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Role of Nanoparticles in Diagnosis and Management of Parasitic Diseases: Review Article

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ABSTRACT

Background: An extensive class of materials, nanoparticles (NPs) include particulate compounds with a minimum diameter of 100 nanometers (nm). This is because of their tiny size and huge surface area, which allows them to traverse the blood-brain barrier, enter the respiratory system and be adsorbable through endothelial cells. Today, nanoparticles for drug administration are being studied to increase their sustained release, intracellular penetrability as well as bioavailability, due to the constant development and innovation of nanomedicine.

Objective: To determine how nanoparticles can help diagnose and treat parasitic diseases.

Conclusion: Nanoparticles could be conjugated with proteins and immunoglobulins that could help in specific diagnosis of several parasitic diseases**,** in addition, improved efficacy and reduced harmful side effects can be achieved by immobilizing antiparasitic medicines on or inside nanomaterials.

Keywords: Nanoparticles, Parasitic Diseases.

INTRODUCTION

Particulate compounds that have one dimension smaller than 100 nm at least are known as nanoparticles (NPs) [(1)]. With their tiny size and wide surface area, the colloidal stability and bioavailability of NPs is boosted, allowing them to penetrate blood-brain barriers, enter the pulmonary system and adhere to endothelial cells [(2)].

To be more specific, metal oxide nanoparticles (MONPs) have a number of advantageous properties like simple preparation processes, high stability, ease of engineering to the desired size, shape, and porosity, no swelling variations, ease of functionalization by various molecules, as well as ease of incorporation into both hydrophobic and hydrophilic systems due to the negative charge of the surface, which make them a promising tool for biomedical applications in particular [(3)].

The aim of the present review was to determine how nanoparticles can help diagnose and treat parasitic diseases.

Classification of NPs:

The chemical composition of NPs determines whether they are classified as organic, inorganic, or carbon-based [(4)].

1. **Organic NPs:** liposomes, dendrimers, ferritin, as well as micelles are the most widely used. Non-toxic, biodegradable, and sensitive to heat and light, they can be used in a wide range of applications [(5)].
2. **Carbon based NPs:** carbon nanotubes, fullerenes, carbon nanofibers, carbon black, as well as graphene are some of the subcategories [(6)].
3. **Inorganic NPs:** The term "inorganic **NPs**" refers to those that lack carbon as a constituent part of their structure. Inorganic **NPs** include metal and metal oxide **NPs** and their derivatives.
   A. Metal based **NPs**: cobalt, aluminum, copper, gold, cadmium, silver, and zinc, iron, as well as lead are among the most often utilized metals for nanoparticle synthesis [(4)].
   B. Metal oxides based: Because of their improved reactivity and efficiency, they are predominantly synthesized. Zinc oxide, cerium oxide, aluminium oxide, iron oxide, titanium oxide, as well as silicon dioxide, are the most typically manufactured.

As drug delivery systems, titanium oxide, and zinc oxide (ZnO) NPs are the most often employed oxide NPs [(7)].

ZnO structure:

Cubic zinc, hexagonal wurtzite blende are the most common types. In ambient settings, wurtzite structure is the most stable and consequently the most widely employed type. Wurtzite ZnO is a hexagonal crystal with lattice parameters a = 0.325 nm and c = 0.521 nm and with three primary growth directions: {1010}, {1120} and {0001}. Four oxygen atoms surround each tetrahedral Zn atom [(8)].

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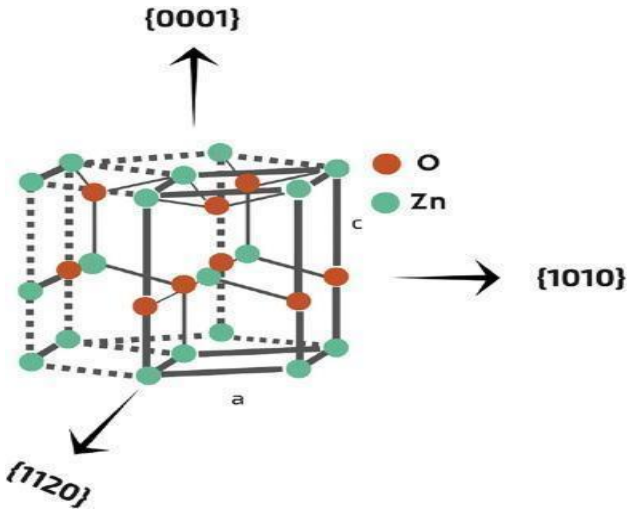

Figure (1): Directions in the ZnO wurtzite structure {0 0 0 1}, {1 1 2 0} and {1 0 1 0} [9]

Methods of ZnO NPs Preparation:

They can be divided into three main methods:

1. Chemical methods:

Physically, they are characterised as solid, liquid (wet chemical techniques), or vapour phase for zinc nanocomposites synthesis. While gas phase synthesis has its advantages, wet chemical approaches are more widely employed and have proven to be useful in the commercial world [10].

