

Application of Nanotechnology on the Treatment of Nematodes Diseases: A Review Article

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ABSTRACT

Background: Nematodes were among the first known human pathogens, and many efforts have been made to develop treatments for them. These infections impose a heavy burden on human populations, especially the poor. Nowadays, intervention and treatment programs have been initiated to control and treat onchocerciasis, lymphatic filariasis, gastrointestinal nematodes, and soil-transmitted helminths. Nanotechnology is being used as a dynamic and dynamic tool in research for the treatment of diseases. Here, we review the application of nanotechnology in treatment of nematode diseases.

Methods: This narrative review was conducted using scientific sites such as Medline, Pubmed Science Direct, and Springer Link databases covering 2000 to 2025 to investigate the application of nanotechnology in nematodes diseases treatment. The terms used included: nanotechnology, nanoparticles, nematodes, nematodes treatment, and nanodrug.

Results: Twenty-eight full-text articles were assessed for eligibility, and from them, 23 selected studies on the application of nanotechnology in the treatment of nematode diseases were selected.

Conclusion: The nanodrugs and nanomedicines are future sources for the development of new drugs with therapeutic applications. Nanotechnology has the potential to be used as antinematodal drugs by modifying the biodistribution of drugs and improving bioavailability.

Keywords: Nanotechnology, Nematodes diseases, Treatment, Review

Introduction

Parasitic diseases are increasingly involved in global major morbidity and mortality (1). Nematode intestinal and tissue infections are a major public health problem worldwide, particularly in low socioeconomic groups. Nowadays, mass chemotherapy is considered an important preventive measure against nematode diseases, especially in endemic areas (2). However, these methods are now ineffective due to the development of resistance in parasites and some side effects

of other traditional treatment methods. Another problem is the uneven access of the drug to the target site, which is responsible for the low efficacy of the drug (3).

Nanoparticles are promising for targeted delivery of antiparasitic drugs due to their unusual physical and chemical properties. Many chemical, physical, and biological techniques, as well as living organisms such as plants, fungi, and bacteria, are good sources for the green synthesis of

nanoparticles. Some of these nanoparticles also have nematicidal properties (4). Therefore, the best strategy to combat parasitic diseases is to develop nanotechnology. Nanotechnology uses materials ranging in size from 0.1 to 100 nanometers and manipulates the atoms and molecules of the material (5). Medicine, microbiology and parasitology began to use delivery systems, nanomaterials, liposomes and polymers, nanocapsules, etc. Nanotechnology has the potential to treat a wide range of parasitic diseases. In this review, we discuss the application of nanotechnology in the treatment of nematode parasitic diseases.

Methods

The articles selected were based on medical resource such as PubMed, Scopus, Web of Science, Google Scholar, Magiran, Iran

Medex, Iran Doc, and SID (as Persian databases) using the terms: nanotechnology, nanoparticles, nematodes, nematodes treatment, and nanodrug from 2000 to 2025. To collect accurate information, search was conducted in all published articles including full texts, abstracts, and summaries of parasitology congresses. Information was obtained from articles in English and Persian. The information in each article was extracted independently by two different authors. A search of the narrative literature yielded 187 references. After removing duplicates, studies unrelated to medical nematodes, and non-compliance with the inclusion criteria, 28 references were screened. This left 23 full-text references for relevance assessment. Then, the following information organized in a table: parasite, nanoparticles, and results. The flow chart of the study selection process is shown in Figure 1.

