Chapter 17

Overview of Nanoparticles and their Role in Management of Parasitic Diseases

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ABSTRACT

Nanoparticles (NPs) belong to a huge group of materials that consist of microscopic compounds with an approximate dimension of 100 nanometers. It's because of their huge circumference and tiny dimensions, which enable them to pass over endothelial cells, enter the circulatory system, and cross the blood-brain barrier. Investigators are constantly looking into ways to improve the long-term absorption, intracellular penetrability, and accessibility of nanoparticles utilized in drug administration due to increasing achievements in nanomedicine. Millions of people worldwide, especially in developing countries, suffer from parasitic infections, for which there are few effective treatments. Drug-resistant parasites have become more common, which emphasizes the need for more effective and safer options for treatment. Parasitic infection or better drug delivery. Since there is currently no vaccine available to prevent the majority of parasite infections, chemotherapy is the main technique for controlling these infections. In the observation and treatment of parasitic infections, nanoparticles have been shown to be valuable instruments that provide novel approaches to address issues such as drug susceptibility and the limited efficacy of traditional treatments. In this review, we look into the potential application of nanomaterials to the diagnosis and cure of parasitic infestations.

KEYWORDS
Nanoparticle's, Drug resistance parasites, chemotherapy, Drug susceptibility, traditional treatment.

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INTRODUCTION

Any substance with a narrowest dimension of hundred nanometers (nm) is known as a nanoparticle (NP). Due to their dimensions being close to those of biological components and molecules, nanotechnology, and nanomaterials are being used more and more in medical research, particularly in oncology and antiparasitic applications, where they may one day be used as disease treatments (Quadir et al., 2017). Due to their narrow dimension and huge surface area, they can be absorbed by endothelial cells and pass across the tight junctions to enter the circulatory system. Regarding nanomedicine, current research on nanoparticles for drug delivery aims to enhance long-term release, intracellular penetration, and bioavailability (Laurent et al., 2008). NPs huge surface area and tiny dimensions allow them to adhere to endothelial cells, enter the circulatory system, and pass across blood-brain barriers, enhancing their colloidal stability and bioavailability. (Rizvi et al., 2018).

Specifically, due to their many beneficial properties, simple preparation, exceptional durability, simplicity in design to the necessary size, shape, and permeability, lack of inflammation variation, simplicity of integration by different molecules, and simplicity of formation into both water-resistance and waterproof systems due to their negative surface charge on metal oxide nanoparticles, or MONPs, they are primarily a useful tool for biological applications (Sanchez-Moreno et al., 2018). Parasites are of great economic importance as they lead to severe economic losses by reducing the health and production of humans and animals (Alvi et al., 2020; Alvi et al., 2021; Alvi et al., 2022; Alvi et al., 2023). Parasitic infections caused by resistant strains of protozoa such as *Plasmodium*, *Leishmania*, *Toxoplasma,* and *Trypanosoma* have become a global health concern, with malaria being a leading cause of illness and death (McCoy et al., 2013; Qamar et al., 2023).The

purpose of the present book chapter was to summarize how useful nanoparticles might be in the detection and management of parasitic diseases.

Classification of NPs

NPs are categorized as organic, inorganic, or carbon-based on the basis of their chemical makeup as shown in Fig.1.