Numerous advantages include the use of inexpensive and easy-to-handle chemicals, as well as simple equipment, and the minimal energy input required by water-based chemical techniques. As a result, nanomaterials may be precisely controlled in terms of their composition, shape, and size by adjusting synthesis parameters during the process [11].

Microemulsions are one of the wet-chemical approaches that we can identify [12], sol-gel synthesis [13], precipitation [14], solvothermal [15] and hydrothermal technique [16].

2. Physical methods:

Thermal evaporation method [17], ultrasonic ablation [18] as well as laser ablation [19] are examples of physical methods.

3. Biological methods:

For the manufacture of nanoparticles, NPs can be derived from natural sources such bacteria, yeasts, fungus, lower plants, and higher angiosperm plant products. Traditional chemical synthesis has significant disadvantages, making the use of biological systems an attractive alternative. One of the advantages of this method is that it does not require the use of harmful or expensive organic solvents, making it more ecologically friendly [20].

Biomedical application of ZnO NPs:

1. Anticancer Activity:

Recent studies have demonstrated that nanomaterial-based nanomedicine, which has great biocompatibility and is easy to functionalize, can overcome the negative effects of chemotherapy, radiotherapy, and surgery. Biocompatible and biodegradable nanoplatforms, such as ZnO NPs, can be selected, and cancer therapeutic applications can be investigated [21].

2. Antibacterial Activity:

ZnO NPs were tested against E. coli by **Jiang *et al.*** [22], who found that they had antibacterial properties. An average of 30 nanometer ZnO particles induced cell death by directly touching the membrane's bilayer and damaging its integrity, according to the study. Incorporating radical scavengers such as mannitol, vitamin E, and glutathione into ZnO NPs might prevent their bactericidal effects, demonstrating that reactive oxygen species (ROS) generation was crucial to the antibacterial effects of ZnO NPs.

3. Diabetes Treatment:

Keeping insulin's structural integrity is well established, and zinc has an active involvement in insulin release from pancreatic cells. Another function of this enzyme is that it helps to synthesis insulin, store it and secrete it [23]. Anti-diabetic properties of zinc have been studied using ZnO NPs, which have been created and tested.

4. Anti-Inflammatory Activity:

Experiments conducted by **Wiegand *et al.*** [24] investigated the impact of ZnO-functionalized textile fibres in the management of oxidative stress in atopic dermatitis (AD). Wearing ZnO materials overnight for three consecutive days resulted in a significant reduction in AD pruritus and subjective sleep quality. Zinc oxide nanoparticles (ZnO NPs) showed remarkable anti-inflammatory effect, according to the work of **Nagajyothi *et al.*** [25] in addition to the related protein expressions of TNFα, COX-2, IL-6, IL-1β and iNOS.

5. Immunomodulatory:

These nanoparticles are commonly found in nutritional products. Immunomodulatory properties were discovered in them. Antigen-specific immune responses in mice were boosted by ZnO NPs. In serum, they increased the synthesis of antigen-specific antibodies, particularly immunoglobulin E (IgE) and immunoglobulin G (IgG). Th2 response was also found to be boosted by ZnO NPs, which increased the generation and activation of cytokines in the body [26].

Research on ZnO's toxicity in mammals:

Toxicology studies on ZnO in living cells, particularly mammalian cells, have yielded mixed results. ZnO has been demonstrated to be biocompatible and harmless in certain investigations, but newer studies have indicated that ZnO can be hazardous to mammalian cells both in vivo and in vitro. These investigations have shown that the toxicity of ZnO is dose-dependent. The therapy of malignant, pathogenic, and leukemic T cells relies on this level of toxicity as well. Drug resistance, which is a serious issue in the pharmaceutical sector, can be solved with the help of these NPs [27].

