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[A Review Article]

Nanotechnology and Nanomedicine-Based Strategies in Parasitic Infection

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Abstract

PARASITIC infections remain a major global health burden, particularly in low-resource settings, where conventional therapies face challenges such as toxicity, drug resistance, and limited efficacy. Nanotechnology has emerged as a transformative approach, offering innovative solutions for diagnosis, treatment, and prevention of these diseases. Nanoparticles enhance the solubility, stability, and bioavailability of drugs, while enabling targeted delivery and reducing side effects. In diagnostics, nanobiosensors and nanoparticle-based assays provide rapid, sensitive, and cost-effective alternatives to traditional techniques. Vaccine development has also benefited from nanotechnology, with nanocarriers improving antigen stability, immune responses, and delivery efficiency. Nanoparticles, such as metal, metal oxide, and polymeric particles, could lead to an effective method for treating some diseases. Applications span a wide range of parasitic diseases, including malaria, leishmaniasis, toxoplasmosis, human African trypanosomiasis, and Chagas disease, with promising outcomes in both experimental and clinical contexts. Despite significant progress, further research is required to address safety, cost, and large-scale implementation challenges.

Keywords: Nanotechnology, Nanomedicine, Nanodiagnostics, Parasitic diseases.

Introduction

Parasitic infections cause substantial global morbidity and mortality, particularly in resource-limited regions. In 2021, malaria accounted for 619,000 deaths, with 95% of cases and 96% of deaths reported in Africa; 80% of fatalities were among children under five. Leishmaniasis affects 700,000 to 1 million people annually, with 85–95% of cases being cutaneous and 50,000–90,000 being visceral forms. Human African trypanosomiasis endangers 70 million individuals in sub-Saharan Africa and is fatal if untreated, while Chagas disease affects 6–7 million people, mainly in Latin America [1].

Toxoplasmosis, caused by the intracellular protozoan parasite *Toxoplasma gondii*, is another globally prevalent parasitic infection, particularly hazardous for immunocompromised individuals and pregnant women, where it may result in congenital anomalies, encephalitis, or pneumonitis. Conventional therapy with pyrimethamine and sulfadiazine are limited by severe side effects, poor bioavailability, and ineffectiveness against latent bradyzoite cysts. Drug resistance has also been reported, and vaccine development attempts remain unsuccessful. Nanotechnology-based strategies offer promising alternatives. In therapeutics, nanoparticles can cross biological barriers, including the blood–brain barrier, and improve delivery of existing drugs such as spiramycin, curcumin, and atovaquone.

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Liposomes, polymeric nanoparticles, chitosan-based carriers, and metallic nanoparticles (e.g., silver, gold, selenium) have demonstrated enhanced anti-*Toxoplasma* activity, reduced parasite burden in animal models, and lower host toxicity compared to traditional treatments.Nanotechnology offers advanced diagnostic solutions for toxoplasmosis, overcoming the limitations of conventional methods like serology and PCR tests, which are often slow, expensive, and inaccessible. By utilizing nanoparticles such as gold or magnetic materials, nano-biosensors facilitate rapid, highly sensitive, and portable detection of T. gondii. This enables point-of-care testing, crucial for early diagnosis and management in high-risk groups as pregnant women and immunocompromised patients [2].

Conventional antiparasitic drugs such as pentamidine, nifurtimox, chloroquine, and artemisinin derivatives are used to eliminate or inhibit parasite growth. Miltefosine and amphotericin-B have replaced antimonial drugs in leishmaniasis treatment. However, drug resistance, adverse effects (e.g., headache, nausea, vomiting, abdominal pain), limited species coverage, and high cost remain key challenges [3].Nanotechnology offers innovative solutions to overcome these barriers. Nanoparticles enhance drug solubility, cellular permeability, and bioavailability while reducing toxicity. These particles can penetrate parasite-infected cells, prolong drug circulation, and enable sustained release. Surface modification with ligands allows targeted delivery and detection of disease-specific biomarkers [4].