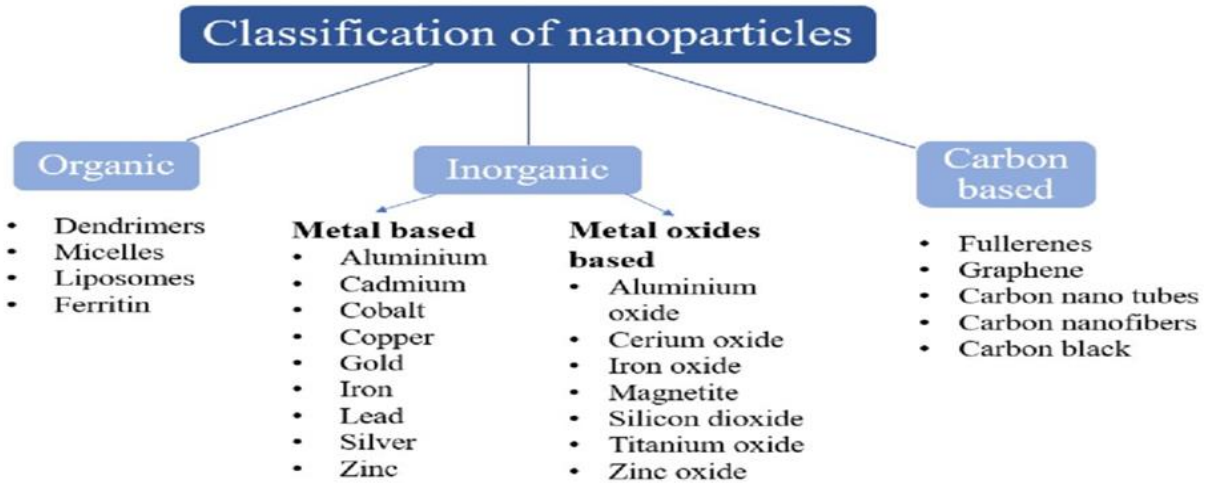

Fig. 1: Classification of Nanoparticles. (Mehta et al., 2023).

Organic NPs

This class of nanoparticles, called organic nanoparticles, is made up of biological molecules that are 100 nanometer or less. (Qi and Zhang, 2022). Recognized nanoparticles and polysaccharides in this class include iron, microorganisms, liposomes, and dendrimers. Two kinds of nanoparticles with hollow interiors known as Nanocapsules include micellar and liposomes. Both of them have sensitivity to electromagnetic radiation, which includes warmth and luminosity (Esakkimuthu et al., 2014). These are safe to use and washable as well. They are better options for medicine delivery due to their unique characteristics. The size, composition, surface shape, and other features are important, but overall pharmaceutical-carrying capacity, strength, and application methods an absorbed medication complex or an entrapped drug system affect their efficiency and range of uses (Hamidi et al., 2008). Since organic nanoparticles are effective and may be administered into specific body sections, they are widely used in the biomedical industry, including in the medicine delivery system (Gholamali et al., 2020).

Carbon-based NPs

Carbon has been a vital component in the development of humanity's culture on the planet. It forms connections with other materials that are unparalleled in strength. Because of their unique physicochemical properties, biocompatibility, and changeable surface science, carbon-based nanoparticles (NPs) represent a different class of nanomaterials with significant properties that stand out sufficiently to be noted in numerous sectors, including medication (Xin et al., 2019). Grapheme, oxides of carbon, fullerenes, carbon microfibers, and carbon black are some of the subcategories (Saravanakumar2017**).**

Inorganic Nanoparticles

"Inorganic NPs" are frequently referred to as NPs whose structure does not contain any carbon. Metals and oxide-based NPs, as well as their byproducts, are classified as inorganic NPs.

Metal-Based Nanoparticles

Metal-based nanoparticles can be obtained from Metals such as aluminum (Al)(Ghanta and Muralidharan, 2013), cadmium (Cd) (Prakash et al., 2010), cobalt (Co)(Mondal et al., 2015), copper (Cu) (Din and Rehan, 2017), and gold (Au) (Jamkhande et al., 2019) are often used in the creation of nanoparticles. Metal nanoparticles have exceptional UV-visible sensitivity as well as electrical, beneficial, heating, and antimicrobial abilities because of their huge volume-to-volume-to-surface relations and quantum impacts (Wang, 2000).

