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Prospective Review

Nanotechnology-based Approaches for the Treatment of Toxocariasis: A Prospective Review

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ABSTRACT

Toxocariasis, caused by *Toxocara* parasites, is a prevalent parasitic disease affecting millions of people worldwide. Conventional anthelmintic drugs for toxocariasis face challenges such as limited efficacy and potential adverse effects, necessitating exploring alternative therapeutic strategies. Nanotechnology has emerged as a promising approach for the treatment of toxocariasis. This prospective review provides an overview of the potential of nanotechnology in toxocariasis treatment and highlights critical advancements in the field. The current review aimed to provide an overview of toxocariasis and the current challenges in its treatment, such as limited efficacy and potential adverse effects. It emphasized the need for novel therapeutic approaches to overcome these limitations. The subsequent section focused on nanoparticle-based drug delivery systems, discussing the nanoparticles used in toxocariasis treatment, their advantages, and strategies for enhancing drug delivery efficiency. Nanotechnology in targeted therapy is a great strategy for treating toxocariasis. It explored targeting *Toxocara* parasites using nanoparticles, surface modifications for enhanced targeting, and controlled release and sustained drug delivery techniques. Nanodiagnostics and imaging techniques in diagnosing and monitoring provide promising futures for controlling toxocariasis. It explored the use of nanosensors for the sensitive detection of *Toxocara* parasites and various imaging modalities for parasite visualization. These advancements enabled timely intervention and personalized treatment strategies. Furthermore, the application of nanotechnology in vaccine development is fruitful for preventing toxocariasis. It highlights the use of nano vaccines for enhanced immune responses, controlled antigen delivery, and targeted immune cell activation. In conclusion, nanotechnology holds immense potential in the treatment of toxocariasis. Its unique features, such as targeted drug delivery, enhanced diagnostics, and improved vaccine efficacy, offer promising avenues for more effective and personalized approaches. Addressing evaluation, regulatory approval, cost-effectiveness, and scalability challenges is crucial for successful translation into clinical practice. The advancements in nanotechnology can potentially revolutionize toxocariasis treatment and improve patient outcomes.

1. Introduction

Zoonotic diseases transmitted between animals and humans threaten global public health[1,2]. These diseases can arise from various pathogens, including parasites[3-5], bacteria, fungi, and viruses, and their impact on human health can range from mild to severe, sometimes even causing epidemics[6,7].

Toxocariasis is a parasitic infection caused by the larvae of *Toxocara* species, mainly *Toxocara canis* and *Toxocara cati*[8]. It is a prevalent zoonotic disease worldwide, affecting both humans and animals[9]. The infection occurs through the ingestion of *Toxocara* eggs present in contaminated soil or by the consumption of undercooked meat containing the

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parasite larvae[10]. Toxocariasis can lead to three major forms of visceral larva migrans, ocular larva migrans, and covert toxocariasis[11].

Despite efforts to control and treat toxocariasis, current treatment methods face several challenges[12]. Conventional anthelmintic drugs, such as albendazole and mebendazole, have some limitations, particularly against Toxocara's larval stages[13,14]. Additionally, these drugs often exhibit poor bioavailability and limited distribution to the target sites within the body. Furthermore, developing drug resistance in *Toxocara* parasites poses a significant hurdle in achieving successful treatment outcomes. Investigating alternative therapy approaches is necessary due to the side effects of current drug therapies and safety concerns.

Nanotechnology has emerged as a promising approach for improving the treatment of toxocariasis[15]. By harnessing the unique properties of nanomaterials, nanotechnology offers potential solutions to overcome the limitations of conventional therapies[16,17]. One of the critical advantages of nanotechnology-based approaches is the ability to deliver drugs to the target sites precisely[18]. Nanoparticle-based drug delivery systems enable controlled and sustained release of anthelmintic agents, enhancing their therapeutic efficacy and reducing side effects[19]. Moreover, nanotechnology provides opportunities for targeted therapy by functionalizing nanoparticles with ligands that can specifically recognize and bind to *Toxocara* parasites, increasing drug accumulation at the infection sites[20].