Nanomedicine applies nanometer-scale (0.1–100 nm) tools for diagnosis, prevention, and treatment. Nanoparticles (NPs), <100 nm in at least one dimension, have a high surface area-to-mass ratio and distinct reactivity [5]. These properties offer advantages over traditional agents, especially in drug delivery and imaging [6].Biosynthesis of NPs using organic compounds (vitamins, proteins, lipids, plant extracts) produces or metal/metal oxide NPs with enhanced bioavailability due to their surface-area-to-diameter ratio. NPs of this scale interact closely with cellular machinery and enable imaging and diagnostic capabilities [7].

In diagnostics, nanobiosensors were used nanomaterials with unique physical and chemical properties offer faster, more sensitive and noninvasive alternatives to microscopy and molecular tests, which are often costly, time-consuming, and require skilled personnel. These approaches are especially promising for deployment in remote or low-resource settings [8]. Nanotechnology has also enhanced vaccine development. Traditional parasitic vaccines, whether live attenuated, inactivated, or subunit, often encounter limitations in safety and effectiveness. Nanoparticle-based vaccine systems offer improved antigen stability, stronger immune activation, and precise delivery. Additionally, they allow simultaneous delivery of antigens and adjuvants, thereby increasing immunogenicity and contributing to the creation of safer and more efficient vaccines [9]. Although, nanotechnology shows considerable promise across therapeutic, diagnostic, and preventive dimensions in parasitic disease control. Further studies are needed to translate these advances into accessible, cost-effective, and scalable clinical solutions (Figure 1) [10].

Classification of Nanoparticles

1. Carbon-Based NPs: Include fullerenes (C60), carbon nanotubes (CNTs), graphene, and others, fabricated via laser ablation, arc discharge, or chemical vapor deposition (CVD) [11]. 2. Inorganic-Based NPs: Include gold (AuNPs), silver (AgNPs), zinc oxide (ZnO), silicon, and ceramic particles. AuNPs, especially quasi-spheres synthesized in aqueous phase, exhibit red color and tunable optical properties [12].

2. Inorganic nanoparticles (such as gold, silver, silica, iron oxide, and quantum dots) have promising applications in drug delivery, imaging, and cancer therapy, as well as in food preservation but their use exhibits a safety concern as their small size and high surface reactivity allow them to interact strongly with biological systems, which can lead to oxidative stress, inflammation, genotoxicity, and disruption of cellular signaling. Some inorganic nanoparticles tend to invade the biological pariers and accumulate in different organs like the liver, spleen, kidneys, placenta and brain due to its very small size and limited biodegradability, raising risks of long-term toxicity. Additionally, dose, size, shape, and surface chemistry strongly influence toxicity profiles, making careful design and regulation essential before clinical use. Consequently, it is recommended for conducting preliminary assessments, including studies on cytotoxicity and long-term impacts. It is necessary to evaluate on a case-by-case basis prior to its widespread application [13].

3. Organic-Based NPs: Comprise dendrimers, micelles, liposomes, and polymer NPs. Dendrimers are monodisperse, 3D, biocompatible carriers for antiparasitic drugs. Polymeric NPs can be nanospheres (solid) or nanocapsules (encapsulating core). Lipid NPs (10–1000 nm) consist of lipid cores and surfactant-stabilized surfaces, used in drug delivery and RNA therapies [14].

4. Composite-Based NPs: Combine multiple NP types or bulk materials, including hybrids like metal-organic frameworks [15].

Applications of Nanomedicine in Drug Delivery

Nanoparticles (NPs) enhance drug delivery by improving bioavailability, minimizing side effects, and allowing precise dosing. Their small size increases surface area-to-volume ratio, facilitating parenteral administration. Their size similarity to cellular machinery enables use in both therapy and diagnostics, with properties like size-dependent magnetism and optical responsiveness. Compared to bulk materials, NPs show enhanced reactivity and surface interactions, which aid in overcoming the limitations of conventional therapies. Their efficacy extends to subtle applications such as cerebral infections [16].