Metal Oxide-Based Nanoparticles

Examiners have been paying increasing attention to metal oxides in the last several years. Ionic compositions consisting of a mixture of negative oxygen ions and positive metallic ions are called metal oxides. The electrostatic interactions among the charged metal ions and the adverse oxygen ions produce powerful and long-lasting ionic bonds (Devan et al., 2012). The goal of creating these oxide-based particles is to change the characteristics of their metal-based equivalents. To profit from their increased reactivity or efficacy. (Tai et al., 2007). Synthesized metal oxide nanoparticles are common. SiO_2, TiO_2, ZnO, and Al_2O_3 are among the oxides that are most frequently manufactured (Bulychev, 2022; Fayad

and Dhahad, 2021; Song et al., 2021). Zinc oxide (ZnO) and titanium oxide are the oxide nanoparticles (NPs) that are most commonly utilized as drug delivery methods.

Zinc Oxide NPs

Although a number of zinc oxide (ZnO) nanoparticles (NPs) are proving to be effective in a variety of technical areas ZnO NPs have gained a lot of attention lately. This is because of its remarkable and enticing qualities, which include excellent resistance to chemicals, high sunlight absorption, a high electrochemical coupling coefficient, and a broad range of photon intake (Kołodziejczak-Radzimska and Jesionowski, 2014). ZnONPs are mostly used as photosynthetic catalysts for biological sensors, energy sources, antibacterial, antiparasitic, anti-cancer, and vaccine systems, as well as biological imaging resources (Talebian et al., 2013; Al Faleh et al., 2023).

Techniques for Preparing ZnONPs

There are three main methods:

Chemical Processes

Zinc nanocomposites can be produced in three different phases: liquid (by wet chemical processes), vapor phase, and solid. A gas phase synthesis provides advantages, but wet chemical techniques are more widely applied and have shown successful in the commercial world. (Kursawe M et al.2005). A few advantages are the use of controllable, reasonably priced chemicals, the use of basic apparatus, and the least amount of energy needed for chemical reactions involving water. Therefore, the composition, shape, and size of nanomaterials may be precisely controlled by adjusting the synthesis variables during the process (Van den Rul, 2006). We can designate microemulsions as one of the wet-chemical techniques. (Elen et al., 2011) sol-gel synthesis (Ristić et al., 2005) precipitation (Sepulveda-Guzman et al., 2009) and hydrothermal Technique (Xu L et al. 2009).

Physical Processes

Two examples of physical approaches are laser ablation and ultrasonic ablation, as well as the thermal evaporation method (Zou C et al., 2015).

Biological Processes

Natural sources such as lower plants, products of higher angiosperm plants, yeasts, bacteria, and fungi can all create NPs. Considering all of its limitations, using biological systems is a compelling substitute for traditional chemical synthesis. Because this approach does not require the use of expensive or dangerous organic solvents, it has the advantage of being more environmentally friendly (Yuvakkumar et al., 2014).

Biomedical Application of zinc Oxide NPs

Zinc Oxide's Antibacterial Properties

The in vitro antibacterial activity of nanomaterials can be assessed using a variety of methods, including the medium diluting technique accompanied by population measures, the gel dilution approach, the disc diffusion test, the microtiter plate-based approach, the flow cytometry survival test kits, and the conductometric tests (Espitia et al.2012). The anti-microbial activity of ZnO NPs has been evaluated against a variety of bacteria, including *P. aeruginosa, E. coli, B. subtilis*, and *S. aureus*, as well as monoderm and diderm bacteria. The exterior membranes of diderm bacteria are covered with a fine sheet of peptidoglycan and lipopolysaccharide. This layer blocks the entry of negatively charged molecules into ROS (Russell et al. 2003). Both monoderm and diderm bacteria are susceptible to the potent antibacterial properties of zinc oxide. Nevertheless, particle size has a remarkable impact on ZnO antimicrobial effectiveness. It has been found that ZnO antimicrobial activity is high when the atom size is reduced. (Czyżowska and Barbasz, 2022).