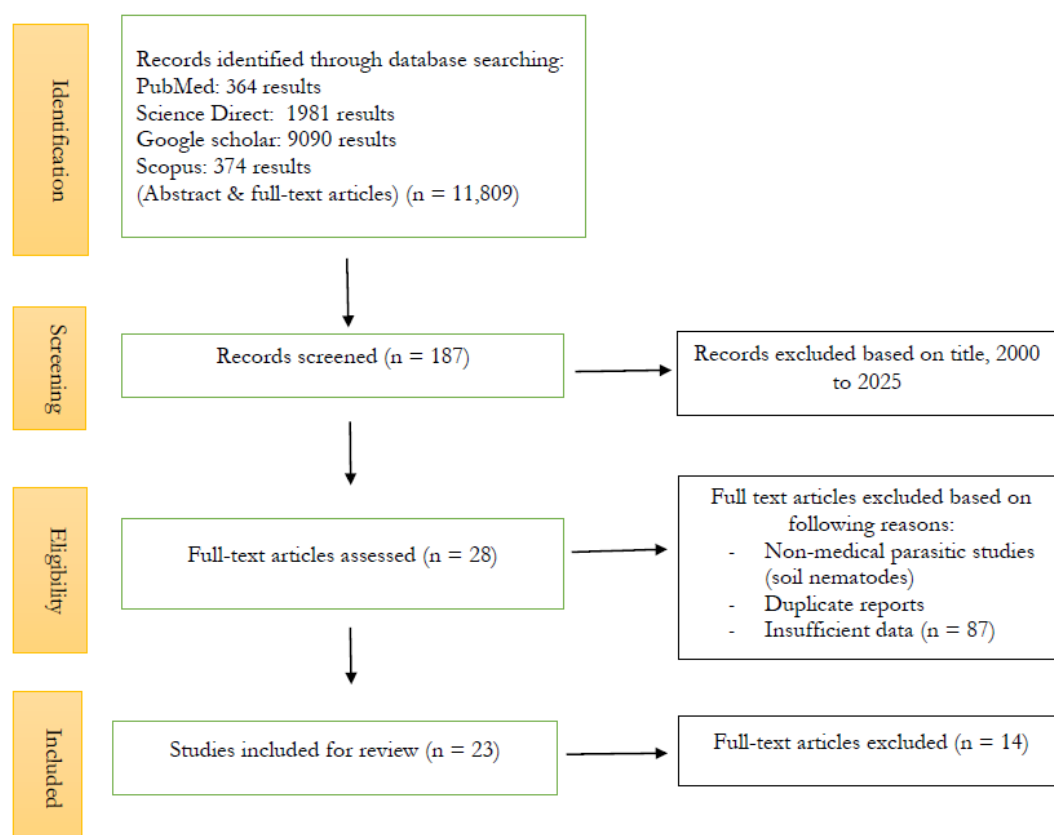


Figure 1: Flowchart of the study selection process from the literature search

Results

After selecting articles, the authors recorded relevant information in a standard data extraction form. Table 1 summarizes the parasitic nematodes treated with nanotechnology particles. A summary of 23 studies (eight *Trichinella spiralis*, five *Brugia malayi*, four *Haemonchus contortus*,

two filarial nematodes, two *Toxocara* spp., one *Wuchereria bancrofti*, and one *Ascaris* spp.) evaluating the role of pharmaceutical nanoparticles in nematode parasites is shown in Table 1. Nanoparticles such as metal nanoparticles alone or loaded with antiparasitic drugs, encapsulated, plant biosynthesis, nanocrystalline or other types were used for drug delivery.

Table 1: Base line parasitic nematodes to treatment by nanotechnology of the included studies