Nanotechnology in Parasitic Disease Diagnosis

Toxoplasmosis: Immunomagnetic bead-ELISA using anti-T. gondii IgG-coated magnetic NPs improved antigen capture over standard ELISA. Gold NPs enabled specific agglutination with good concordance to ELISA. A gold-NP-based LFIA using PMAA-modified particles detected TORCH IgM with 100% sensitivity and specificity [17].

Leishmaniasis: Gold NPs conjugated with oligonucleotide probes detected Leishmania DNA via pH-dependent color change red in presence of target, purple otherwise [18].

Malaria: Magnetic core/silver shell NPs enhanced resonance Raman spectroscopy for early detection of β-hematin. Gold-NP-based fluorescence immunoassays detected Plasmodium falciparum Hsp70 antigens via Cy3B quenching [19].

Cryptosporidiosis: Gold-NP probes targeting C. parvum 18S rRNA formed hybridized networks detectable by spectroscopy. HSP70 mRNA was also detected using goldNPs [20].

Nanomedicine in Treatment of Parasitic Diseases

Nanoparticle-based systems, including liposomes and solid or hydrophobic carriers, offer sustained-release and pathogen-targeted delivery. They address resistance by enhancing cellular drug uptake [21].

Parasitic Diseases Management

Nanoparticles such as liposomes, solid lipid nanoparticles (SLNs), polymer-based carriers, nanosuspensions, and metallic nanoparticles (e.g., gold, silver, carbon) are under extensive investigation for antiparasitic drug delivery [23]. These systems improve therapeutic efficacy and address diagnostic limitations. Traditional parasitological and immunological tests often suffer from cross-reactivity and low accuracy, while nanotechnology-based diagnostics offer improved sensitivity and specificity [24].

Liposomes

Liposomes are lipid bilayer vesicles ranging from 0.025 to 2.5 µm. They can encapsulate drugs in their aqueous core or lipid membrane, enhancing stability, circulation time, and reducing toxicity. Liposomes have shown efficacy in treating malaria, leishmaniasis, and Chagas disease. They have also proven superior to conventional antifungals in systemic infections caused by *Candida albicans* and *Aspergillus fumigatus*, with enhanced tissue penetration [25]. Their pharmacokinetics can be improved by modifications such as immunoliposomes (antibody-tagged) or peptide-functionalized liposomes, allowing targeted delivery. Liposomes are biocompatible and biodegradable, solubilize hydrophobic drugs, and protect against degradation. They can enter macrophages during phagocytosis, enabling intracellular delivery. These properties make them ideal for controlled, targeted antiparasitic therapy [26]. Overall, liposomes found to improve drug delivery and often reduce systemic toxicity compared to free drugs, but they still carry risks like infusion reactions, immune activation, liver/spleen accumulation, and drug-specific toxicities (e.g., hand-foot syndrome with liposomal doxorubicin) [27].

Solid Lipid Nanoparticles (SLNs)

SLNs are spherical particles (<1000 nm) composed of solid lipids stabilized by surfactants. They protect drugs from enzymatic degradation and allow controlled release. SLNs are non-toxic, biodegradable, and suitable for hydrophilic or hydrophobic drugs [28]. However, challenges like lipid crystallization, drug leakage, gelation, and polymorphic transitions limit their performance. Despite this, SLNs enhance intracellular targeting, reduce doses, minimize toxicity, and outperform conventional carriers. Their scalability and compatibility make them promising for use in resource-limited areas [29].

Nanosuspensions

Nanosuspensions are colloidal dispersions of poorly soluble drugs in nanocarriers, often <1 µm. They enhance solubility, bioavailability, and controlled release. Poor solubility and low bioavailability are common issues with antiparasitic drugs, contributing to treatment failure and resistance [30]. Nanosuspensions of antiparasitic agents have shown improved therapeutic profiles in animal models, enabling lower doses, better compliance, and reduced costs. However, safety, targeting specificity, and off-target effects must be critically assessed through multidisciplinary approaches [31].