Anti-Inflammatory Activity of ZnO

Nanoparticles have been more and more well-liked as anti-inflammatory medicines in recent decades. Their huge surface area to volume ratio gives them significant surface reactive properties that enhance their physical transit and contact with the biological membrane. ZnO NPs are easily absorbed across biological membranes due to their nanoscale size. Previous studies have demonstrated a considerable anti-inflammatory impact of zinc oxide nanoparticles. (M. Ilves, et al. 2014). Common antibacterial strategies for zinc oxide nanoparticles include preventing the expression of the enzyme that produces nitric oxide. (Cortese-Krott et al., 2014). inhibition of myeloperoxidase and pro-inflammatory cytokine release along with the corresponding protein expressions.

Immunostimulant Activity of ZnO

Zinc oxide (ZnO) immunomodulatory activity is its capacity to regulate or influence the body's immune response. Research suggests that ZnO nanoparticles may possess immunomodulatory properties that impact various immune cells and processes (Mehessen et al., 2023). Zinc oxide (ZnO) nanoparticles have been found to affect the activity of T cells, B cells, dendritic cells, and macrophage function, among other immune cells. They exhibit the capacity to regulate

phagocytosis, antigen presentation, and the production of cytokines, among other immune response modulation mechanisms. These nanoparticles are often found in nutritious foods and drinks. Their capacity to modulate immunity was discovered. ZnO NPs enhanced mice's immune responses specific to antigens. Serum levels of antibodies specific to antigens, namely IgE and IgG, were higher. It was also found that ZnO NPs improved the Th2 response by raising the body's activation and synthesis of cytokines (Roy et al., 2014).

Beneficial Effects of zno-nps in Different Animal Species

Because of their remarkable biocompatibility, affordability, and low toxicity, zinc oxide nanoparticles are among the most frequently used metal oxide nanoparticles in a variety of animal species (Table 1) for biological, medicinal, and industrial applications.

species	Benefits of ZNO NP in Different Animal Species
Mice	Shown antibacterial and antidiabetic properties, increased spermatogenesis, lipid profile, and neurotransmitter stability (Pati et al., 2014).
Rats	Exhibited signs of antidiabetic activity, analgesic efficacy via nociception inhibition, and improved lipid profile (El-Maddawy and Abd El Naby, 2019).
Pigs	Increase in body weight, increased the duodenal villi's length, enhanced gut morphology, and heightened immunological response (Wang et al., 2017).
Rabbits	Demonstrated the ability to repair tendon damage and liver protection against aflatoxicosis by the use of free radicals (Atef et al., 2016).
Equine	Increased gas generation, better gut health, and decreased mineral release in the feces, increased wound healing, and higher feed digestibility (Adegbeye et al., 2019).
Poultry	Gain in body weight, better lipid profile, enhanced dite adaptation, and elevated antioxidant activity (Zahra et al., 2017).
Fish	Provide antibacterial properties against fish infections, enhance fish zinc bioavailability and intestine absorption, and raise MCHC and RBC values.
Cattle	Shown antimicrobial properties, enhanced the state, enhanced mastitis, enhanced milk output, and enhanced rumen fermentation (Bai et al., 2018).

Toxicity of zno-np in Animals

It is thought that the release of Zn+ ions from the nanoparticles is what gives ZnO-NPs their poisonous characteristics. Consequently, even for brief periods of time, a high concentration of ZnO-NPs in food can make animals poisonous to zinc. (Underwood and Van Eps, 2012). Moreover, ZnO-NPs resulted in hemolysis, lowering erythrocyte parameters, platelet count, serum haptoglobin content, and many liver histological abnormalities (Ibrahim et al., 2017). Evidence that these nanoparticles have detrimental effects in a range of animal models has stimulated research on the potential dangers and toxicity mechanisms of these particles. Studies have shown that exposure to ZnO-NP might result in harmful physiological responses like oxidative harm, irritation, DNA damage, and harm to organs (Shahzad et al., 2019).