In addition to drug delivery, nanotechnology also plays a crucial role in diagnosing and monitoring toxocariasis[21]. Nanosensors and nanomaterial-based diagnostic platforms offer increased sensitivity and specificity for detecting *Toxocara* antigens or antibodies, enabling early diagnosis and timely intervention[22]. Furthermore, advanced imaging techniques utilizing nanomaterials allow for the visualization of parasite migration and localization, aiding in disease monitoring and treatment evaluation. Nanotechnology holds promise in the development of vaccines against *Toxocara* parasites as well.

Toxocara antigens can be used in nanovaccines with better antigen presentation and immunogenicity, resulting in more potent immune responses[23]. Such nano vaccines have the potential to provide long-lasting protection against toxocariasis and reduce the burden of the disease[20,24].

Nanotechnology presents promising possibilities for addressing toxocariasis, a parasitic infection. However, ensuring safety and biocompatibility are crucial aspects that must be prioritized in developing and implementing nanotechnology-based treatments. The potential toxicity of nanomaterials needs to be thoroughly evaluated, and the development of biocompatible nanocarriers is essential to ensure the safe administration of therapeutic agents[25,26]. Furthermore, regulatory and ethical aspects surrounding the use of nanotechnology in healthcare must be addressed to facilitate its translation into clinical practice[27].

However, further research is needed to optimize nanomaterial design, assess long-term safety, and establish the efficacy of nanotechnology-based interventions in clinical settings. Integrating nanotechnology into toxocariasis treatment can revolutionize patient care and contribute to the control and eradication of this parasitic infection.

2. Nanoparticle-based drug delivery systems

Nanoparticles employed in toxocariasis treatment have emerged as possible choices for treating toxocariasis. Various types of nanoparticles have been investigated for their potential to deliver anthelmintic drugs effectively.

2.1. Applications

2.1.1. Liposomes

Liposomes are spherical vesicles composed of lipid bilayers encapsulating hydrophobic and hydrophilic drugs. These nanoparticles offer versatility in drug delivery due to their ability to accommodate a wide range of therapeutic agents[28]. Liposomes have been explored in the delivery of anthelmintic drugs against *Toxocara* parasites[29]. In order to improve stability, drug encapsulation efficiency, and targeting capabilities, it may be necessary to make modifications to the surface of liposomes.

2.1.2. Polymeric nanoparticles

Polymeric nanoparticles are synthesized from biocompatible polymers, such as poly lactic-co-glycolic acid, polyethylene glycol, and chitosan. These nanoparticles offer tunable properties, including particle size, drug release kinetics, and surface charge. Polymeric nanoparticles can encapsulate and protect anthelmintic drugs, allowing sustained drug release[24]. Surface modifications of polymeric nanoparticles can improve their targeting abilities by incorporating ligands that specifically recognize *Toxocara* parasites[30].

2.1.3. Solid lipid nanoparticles

Solid lipid nanoparticles (SLNs) are colloidal systems of solid lipids dispersed in an aqueous medium. The SLNs have shown promise in the delivery of anthelmintic drugs for treating toxocariasis[31]. These nanoparticles offer advantages, such as high drug-loading capacity, good biocompatibility, and stability. The controlled release of drugs from SLNs ensures sustained drug levels at the target site, enhancing therapeutic efficacy[15].

2.1.4. Metallic nanoparticles

Metallic nanoparticles, such as silver and gold, have also been investigated for their potential in toxocariasis treatment[32]. These nanoparticles exhibit antimicrobial properties that can aid in parasite eradication. Metal nanoparticles can be functionalized with anthelmintic drugs or surface-modified to improve their targeting capabilities and enhance drug delivery efficiency[33]. Additionally, the unique physicochemical properties of metal nanoparticles, such as their surface plasmon resonance, can improve imaging and therapeutic applications. The advantages of nanoparticle-based drug delivery systems offer several benefits over conventional drug formulations, making them promising for toxocariasis treatment.

2.2. Advantages of nanoparticle applications

Nanoparticles can encapsulate and release drugs in a controlled manner, ensuring sustained drug levels at the infection site[34]. This controlled release profile enhances therapeutic efficacy and reduces the frequency of drug administration.

2.2.1. Improved drug stability

Nanoparticles can protect drugs from degradation, enhancing their stability and prolonging their shelf life[35,36]. This characteristic is important for anthelmintic medications with limited stability under physiological conditions.