Polymer-Based Nanoparticles

These nanoparticles (<1000 nm) are made from synthetic or natural polymers like poly(lactic-co-glycolic acid) (PLGA), polyethylene glycol (PEG), and chitosan. They allow controlled drug release, stability, and biocompatibility. The therapeutic agent is housed in the core, while the outer polymer shell modulates drug release via diffusion or degradation. Surface functionalization with ligands or antibodies improves tissue-specific targeting. These properties support their use in drug delivery, gene therapy, and imaging for parasitic diseases [32].

Nanotechnology-Based Vaccines

Nanovaccines improve antigen delivery, stability, and immune response for parasitic diseases. Incorporating adjuvants enhances immunogenicity. Nanoparticle carriers promote antigen trafficking to lymph nodes and antigen-presenting cells, resulting in strong immune responses. DNA vaccines delivered via nanoparticles showed efficacy in murine leishmaniasis models [33]. Virus-like particles (VLPs) are self-assembling, non-infectious nanoparticles mimicking viral structures. They have been applied in malaria and schistosomiasis research, where VLPs efficiently deliver antigens and elicit potent immune responses. They preserve native B-cell epitopes, require no inactivation, and allow scalable production [34].

Employment of Nanotechnology in Parasitic Diseases

Toxoplasmosis

Toxoplasma gondii is an obligate intracellular parasite threatening immunocompromised individuals and pregnant women. Standard therapy with pyrimethamine and sulfadiazine has poor bioavailability, severe side effects, and fails against latent tissue cysts, with growing drug resistance worsening outcomes [35]. Nanotechnology offers alternatives through liposomes, polymeric nanoparticles (PLGA, chitosan), solid lipid nanoparticles, and metallic carriers (silver, gold, selenium) that improve solubility, stability, and blood–brain barrier penetration. Spiramycin-loaded chitosan nanoparticles showed higher bioavailability and efficacy than free spiramycin, lowering parasite burden and extending survival in mice. Curcumin nano-emulsions and silver nanoparticles reduced tachyzoite counts, brain cysts, and drug-induced liver toxicity in animal models [36]. Nanoparticle-based biosensors using gold or magnetic materials provide rapid, sensitive detection of *T. gondii* antigens or DNA, enabling early, point-of-care diagnosis critical for pregnant and immunocompromised patients. Liposomal vaccines carrying *T. gondii* antigens enhanced humoral and cellular immunity, decreasing parasite transmission and congenital infection in experimental studies [37]. Nanotechnology strengthens toxoplasmosis control by improving treatment efficacy, enabling faster diagnostics, and boosting vaccine responses, though further optimization and safety evaluation remain essential before clinical application [38].

Leishmaniasis

Leishmaniasis, caused by *Leishmania* spp., manifests as cutaneous, mucocutaneous, and visceral forms. Current drugs, including antimonials, amphotericin B, miltefosine, and paromomycin, have side effects, resistance issues, and delivery challenges, especially as the parasite resides inside macrophages [39]. Nanoparticles (NPs) enable targeted delivery to infected cells. Liposomal amphotericin B (L-AmB), encapsulated in lipids like phosphatidylcholine and cholesterol, reduces toxicity via slow, site-specific release, improving tissue distribution and drug half-life. Human trials show L-AmB has minimal side effects, high cure rates, and flexible dosing, leading WHO to recommend it as a first-line therapy [40].