Function of Nanomaterials in the Identification of Parasitic Illnesses

Malaria

The identification of malaria antigens was demonstrated to be effective when various parasite heat shock proteins 70 (HSP 70) were combined to metallic nanoparticles modified with monoclonal antibodies; and polyester NPs coupled to polyclonal anti-*P. Falciparum* IgG antibodies produced highly precise outcomes. Improved resonance for the detection of β-hematin or hemozoin Raman spectroscopy and atomic force microscopy were used to successfully screen blood films. Utilizing a magnetic field to gather information allows for the prior identification of malaria. (Yuen C et al.2013**).** A new method of diagnosing malaria was developed using nanotechnology. Using a quantum-magnetic droplet test, serum or urine carrying *P. falciparum* (PF) protein 2 (HRP2 protein 2; high in histidine) can be recognized. Anti-HRP2 antibodies and magnetic beads can be used to capture the target protein. Following that, it can be purified and identified using quantum dot technology (Castro-Sesquen et al., 2016).

Leishmaniasis

Agents significantly increased the isothermally of Leishmaniasis DNA in blood tests from sick dogs by using gold nanoparticles, specific Leishmania spp. markers, and a sticky cushion. The nanoparticles' electrocatalytic response was reliable for the speedy detection of amplified DNA. This method of diagnosing visceral leishmaniasis (VL) has been shown to be more accurate and cautious than traditional PCR methods. (de la Escosura-Muñiz et al., 2016).

Toxoplasmosis

When antigen-coated gold nanoparticles are used in the reducing agent differentiation verification procedure, the results of an ELISA correlate. To improve the reliability of extracting circulating surface antigens, the examiner used an

immunomagnetic tablet coated with a polyclonal counteracting agent for *T. gondii* IgG that was wrapped in sticky nanoparticles (Wang et al., 2004). Further, *T. gondii* clinical techniques that make use of nanomaterials include modern detection strategies, such as measuring assays of DNA with nanoparticles (Sousa et al., 2021). Considerable improvement has been made in terms of affectability, specificity, and adequateness with the addition of intriguing and luminous nickel nanoparticles (CdTE/Ni mQD) nanodot assays to diagnostic frameworks for the detection of *T. gondii* DNA. (Assolini et al., 2017).

Amebiasis

The research has shown that luminous nanoparticles based on artificial antiparasitic silica, *Entamoeba histolytica* IgG1, have a significant perceptivity to identify amebiasis with no interaction with other protozoa (Hemadi et al., 2015).

Cryptosporidiosis

The mRNA of *C. parvum* oocytes, was combined with gold nanoparticles. When stool samples are analyzed, oocyst nucleic acids from *C. parvum* can be identified using two gold NP probes functionalized with oligonucleotides that match the 18S rRNA sequences of the bacterium (Weigum et al., 2013).

Schistosomiasis

The majority of research has relied on the identification of *Schistosoma* antigens. An example is an enzyme affinity test known as the magnetic affinity enzyme-linked immunoassay. The MEIA test is carried out depend on the production of specific antibodies in response to the aspect of larval antigens. Magnetic beads with functional polymer components and superparamagnetic nanoparticles are used in the MEIA test. Furthermore, distinctive functional groups were added to magnetic beads to enable them to form bonds with charged molecules. Molecular targets were placed on magnetic beams and then the reactive system was exposed to the magnetic field thus, via magnetic separation, an immunological complex was obtained. A distinct type of metallic nanoparticle was employed in colloidal gold, an additional diagnostic technique. Because Ig-bonded colloidal gold can connect with biological macromolecules like immunoglobulins, it is a useful tool for important clinical diagnostic research. Schistosomal antigen creates an immunological combination with IgG–colloidal gold during the diagnostic procedure (Wu et al., 2018).