Nanoparticles in parasitic diseases:

Role of NPs in diagnosis of parasitic diseases:

Malaria:

Heterologous P. falciparum heat shock protein 70 (HSP 70) coupled to gold NPs and functionalized with anti-HSP 70 monoclonal antibodies demonstrated effectiveness in the detection of malaria antigens. Polystyrene NPs coupled to polyclonal anti-P. falciparum IgG antibodies yielded very specific results. The detection of hemozoin or β-hematin utilizing surface-enhanced resonance Raman spectroscopy (SERRS) and atomic force microscopy (AFM) proved successful in screening blood films. Tuning the core and shell with a silver shell allowed magnetic field to be employed in SERRS. Early detection of malaria is possible due to the accumulation of β-hematin as a result of this adjustment [(28)].

Toxoplasmosis:

According to **Wang and colleagues** [(29)], the use of antigen-coated gold NPs for antibody detection yielded results that were consistent with those obtained by using an enzyme-linked immunosorbent assay (ELISA). T. gondii IgG polyclonal antibodies coated with magnetic NPs (SAG1) were used in an immunomagnetic bead (IMB)-ELISA approach to better capture circulating surface antigens.

Cryptosporidiosis:

Conjugated with gold NPs, HSP70 was used to target Cryptosporidium parvum (C. parvum) oocyte HSP70 mRNA. Oocyst nucleic acids from C. parvum can be detected in stool samples using a pair of oligonucleotide-functionalized gold NPs probes corresponding to the 18s rRNA sequences of C. parvum [(30)].

Amebiasis:

An amebiasis diagnostic method based on fluorescence silica NPs and monoclonal anti-Entamoeba histolytica IgG1 demonstrated significant sensitivity results without cross-reaction with other protozoa, according to the study [(31)].

Leishmaniasis:

Isothermal amplification of leishmania DNA in blood samples from infected dogs was performed using gold NPs coupled with tagged leishmania spp. primers and a magnetic bead. The quick detection of amplified DNA was shown to be possible thanks to the electrocatalytic activity of NPs. The previous PCR method for diagnosing visceral leishmaniasis (VL) was shown to be less sensitive and more expensive than this method [(32)].

Role of NPs in treatment of parasitic diseases:

As the sole method of therapy:

Treatment of VL can be improved by NPs targeting infected macrophages. Animals infected with giardiasis were treated with silver, chitosan (CS), and curcumin NPs, which had the greatest effect and a complete cure. Toxoplasmosis in experimental animals was treated with either silver or CS alone or in combination. The parasite burden in the liver and spleen was significantly reduced by the combined treatment. Tachyzoites were shown to be unable to move and distorted in shape by microscopic analysis [(33)].

As a drug delivery system:

Wild-type resistant strains of VL were treated with quercetin conjugated with gold NPs. When compared to CS-free control medicines, amphotericin B and rifampicin showed substantial results in treating VL.

Leishmania major (L. major) ulcers in mice treated with glucantime liposomes were effectively treated by the topical application of glucantime in mice. It reduces the size of the lesion and the parasite burden in the spleen. The efficiency of triclabendazole in the treatment of fascioliasis was improved by using soil fungus Trichoderma harzianum conjugated with silver NPs [(34)].

When treating schistosomiasis mansoni (S. mansoni), liposome praziquantel (300 mg/kg) reduced the worm burden, the number of worms and eggs found in the faeces and the number of tumours found in the liver. As a single oral dose of 20 mg/kg of miltefosine, an anticancer drug, it was compared to praziquantel's efficacy in S. mansoni-infected mice. S. mansoni's potential and nanomedicine's capacity to deliver drugs efficiently were demonstrated by the results [(34)].

Immunization and vaccination:

It is important to note that the antigenicity of conjugated or adsorbed antigens can be enhanced by the addition of NPs. Adaptive and innate immune responses can be elicited by NPs. Aside from that, their large specific surface area and functionality make them ideal for use as antigen carriers in order to improve antigen processing and display. Most vaccines' half-lives can be extended thanks to the regulated release of antigens provided by NPs. Additionally, they can serve as immunological potentiators on their own [(35)].

CONCLUSION

NPs could be conjugated with proteins and immunoglobulins that could help in specific diagnosis of several parasitic diseases, in addition, improved efficacy and reduced harmful side effects can be achieved by immobilizing antiparasitic medicines on or inside nanomaterials.

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