Other formulations include PLGA-based amphotericin B NPs for cutaneous leishmaniasis, and mannose-targeted chitosan NPs that enhance macrophage uptake and stability. Carbon-based nanocarriers (graphene, CNTs) also show high efficacy with low toxicity [41].For vaccination, PLGA nanovaccines induce strong humoral and T-cell responses. In *L. infantum*-infected C57BL/6 mice, a PLGA-peptide-MPLA formulation cut liver parasite load by 72.81% and spleen by 61.98% at one month; by month two, reductions reached 64.4% and 73.64%, respectively. In BALB/c mice, similar vaccines elevated IFN-γ, IL-2, and TNF-α [22, 42]. Nanovaccines enhance antigen uptake by dendritic cells and macrophages through phagocytosis or receptor-mediated endocytosis. The internalized antigens are processed and presented via MHC I and II pathways, stimulating both $CD8^+$ cytotoxic and $CD4^+$ helper T cells. This dual activation leads to the secretion of Th1-type cytokines such as IFN-γ, IL-2, and TNF-α, which further activate macrophages to destroy intracellular amastigotes. Concurrently, B-cell activation and antibody production reinforce the humoral response, providing long-term immunity against *Leishmania* infection. The coordinated cellular and humoral responses depicted highlight the broad immunostimulatory potential of nanovaccine formulations (fig. 2) [22].

Malaria

Malaria, caused by *Plasmodium* spp., faces hurdles like drug resistance and poor patient compliance. NPs offer targeted delivery to infected red blood cells (iRBCs), boosting efficacy while minimizing toxicity [43]. Chloroquine-loaded chitosan NPs with DHA achieved parasite inhibition at 1 nM vs. 100 nM for free drug. PEGylated liposomes loaded with artemisinin-curcumin showed 100% cure and sustained drug release in vivo. Polymeric microparticles (e.g., primaquine) improved liver retention but underperformed compared to the free drug [44]. Metal NPs like mesoporous ferrite exploit magnetic targeting to release artemisinin near hemozoin-rich iRBCs. AuNPs aid in delivering drugs to parasite membrane proteins. PEI NPs deliver genes, while chitosan NPs target *Plasmodium* genes via dsRNA. NPs also serve as malaria vaccine carriers. AuNPs carrying *P. falciparum* CSP antigen induced strong antibody responses that blocked transmission in animal models. For diagnosis, antibody-functionalized AuNPs detect malaria biomarkers like HRP2 early in infection [45].

Human African Trypanosomiasis (HAT)

HAT, caused by *Trypanosoma brucei* and transmitted by tsetse flies, progresses from nonspecific symptoms to fatal neurological involvement. Current drugs—pentamidine, melarsoprol, NECT—have toxicities and limitations [46]. Nanotechnology offers alternatives. Pentamidine-loaded NMOFs with PEG coating reduced parasitaemia and prolonged survival in mice. Antibody-coated NPs target parasite surface glycoprotein VSG, enabling drug delivery via endocytosis. Liposomes and solid lipid NPs (SLNs) loaded with pentamidine increased brain delivery; 87% of encapsulated drug reached the CNS versus much less with free drug [47].

Chagas Disease

Caused by *T. cruzi*, Chagas disease has acute and chronic stages involving cardiac and neurological damage. Nifurtimox and benznidazole—hydrophilic drugs—struggle to penetrate host cells and reach intracellular amastigotes [48]. Nanocarriers like liposomes, PACA, and chitosan-coated NPs improve drug delivery, pharmacokinetics, and cell penetration. Benznidazole-loaded NPs showed higher in vitro potency compared to the free drug. Nifurtimox-loaded PACA NPs enabled sustained release over 24 h and reduced parasitaemia. Chitosan-coated NPs with benznidazole improved stability. SLNs loaded with S-benzyl dithiocarbazate outperformed benznidazole in both in vivo and in vitro trials. Gold NPs efficiently delivered drugs across parasite membranes [24]. For vaccines, nanocarriers enhance antigen delivery and immune activation in animal studies. Diagnostics using NPs include urine antigen detection and devices like Nanopoc or electrochemical sensors for antibody detection. offering improvements in sensitivity and time efficiency [49].