Trypanosomiasis (Chagas' disease)

Nanomaterials, like metallic nanoparticles, have been used in recent years to diagnose Chagas disease. These identification instruments should be used in an integrated microflow system connected to an electrode pull with carbon screens (Quijia Quezada et al., 2019). Its purpose is to measure certain IgG antibodies present in serum. It employs *Trypanosome cruzi* proteins that have been isolated from epimastigotes and functionalized on AuNPs. 3.065 ng/mL was determined to be the test's lower detection limit, and the coefficients of variation between tests were lower than 6.95% (Quijia Quezada et al., 2019). The Chunap test, also known as the Chagas' urine nanoparticles test, is used to diagnose congenital Chagas disease early. Its foundation is the identification of antigens released by trypomastigote forms using Western blot analysis (Choudhury, 2021). Because tryptan blue and polyunsaturated N-isopropylacrylamide are used to functionalize nanoparticles that can collect and concentrate *T. cruzi*, the sensitivity and specificity of a urine-based test are roughly 95% (Quijia Quezada et al., 2019).

Nanoparticles in Parasitic Diseases

Kinds of NPs that are Susceptible to Parasites

Type of nanoparticle	Parasite	Results
Silver, chitosan, and curcumin NPs	*Giardia lamblia*	When the three nanoforms were combined, the fighting effect was maximized. It was discovered that the parasite had disappeared from the intestine and stool (Said et al., 2012).
Ag-NPs	*Leishmania Tropica*	Ag-NPs significantly reduced promastigotes' metabolic activity and rate of proliferation, exhibiting antileishmanial effects (Ponarulselvam et al., 2012).
LCu(CH3COO)2 and LCuCl2	*P.falciparum*	Significant antimalarial activity against the parasites was demonstrated by the two substances (Tripathy et al., 2012).
Gold NPs	*Leishmania major*	Compared to MW alone, when promastigotes and amastigotes were exposed to microwave radiation, the presence of GNPs was more lethal (Alshamiri et al., 2021)
Chitosan and silver	*T. gondii*	The results show that using AgNPs either by themselves or in conjunction with chitosan has shown promising anti-Toxoplasma capacity.
Nano-Nitazoxanide (NTZ)	*Cryptosporidium parvum*	On day six, nano nitazoxanide showed efficacy against parasites.
Silver NPs	*Plasmodium falciparum*	When applied to P. falciparum, the AgNPs exhibited antiplasmodial action (Mohapatra et al., 2010).

NPs' Function in Treating Parasitic Illnesses

As a Sole Method Therapy

NPs that specifically target infected macrophages can enhance the treatment of VL. AgNPs, and curcumin NPs were used to treat giardiasis-infected animals. Curcumin NPs provided the most effective and comprehensive treatment. Experimental animals with toxoplasmosis were treated with silver alone, and used in combination. The combined treatment dramatically decreased the parasite load in the spleen and liver. Microscopic research revealed that tachyzoites were deformed in shape and unable to move (Said et al., 2012).

As a Drug Delivery System

Treatment was administered to VL strains resistant to the wild type using gold nanoparticle quercetin-conjugated strains. Comparing drugs with amphotericin B and rifampicin, two treatments for VL, demonstrated a substantial level of effectiveness. *L. major* ulcers in mice treated with glucantime liposomes were successfully healed with topical application of glucantime. It drops the number of parasites and the extent of the splenic lesion. *Trichoderma harzianum,* a soil fungus, was conjugated with silver nanoparticles to increase the effectiveness of triclabendazole in treating fascioliasis. (Gaafar et al., 2014). Liposomal praziquantel (300 mg/kg) decreased the parasite load, the number of worms and eggs in the feces, and the number of liver tumors when cure *Schistosom mansoni*. In *S. mansoni*-infected mice, the effectiveness of miltefosine, an anticancer medication, was compared to that of praziquantel at an oral dosage of 20 mg/kg. The outcomes indicated the potential of *S. mansoni* and the effectiveness of nanomedicine in drug delivery (Gaafar et al., 2014).

Immunization and Vaccination

It's crucial to remember that adding NPs can increase the antigenicity of conjugated or adsorbed antigens. NPs have the ability to trigger both innate and adaptive immune responses. Aside from that, they are perfect for usage as antigen bearers to enhance antigen processing and display due to their enormous specific surface area and activity. Because NPs release antigens in a regulated manner, most vaccinations have longer half-lives. They can also act as independent immunological potentiators (Kheirollahpour et al., 2020).

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