No.	Parasite	Nanoparticles	Results	References
1	<i>Trichinella spiralis</i>	Chitosan (CH) nanoparticles singly or combined with albendazole	Results showed significant reduction in all treated groups with the highest reduction rate of adult 99.1%.	(6)
2	<i>T. spiralis</i>	Chitosan (CH) nanoparticles alone or loaded with full and half dose albendazole	Results revealed a significant improvement in all treated groups with the highest reduction rate (97.3%) of muscle larval counts. A significant decrease in inducible nitric oxide synthetize (iNOS) expression in muscle tissues was in mice treated by CH loaded with a full dose of ABZ (Albendazole) compared to control group	(7)
3	<i>T. spiralis</i>	Mebendazole loaded to silver nanoparticles (AgNPs)	Our results revealed that each of the three lines of treatment (mebendazole alone, AgNPs alone and mebendazole loaded to AgNPs) showed significant ($p \leq 0.001$) reduction in the mean larval count compared to the infected control.	(8)
4	<i>T. spiralis</i>	Chemically and biosynthesized (<i>Commiphora myrrha</i> extract) silver nanoparticles	The results showed complete inhibition of the infectivity of ML exposed to sublethal doses of chemical and myrrh 36prepared AgNPs when used to infect animal models.	(9)
5	<i>T. spiralis</i>	NLCs for oral delivery of albendazole	In the migrating phase reduced larval count by 62.9, 99.6 and 89.5 % after administration of suspension, coated and uncoated NLCs, respectively.	(10)
6	<i>T. spiralis</i>	Chitosan, cellulose derivatives, and poloxamer	This analysis indicated that the microcrystals made with hydroxyethyl cellulose or chitosan appear to be the best options to optimize oral absorption of the active pharmaceutical ingredient.	(11)
7	<i>T. spiralis</i>	Niosomal versus nanocrystalline Ivermectin (IVM)	Niosomal IVM efficacy exceeded the nanocrystalline IVM in treatment of different phases of trichinellosis.	(12)
8	<i>T. spiralis</i>	MBZ with chitosan and zinc oxide nanoparticles	The results of adult worm count in all treated groups showed the highest percentage reduction (96.4%).	(13)
9	<i>Brugia malayi</i>	Ivermectin, doxycycline, polyanhydride nanoparticles	The use of a biodegradable polyanhydride nanoparticle-based platform for the co-delivery of the antibiotic doxycycline with the antiparasitic drug, ivermectin, to reduce microfilarial burden and rapidly kill adult worms. When doxycycline and effective killing of adult female <i>B. malayi</i> filarial worms was achieved with approximately 4,000-fold reduction in the amount of drug used. Additionally the time to death of the microfilaria was also significantly reduced (five-fold).	(14)
10	<i>B. malayi</i>	Ivermectin in chitosan-alginate nanoparticles	To substantiate increase in MIF activity, pharmacokinetics study which revealed a greater peak plasma concentration (45.3 ± 1.79 ng/mL), area under the concentration curve (298 ± 38.7 ng d/mL)	(15)