2.2.2. Enhanced drug solubility and bioavailability

Many anthelmintic drugs used in toxocariasis treatment have poor solubility, leading to limited bioavailability. Nanoparticles can improve drug solubility by incorporating hydrophobic drugs within their hydrophobic cores or modifying the drug's physicochemical properties[37]. This could improve drug absorption and systemic distribution[38,39].

2.2.3. Targeted drug delivery

Nanoparticles can be surface-modified with targeting ligands, such as antibodies or peptides, that specifically recognize and bind to *Toxocara* parasites. This active targeting facilitates the accumulation of drugs at the infection site, enhancing treatment efficacy while minimizing off-target effects.

2.2.4. Versatility in drug encapsulation

Nanoparticles can encapsulate various drugs, including hydrophobic and hydrophilic compounds. This versatility allows for the delivery of different anthelmintic agents, combination therapies, or co-delivery of multiple medications, enabling synergistic effects and improving treatment outcomes[40].

2.3. Strategies for enhancing drug delivery efficiency

Several methods can be employed to enhance drug delivery efficiency using nanoparticles, optimizing their therapeutic potential for toxocariasis treatment.

2.3.1. Surface modification

Surface modifications of nanoparticles can enhance their targeting capabilities and improve interactions with *Toxocara* parasites[41].

2.3.2. Stimuli-responsive nanoparticles

Stimuli-responsive nanoparticles can be designed to release drugs in response to specific triggers at the injection site. For example, pH-sensitive nanoparticles can exploit the slightly acidic microenvironment associated with parasites, triggering drug release at the target site. Additionally, stimuli-responsive nanoparticles can respond to enzymatic activity or temperature changes, allowing controlled drug release tailored to the specific needs of toxocariasis treatment[42,43].

2.3.3. Combination therapy

Nanoparticles offer the opportunity for combination therapy by co-encapsulating multiple drugs within a single nanoparticle system. This approach allows for synergistic effects, where drugs can act on various parasite life cycle stages or target different molecular pathways[44]. Combination therapy can enhance treatment efficacy and minimize the possibility of drug resistance.

2.3.4. Particle size and surface electric charge optimization

Nanoparticles' size and surface electric charge play a crucial role in their cellular uptake and biodistribution. Nanoparticles with an optimal particle size can efficiently penetrate tissues and cross biological barriers, facilitating their accumulation at the injection site[45]. Surface charge optimization can enhance interactions with cell membranes, improving cellular uptake and internalization of nanoparticles[46].

3. Nanodiagnostics and imaging techniques

Nanosensors for toxocariosis diagnosis nanotechnology has revolutionized the field of diagnostics by enabling the development of highly sensitive and specific nanosensors to detect *Toxocara* parasites. These nanosensors can detect parasite-specific biomarkers or antigens, allowing for rapid and accurate diagnosis of toxocariasis.

3.1. Biosensors

Biosensors based on nanotechnology principles can detect and quantify specific biomarkers or antigens associated with *Toxocara* parasites[47]. On the surface of nanoparticles, there is a small component known as a recognition element. This element can recognize and interact with samples from patients. Antibodies and aptamers are recognition elements that can be used.

The binding event is then transduced into a measurable signal, providing sensitive and specific detection of the parasites[48].

3.2. Quantum dots

Quantum dots (QDs) are semiconductor nanoparticles that emit fluorescent light when excited by an external light source. These nanocrystals have unique optical properties, such as size-dependent emission and high photostability, making them ideal for diagnostic applications. QDs can be functionalized with specific targeting molecules, enabling their binding to *Toxocara* parasites[42]. The fluorescence emitted by the QDs can be detected and quantified, providing a sensitive and reliable method for parasite detection[49,50].

With advanced imaging techniques, nanotechnology has provided an ability to diagnose and locate *Toxocara* parasites within the human body. These imaging techniques provide valuable insights into the parasite's location, distribution, and interaction with host tissues.