Potential Adverse Effects and Safety Considerations of Nanotechnology-Based Antiparasitic Drugs

Although nanotechnology-based formulations offer significant therapeutic advantages, their potential adverse effects must be carefully evaluated before widespread clinical application. Toxicity may arise from factors such as nanoparticle composition, size, surface charge, and accumulation in vital organs including the liver, kidneys, and brain. Some inorganic nanoparticles, like silver or gold, can induce oxidative stress, inflammation, or genotoxicity if not properly engineered or dosed [50]. Regulatory agencies, including the World Health Organization (WHO), and the U.S. Food and Drug Administration (FDA), emphasize the need for comprehensive preclinical and clinical safety evaluations, covering cytotoxicity, immunogenicity, biodistribution, and long-term biocompatibility [51].

Future Perspectives and Concluding Remarks

Therapeutic Potential of Nanoparticles

Nanoparticles (NPs) offer promising improvements in parasitic disease management by enhancing drug delivery, bioavailability, and efficacy while minimizing toxicity. They can target intracellular forms, like amastigotes, which are often inaccessible to conventional drugs. Nanovaccines and nanosensors further extend applications in control and diagnosis [52, 53].

Challenges and Ethnobotanical Integration

Despite established synthesis methods, biomedical application is limited by concerns over cytotoxicity and environmental effects. Ethnobotanical products are explored as alternatives but face challenges like poor drug targeting. NPs may overcome these by enhancing targeted delivery, as shown in various promising studies [54, 55].

Commercialization and Market Trends

NP-based therapeutics—including liposomes, pegylated biologics, gels, nanocrystals, emulsions, and metallic NPs—have entered clinical use, with multiple formulations on the global market. These advanced formulations provide higher value over conventional drugs. In 2022, the parasitic disease treatment market reached USD 1.7 billion and is projected to grow at a 5% CAGR, reaching USD 2.6 billion by 2031 (Grand View Research, Inc.) [22].

Conclusion

Although Nanotechnology represents a powerful and versatile platform for advancing the management of parasitic diseases. By enhancing drug delivery, improving diagnostic accuracy, and strengthening vaccine development, nanomedicine offers solutions to many of the limitations associated with conventional therapies. Liposomes, polymeric carriers, metallic nanoparticles, and nano-biosensors have all demonstrated remarkable potential in overcoming drug resistance, reducing toxicity, and enabling targeted interventions. While experimental and early clinical studies show encouraging outcomes, translation into routine clinical practice requires further investigation into long-term safety, cost-effectiveness, and large-scale production. Integration of nanotechnology into parasitic disease control strategies could significantly reduce the global burden of these infections and pave the way for more effective, accessible, and sustainable healthcare solutions. Further researches needed to ensure that this technology does not cause cellular toxicity, chronic toxicity over long-term use, or any other risks to human health.

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Declaration of Conflict of Interest

The authors declare that there is no conflict of interest.

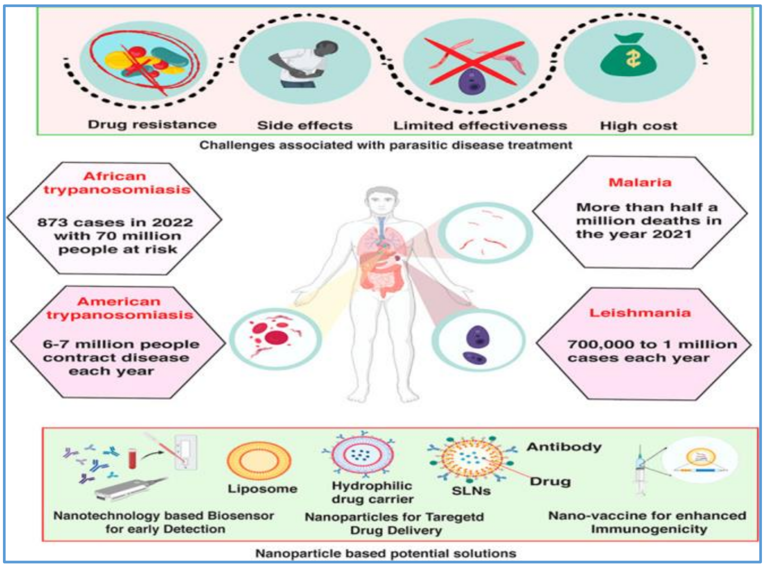

Fig. 1. Nanoparticles based potential solutions [22].

