role of Pseudomonas aeruginosa and Staphylococcus aureus. *Expert Review of anti-Infective Therapy*, *13*(5), 605-613.

Shahid, S., Ejaz, A., Javed, M., Mansoor, S., Iqbal, S., Elkaeed, E. B., Alzhrani, R. M., Alsaab, H. O., Awwad, N. S., Ibrahium, H. A., Fatima, U., Zaman, S., and Nazim Sarwar, M. (2022). The Anti-Inflammatory and Free Radical Scavenging Activities of Bio-Inspired Nano Magnesium Oxide [Original Research]. *Frontiers in Materials*, *9*. https://doi.org/10.3389/fmats.2022.875163

Sindhu, R. K., Yadav, S. K., Kaur, A., Kumar, M., and Kumar, P. (2022). X-Ray Fluorescence: Current Trends and Future Scope. *X-Ray Fluorescence in Biological Sciences: Principles, Instrumentation, and Applications*, 623-646.

Song, M.-S., Zeng, R.-C., Ding, Y.-F., Li, R. W., Easton, M., Cole, I., Birbilis, N., and Chen, X.-B. (2019). Recent advances in biodegradation controls over Mg alloys for bone fracture management: A review. *Journal of Materials Science and Technology*, *35*(4), 535-544.

Spellberg, B., and Gilbert, D. N. (2014). The future of antibiotics and resistance: a tribute to a career of leadership by John Bartlett. *Clinical Infectious Diseases*, *59*(suppl_2), S71-S75.

Ssekatawa, K., Byarugaba, D. K., Angwe, M. K., Wampande, E. M., Ejobi, F., Nxumalo, E., Maaza, M., Sackey, J., and Kirabira, J. B. (2022). Phyto-Mediated Copper Oxide Nanoparticles for Antibacterial, Antioxidant and Photocatalytic Performances [Original Research]. *Frontiers in Bioengineering and Biotechnology*, *10*. https://doi.org/10.3389/fbioe.2022.820218

Stoimenov, P. K., Klinger, R. L., Marchin, G. L., and Klabunde, K. J. (2002). Metal oxide nanoparticles as bactericidal agents. *Langmuir*, *18*(17), 6679-6686.

Stojadinovic, A., Carlson, J. W., Schultz, G. S., Davis, T. A., and Elster, E. A. (2008). Topical advances in wound care. *Gynecologic Oncology*, *111*(2), S70-S80.

Sun, Y., Chen, D., Pan, Y., Qu, W., Hao, H., Wang, X., Liu, Z., and Xie, S. J. D. D. (2019). Nanoparticles for antiparasitic drug delivery. *26*(1), 1206-1221.

Tang, J., Guan, H., Dong, W., Liu, Y., Dong, J., Huang, L., Zhou, J., and Lu, S. (2022). Application of compound polymyxin B ointment in the treatment of chronic refractory wounds. *The International Journal of Lower Extremity Wounds*, *21*(3), 320-324.

Thapa, R. K., Kiick, K. L., and Sullivan, M. O. (2020). Encapsulation of collagen mimetic peptide-tethered vancomycin liposomes in collagen-based scaffolds for infection control in wounds. *Acta Biomaterialia*, *103*, 115-128.

Timashev, P., Bardakova, K., Minaev, N., Demina, T., Mishchenko, T., Mitroshina, E., Akovantseva, A., Koroleva, A., Asyutin, D., and Pimenova, L. (2016). Compatibility of cells of the nervous system with structured biodegradable chitosan-based hydrogel matrices. *Applied Biochemistry and Microbiology*, *52*, 508-514.

Trumbo, P., Schlicker, S., Yates, A. A., and Poos, M. (2002). Dietary reference intakes for energy, carbohydrate, fiber, fat, fatty acids, cholesterol, protein and amino acids.(Commentary). *Journal of the American Dietetic Association*, *102*(11), 1621-1631.

Vera, J., Herrera, W., Hermosilla, E., Díaz, M., Parada, J., Seabra, A. B., Tortella, G., Pesenti, H., Ciudad, G., and Rubilar, O. (2023). Antioxidant Activity as an Indicator of the Efficiency of Plant Extract-Mediated Synthesis of Zinc Oxide Nanoparticles. *Antioxidants*, *12*(4), 784. https://www.mdpi.com/2076-3921/12/4/784

Viswanathan, V. (2014). Off-label abuse of antibiotics by bacteria. *Gut Microbes*, *5*(1), 3-4.

Wang, Y., Yu, L., Kong, X., and Sun, L. J. I. j. o. n. (2017). Application of nanodiagnostics in point-of-care tests for infectious diseases. 4789-4803.

Wu, Y.-K., Cheng, N.-C., and Cheng, C.-M. (2019). Biofilms in chronic wounds: pathogenesis and diagnosis. *Trends in Biotechnology*, *37*(5), 505-517.

Xu, Z., Zha, X., Ji, R., Zhao, H., and Zhou, S. (2023). Green Biosynthesis of Silver Nanoparticles Using Aqueous Extracts of Ageratum Conyzoides and Their Anti-Inflammatory Effects. *ACS Applied Materials and Interfaces*, *15*(11), 13983-13992. https://doi.org/10.1021/acsami.2c22114

Zahoor, S., Sheraz, S., Shams, D. F., Rehman, G., Nayab, S., Shah, M. I. A., Ateeq, M., Shah, S. K., Ahmad, T., Shams, S., and Khan, W. (2023). Biosynthesis and Anti-inflammatory Activity of Zinc Oxide Nanoparticles Using Leaf Extract of Senecio chrysanthemoides. *Biomed Research International*, 3280708. https://doi.org/10.1155/2023/3280708

Zazo, H., Colino, C. I., and Lanao, J. M. (2016). Current applications of nanoparticles in infectious diseases. *Journal of Controlled Release*, *224*, 86-102.

Zhang, P., Gong, J., Jiang, Y., Long, Y., Lei, W., Gao, X., and Guo, D. J. P. (2023). Application of silver nanoparticles in parasite treatment. *15*(7), 1783.

Zhang, Y., Cui, L., Lu, Y., He, J., Hussain, H., Xie, L., Sun, X., Meng, Z., Cao, G., and Qin, D. (2022). Characterization of silver nanoparticles synthesized by leaves of Lonicera japonica Thunb. *International Journal of Nanomedicine*, 1647-1657.