3.3. Magnetic resonance imaging

Nanoparticles can be engineered to possess magnetic properties, enabling their detection by magnetic resonance imaging (MRI). By incorporating iron oxide nanoparticles or other contrast agents, specific to *Toxocara* parasites into the nanoparticle formulation, parasites can be visualized with high resolution in real-time[51-53]. MRI-based imaging techniques offer excellent soft tissue contrast and depth penetration, facilitating the visualization of parasites *in vivo*[54,55].

3.4. Fluorescence imaging

Nanoparticles with fluorescent properties, such as organic dyes or quantum dots, can be utilized for fluorescence imaging of *Toxocara* parasites. These nanoparticles can be functionalized to bind to parasites, explicitly allowing for their selective visualization[56]. Fluorescence imaging techniques provide high sensitivity, allowing for detecting even low parasite burdens[57]. In addition, advanced fluorescence imaging techniques, such as confocal microscopy and multiphoton imaging, offer enhanced resolution and three-dimensional imaging capabilities[58].

3.5. Positron emission tomography imaging

Nanoparticles labeled with positron-emitting radionuclides can be used for positron emission tomography (PET) imaging of *Toxocara* parasites. The radiolabeled nanoparticles can target the parasites through surface modifications or specific binding ligands[59]. The PET imaging provides quantitative and functional information about parasite distribution and metabolic activity, enabling the monitoring of disease progression and treatment response[60].

Advancements in early detection and monitoring nanodiagnostics and imaging techniques have significantly contributed to improvements in the early detection and monitoring of toxocariasis. By enabling sensitive and specific detection of parasites, these techniques facilitate early intervention and treatment, leading to improved patient outcomes.

4. Advantages of diagnostic technique

4.1. Point-of-care diagnostics

Nanosensors and portable diagnostic devices offer the potential for point-of-care testing, allowing rapid and on-site detection of Toxocara parasites[61]. These technologies eliminate the need for centralized laboratories and extensive sample processing, enabling early diagnosis and timely treatment initiation[62].

4.2. Theragnostic

The integration of diagnostics and therapeutics, known as theragnostic, has emerged as a powerful approach to personalized medicine[63]. Nanoparticles can be designed to serve dual functions by combining diagnostic capabilities with targeted drug delivery.

Theragnostic nanomedicine is a way to treat diseases by putting both diagnostic agents and medicines in tiny particles. It can help doctors check how well the treatment is working while also giving the medicine right to the parasites[64].

4.3. Longitudinal monitoring

Nanotechnology-based imaging techniques enable longitudinal parasite load and disease progression monitoring[65]. By repetitively imaging the same host over time, the effectiveness of therapeutic interventions can be assessed, and treatment regimens can be adjusted accordingly. Longitudinal monitoring provides valuable insights into parasite clearance dynamics and host-parasite interaction, guiding clinical decision-making.

5. Nanomaterials in vaccine development

Nanovaccines for toxocariasis prevention nanotechnology has emerged as a promising platform for developing nano vaccines to prevent toxocariasis. Nanovaccines utilize nanomaterials as carriers or adjuvants to enhance the immune response to *Toxocara* antigens, improving vaccine efficacy.

5.1. Nanoparticle-based antigen delivery

Nanoparticles, such as liposomes, polymeric nanoparticles, or virus-like particles, can deliver *Toxocara* antigens to the immune system[24,66]. These nanoparticles offer several advantages, including protection of antigens from degradation, sustained release of antigens, and efficient uptake by antigen-presenting cells[15]. By presenting the antigens in a controlled manner, nano vaccines can enhance antigen presentation and promote robust immune responses[67].

5.2. Adjuvant incorporation

Adjuvants are substances that enhance the immune response to vaccines[68]. Nanomaterials can serve as adjuvants in nano vaccines, stimulating the immune system and promoting a more robust and long-lasting response to *Toxocara* antigens. Various nanomaterials, such as nanoparticles or microparticles, can be engineered to encapsulate or adsorb adjuvants, allowing for controlled release and targeted delivery to immune cells[69,70].

Enhancing vaccine efficacy and immunogenicity nanomaterials offer unique opportunities to strengthen vaccine efficacy and immunogenicity against *Toxocara* parasites. The immune response can be modulated and optimized for maximum effectiveness by incorporating specific features and properties into nano vaccines.