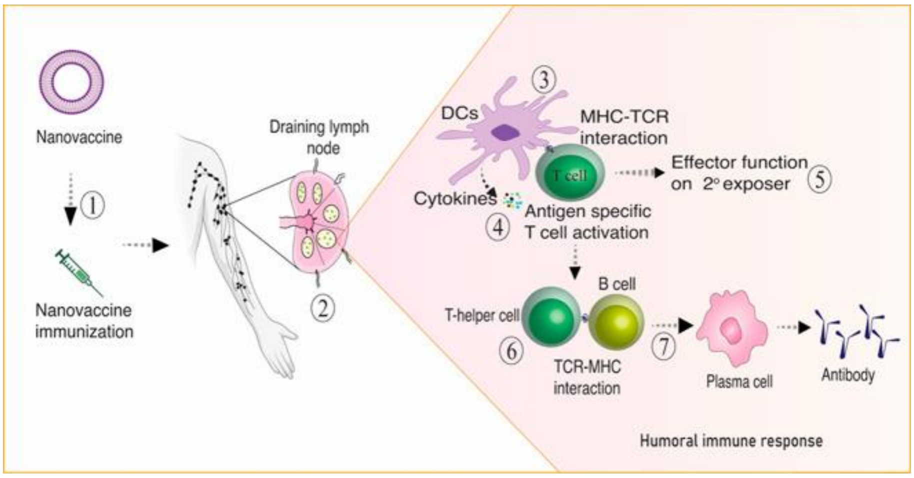

Fig. 2 illustrates the immune pathway activated by nanovaccines [22].

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الاستراتيجيات القائمة على تقنية النانو والطب النانوي في مكافحة العدوى الطفيلية: بحث مرجعي

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الملخص

تُمثِّل العدوى الطفيلية أحد أبرز الأعباء الصحية عالميًا، ولا سيّما في البيئات محدودة الموارد، حيث تواجه العلاجات التقليدية معوّقات عدة، من بينها السُمّية الدوائية، وتطوّر مقاومة الأدوية، وضعف الفاعلية العلاجية. وقد وجد طفيل التوكسوبالزما في جميع أنحاء العالم. وتقريبًا جميع الحيوانات عرضة للاصابة به. وفي هذا السياق، برزت تقنية النانو كنهج واعد، إذ توفّر حلولًا مبتكرة للتشخيص والعلاج والوقاية من هذه الأمراض. تعمل الجسيمات النانوية على تعزيز ذوبانية الدواء وثباته وتوافره الحيوي، مع إتاحة التوصيل الموجَّه وتقليل الآثار الجانبية. وفي مجال التشخيص، تقدّم المستشعرات النانوية والاختبارات المعتمدة على الجسيمات النانوية بدائل سريعة وعالية الحساسية ومنخفضة التكلفة مقارنة بالأساليب التقليدية. كما أسهمت تقنية النانو في تطوير اللقاحات من خلال تحسين ثبات المستضدات، وتعزيز الاستجابة المناعية، وزيادة كفاءة التوصيل. وتشمل التطبيقات طيفًا واسعًا من الأمراض الطفيلية، بما في ذلك الملاريا، والليشمانيا، وداء المقوسات، وداء المثقبيات الإفريقي البشري، وداء شاغاس، وقد أظهرت نتائج واعدة في كلٍّ من الدراسات التجريبية والسياقات السريرية. وعلى الرغم من هذا التقدّم الملحوظ، فإنّ هناك حاجة ماسّة إلى مزيد من الدراسات لمعالجة التحديات المتعلقة بالسلامة والتكلفة وإمكانية التطبيق على نطاق واسع

الكلمات الدالة: تقنية النانو، الطب النانوي، التشخيص النانوي، الأمراض الطفيلية، توصيل الدواء.