			and extended mean residence time (23.4 ± 8.56 d) of IVM in chitosan–alginate nanoparticles.	
11	<i>B. malayi</i>	Poly (lactic-co-glycolic acid) nanoparticles encapsulated ivermectin (nano-IVM)	Nano-IVM was also found to be effective against adult stage parasites causing 36.67 % worm mortality and 75.89 % in combination with diethylcarbamazine (DEC); however, female sterilization remains almost similar.	(16)
12	<i>B. malayi</i>	PLGA nanoparticles of doxycycline hydrochloride (DOX) (DPNPs)	This targeting resulted in significantly greater <i>in vivo</i> antifilarial activity of DPNPs when compared to DOX solution as gauged by several parameters in <i>B. malayi</i> . Interestingly, the magnification in efficacy was obtained despite equivalent <i>in vitro</i> antifilarial activity of DOX solution and DPNPs against <i>B. malayi</i> worms.	(17)
13	<i>B. malayi</i>	AgNPs	The apoptosis by AgNPs is possibly mediated through peroxynitrite dependent depletion of glutathione (GSH).	(18)
14	<i>Wuchereria bancrofti</i>	<i>Terminalia chebula</i> extract to synthesize AuNPs	AuNPs exhibit superior antifilarial activity against <i>W. bancrofti</i> , and is able to induce oxidative stress and apoptotic cell death in filarial parasite mediated through mitochondria.	(19)
15	Filarial nematode	Poly (vinyl alcohol) capped silver nanoparticles	Ultrasound increased the reaction rate and yield, and improved the quality of the AgNP in terms of regular size distribution. The synthetic route follows the principles of green chemistry. The biocompatible polymer (PVA) capped AgNPs are suitable for the treatment of filarial nematode.	(20)
16	Filarial nematode	Chitosan functionalized with gold nanoparticles (GNPs)	The developed nanoparticle shows no detectable sign of toxicity when evaluated <i>in vitro</i> or <i>in vivo</i> . Therefore, the synthesized green GNPs appear to be a substantial promise as an efficacious broad-spectrum nanotherapeutic agent with safe outcome for clinical attempt.	(21)
17	<i>Ascaris</i> spp. (egg)	AuNPs	Based on this study, AuNPs can significantly reduce the egg count of <i>Ascaris</i> spp. comparing to negative control ($P < 0.05$, t-test)	(22)
18	<i>Haemonchus contortus</i>	<i>Lansium parasiticum</i> aqueous extract protected silver nanoparticles (LAgNPs)	LAgNPs was also quite effective in inhibiting egg hatching, with an IC ₅₀ value of 144.4 ± 3.1 nM at 48h of exposure. Exposure to LAgNPs generated oxidative stress and mediated physical damage in the worms 'tissue.	(23)
19	<i>H. contortus</i>	<i>zinc oxide</i> nanoparticles	ZnO-NPs exerted significant wormicidal effects via induction of oxidative/nitrosative stress and DNA damage.	(24)
20	<i>H. contortus</i>	silver nanoparticles (AgNPs) synthesized extract of <i>Azadirachta indica</i>	1.0 µg/ml concentration induced $85 \pm 2.89\%$ egg hatch inhibition. The experimental plant extract contains reducing properties for the synthesis of AgNPs which, in turn, showed potent anthelmintic properties.	(25)
21	<i>H. contortus</i>	silver and selenium nanoparticles, and extract of <i>Punica granatum</i>	The results showed that the lowest concentration of AgNPs, SeNPs, and extract significantly inhibited egg hatching. Adult <i>H. contortus</i> mortality percentage was also significantly affected by all three agents.	(26)
22	<i>Toxocara canis</i>	Solid lipid nanoparticles (SLN) of albendazole (ABZ)	The anthelmintic efficacy of ABZ-SLN confirmed the reduction in larvae count in the liver, lung, brain and kidney.	(27)
23	<i>T. vitulorum</i>	ZnO and FeO	The results showed that both of the nanoparticles could significantly decrease worm's mobility, increase mortality rate as well as elevate malondialdehyde (MDA) and nitric oxide (NO) content. Super oxide dismutase (SOD) activity was elevated with the low concentration of the nanoparticles but it was decreased in higher ones.	(28)

Discussion

The use of chemical anthelmintics to treat and control nematodes is common. However, these anthelmintics are expensive, and resistance to them has developed over time (29). Mebendazole and ABZ are commonly used to treat *Trichinella spiralis*, but none of these drugs are completely effective against larvae of *T. spiralis* (30). Due to its limited bioavailability and high strength, chitosan (CH) nanoparticles were used alone or in combination with ABZ to treat experimental trichinellosis to be a means of delivering ABZ, improving its therapeutic effect, increase ABZ dissolution rate, to enhance its antiparasitic activity during the muscular phases of *T. spiralis* infection (6, 7). In some cases, antiparasitic drugs have little ability to penetrate into the parasitic cysts, enhanced by the use of nanoparticles. For example, the benzimidazole drugs used to treat trichinellosis has limitations in penetrating into the larvae encysted in muscles. When mebendazole is loaded to silver nanoparticles (AgNP), the anthelmintic effect of mebendazole is improved in treatment of muscular phase of experimental trichinellosis (8, 9). Another example was the use of niosomes to increase the effectiveness of oral IVM against various stages of *T. spiralis* infection. As a result, the effect of niosomal IVM in the treatment of various stages of trichinellosis has gone beyond nanocrystalline IVM (12). A major challenge for the pharmaceutical industry is the poor solubility of most drugs, which leads to bioactivity and reduced delivery.