5.3. Controlled antigen release

Nanoparticles can be designed to release antigens in a controlled manner, mimicking the natural process of antigen presentation[71]. This controlled release profile ensures prolonged exposure of the immune system to *Toxocara* antigens, enhancing the generation of specific immune responses, including T helper 1 and inflammatory cytokines, and the development of immunological memory.

5.4. Targeted delivery to immune cells

Nanoparticles can be functionalized with ligands or antibodies specifically targeting immune cells, such as dendritic cells or macrophages[72]. By delivering *Toxocara* antigens directly to these antigen-presenting cells, nano vaccines promote efficient antigen presentation and activation of the adaptive immune response.

5.5. Co-delivery of antigens and immunomodulators

Nanoparticles can be engineered to co-deliver *Toxocara* antigens and immunomodulatory molecules, such as cytokines or toll-like receptor agonists[20]. This combination enhances the immune response by activating and programming immune cells to generate a more vigorous and sustained immune reaction against the parasites.

5.6. Immune cell activation and maturation

Nanomaterials can be designed to interact with immune cells and trigger their activation and growth[73]. By providing the necessary signals for immune cell activation, nano vaccines facilitate the development of robust and long-lasting immune responses, leading to improved vaccine efficacy[74].

Nanomaterials could be used to make better vaccines for toxocariasis, but there are still obstacles to overcome before they can be used in clinics.

6. Future considerations

6.1. Safety and biocompatibility

The safety and biocompatibility of nanomaterials used in nano vaccines need to be thoroughly evaluated to ensure their suitability for human use. Comprehensive studies on potential toxicities, immune responses, and long-term effects are essential for safely translating nano vaccines into clinical practice.

6.2. Scalability and manufacturing

Researchers need to find ways to make nano vaccines cheaper and easier to make in order to use them more widely. Developing efficient and reproducible manufacturing processes is crucial to enable the large-scale production of nanomaterials and nano vaccines.

6.3. Regulatory considerations

The regulatory landscape of nano vaccines must be defined and streamlined to facilitate their development and approval. Regulatory agencies should establish guidelines addressing nanomaterial-based vaccines, ensuring appropriate evaluation and oversight to expedite their clinical translation.

6.4. Immunological challenges

Toxocara parasites have complex immune evasion mechanisms that challenge vaccine development. Future research should focus on understanding the host-parasite interaction and identifying antigens that can induce protective immune responses against *Toxocara* parasites.

7. Conclusion

Toxocariasis is a challenging parasitic disease, and developing effective treatment strategies is crucial for its treatment. Nanotechnology has emerged as a promising approach in the fight against toxocariasis, offering unique advantages in drug delivery, diagnostics, and vaccine development. Nanoparticle-based drug delivery systems have shown the potential to enhance treatment efficacy through targeted delivery and controlled release of therapeutic agents. Surface modifications and sustained drug delivery techniques further improve targeting capabilities. Nano diagnostics and imaging techniques enable sensitive detection and visualization of *Toxocara* parasites, facilitating early diagnosis and monitoring. Nanomaterials have also shown promise in vaccine development, with nano vaccines offering enhanced immune responses and controlled antigen delivery.

Safety evaluation, scalability of manufacturing processes, regulatory considerations, and cost-effectiveness are critical aspects that need to be addressed.

Collaborative efforts between researchers, regulatory agencies, industry partners, and policymakers are essential to overcome these challenges and successfully implement nanotechnology-based therapies.

Emerging nanotechnologies, such as nano theragnostic and nanorobotics, hold immense potential for targeted therapy and personalized medicine in toxocariasis treatment. Addressing barriers to implementation and fostering public acceptance through transparent communication and ethical considerations are essential for the widespread adoption of nanotechnology in managing toxocariasis.

Declarations

Competing interest

The authors declare no conflict of interest.

Authors' Contribution

Hassan Borji conceptualized the study. All authors developed The methodology collaboratively, ensuring a comprehensive approach to the investigation. The entire team carried out the formal analysis and investigation, collectively contributing to the data collection and analysis process. All authors participated in the writing of the original draft of the manuscript. All authors checked and approved the final version of the manuscript for publication in the present journal.

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Availability of data and materials

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethical considerations

All applicable international, national, and/or institutional guidelines for the care and use of animals were followed.

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