One of these is albendazole, which is used in oral chemotherapy against intestinal parasites due to its broad spectrum of activity, but it has low bioavailability due to its very low solubility in water. Microcrystals formulations based on chitosan and cellulose derivatives increase the solubility of albendazole, to increase its antiparasitic activity, solves this problem

and optimizes the oral absorption of the drug active substance against *T. spiralis* (11). The chitosan coated nanostructured lipid carriers (NLCs) for oral delivery of albendazole enhanced the efficacy of albendazole against *T. spiralis* compared with suspension with chitosan coated NLCs being superior (10).

The current antifilarial treatments are not partially satisfactory due to the deep parasitic location in the human lymphatic system, but improved IVM antifilarial activity using chitosan–alginate nanoparticles prepared by a modified complex coacervation method will further penetrate the drug (15) and also in order to provide an alternative, have constructed ultrafine PLGA nanoparticles of doxycycline hydrochloride (DOX) (DPNPs). Interestingly, the magnification in efficacy was obtained despite equivalent in vitro antifilarial activity of DOX solution and DPNPs against *B. malayi* adult worms (17).

For co-delivery of doxycycline with the antiparasitic drug ivermectin, a biodegradable polyhydride nanoparticle-based system was synthesized to significantly reduce the burden of microfilaria and eliminate *B. malayi*, significantly reducing macrofilaria death time (14). The antifilarial activity of poly (lactic-co-glycolic acid) nanoparticles encapsulated ivermectin (Nano-IVM) against human lymphatic filariid *B. malayi*. Thus, the combination of entrapped IVM with DEC exhibited enhanced microfilaricidal and marginally better macrofilaricidal efficacy than any of the single formulation or drugs combination (16). Silver nanoparticles (AgNPs) induce apoptosis but the cause has not yet been elucidated. A study of apoptosis in the *B. malayi* parasitic model concluded that AgNPs may cause apoptosis through a reduction in glutathione peroxynitrite (GSH) (18).

Chitosan is unique due to its low toxicity and immunogenicity and antimicrobial

activity. The most interesting feature of chitosan is that it is toxic to microorganisms but shows very little toxicity to mammalian cells (31). Chitosan was used together with the terminal extract of *Terminalia chebula* to synthesize gold nanoparticles (AuNPs) and the anti-parasitic activity of *W. bancrofti* was investigated. AuNPs are able to induce oxidative stress and apoptotic cell death in filarial parasites mediated by mitochondria. In addition, the nanomaterials synthesized appeared to be non-toxic to mammalian cells (19). Poly (vinyl alcohol) (PVA) capped stable AgNP with sonochemically synthesized are suitable for the treatment of filarial nematode (20). Green gold nanoparticles (GNPs) synthesized as an effective nanotherapeutic agent with a broad-spectrum and safe results for antifilarial activity are significant promising (21). The zinc oxide (ZnO) and iron oxide (FeO) nanoparticles could significantly decrease *Toxocara vitulorum* mobility, increase mortality rate which does this by exert of oxidative/nitrosative stress (28). The solid lipid nanoparticles (SLN) of ABZ and evaluation of its anthelmintic effect in a mice model after oral administration reduced the number of larvae in liver, lung, brain and kidney, which could be a promising formulation for the treatment of *T. canis* infection (27). The AuNPs could be significantly reduce viability of *Ascaris* spp. egg comparing to negative control. The AuNPs solution might be applicable as a disinfectant system for decontamination of *Ascaris* spp. contamination (22). Nanoparticles can be used in cases where there is resistance to common antiparasitic drugs, for example *Lansium parasiticum* aqueous extract-protected silver nanoparticles (LAgNPs) has been used to against albendazole-resistant gastrointestinal parasite *Haemonchus contortus*. In fact, the results of such research provide an opportunity to find alternative drugs in cases of drug-resistant parasitic helminths (23).

Conclusion

Nanodrugs and nanomedicines are future sources for the development of new drugs with therapeutic applications. Nanotechnology has the potential to be used as antinematodal drugs by modifying the biodistribution of drugs and improving bioavailability.

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Conflicts of Interest

The author declares no conflicts of interest.

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