Antiparasitic Activity of Nanomaterials

A. Najitha Banu, Natasha Kudesia, Neha Rana, Durdana Sadaf, and A. M. Raut

Abstract Parasites continue to cause substantial illness and mortality all over the globe to date. Malaria, Chagas disease, Ascariasis, Leishmaniasis, etc., are the major parasitic infection that carries a tremendous burden of diseases, particularly in tropical and subtropical regions. Antiparasitic drugs are widely used for the control of parasitic diseases, but drawbacks such as low efficacy and short shelf-life limit their utilization. The incompetence of the antiparasitic drugs and the absence of a functional vaccine has prompted the development of a new strategy for the treatment of these diseases. With the continuous development of nanotechnology, nanoparticles have attracted a lot of attention because of their great potential in medical applications. Different nanomaterials function as antiparasitic drug carriers to overcome the difficulties faced during drug delivery. Nanomaterial-based drug delivery system effectively targets the loaded drugs into the sites of infection as well as increases the efficacy of the drugs. While nanoparticles are efficient in the treatment of parasitic diseases, they also demonstrate promising applications in controlling parasite vectors. Currently, research is also being carried out for developing nanovaccines that are suitable candidates to prevent and fight against parasites. This chapter focuses on different nanocarriers developed for antiparasitic drug delivery. The role of nanoparticles in keeping a check on vectors harboring parasitic organisms has also been discussed. In the final section, major challenges and further research on the use of nanoparticles in making potent vaccines are recommended.

Keywords Parasitic infections · Nanotechnology · Drug delivery · Vector control · Nanoparticles · Nanovaccines

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1 Introduction

Since antiquity, human beings and their ancestors are suffered from various diseases which are either caused by infectious pathogens (bacteria, viruses, parasites) or by the process of aging. Parasitic diseases are found throughout the world, but they are mostly endemic in tropical areas leading to morbidity, mortality, and socioeconomic backwardness in these areas [1]. The climate is the primary reason for the high prevalence of parasitic infections in the tropics; high temperatures and humidity are optimal for parasite growth. The infected populations are mostly living in tropical, subtropical, and remote areas where they are far behind the development, as these diseases are closely linked to many socioeconomic factors such as poor sanitation, lack of personal hygiene and health as well as poverty, development in drug resistance, and increase in global tourism [2].

Human parasite infections have a wide range of impacts, ranging from acute symptoms like severe diarrhea or anemia to more long-term issues like growth retardation, chronic limb, and organ enlargement, or blindness. Despite medical advancements, parasitic diseases continue to pose a significant threat to human health and life [3]. Moreover, parasitic infections are not restricted to human beings but are an equal threat to wild and domestic animals wreaking havoc on already poor countries [4]. A parasitic disease is an infectious disease that is caused or transmitted by a parasite, also referred to as parasitosis. A parasite (Greek pará: besides, on; sítos: food) is an organism that lives in or on another organism and derives nourishment at the expense of its host health [5]. Parasites are a wide and multifaceted group of organisms that can be broadly classified into three main categories: protozoa, helminths, and ectoparasites. Protozoa are microscopic, unicellular, heterotrophic organisms that multiply by binary division in people and lead to serious infections from a single cell. Protozoans that thrive in blood or tissue are transmitted with the help of an arthropod vector, whereas intestinal-inhabited protozoans are transmitted by the fecal-oral route. The protozoans are further classified on the mode of locomotion (Fig. 1). Helminths are large (1 mm–1 m long), invertebrate multicellular worms characterized by elongated round (nematodes) or flat bodies (cestode and trematode). Mortality by helminthic diseases is not high, but they have a negative impact on the host's nutritional and immune condition, resulting in low resistance to subsequent infections [6]. Ectoparasites thrive either on the surface of the skin or burrow into it from which they derive their sustenance including lice, ticks, mites, and fleas. Ectoparasites are potential vectors for interspecific and intraspecific disease transmissions.

Several strategies have been undertaken in previous years to combat parasitic diseases. Antiparasitic drugs are used for the control of these diseases. However, the drawbacks of antiparasitic drugs such as toxicity and negative impact on human life could not be ignored. Likewise, as the drugs used in the treatment are so expensive, their use is mostly limited in undeveloped and developing countries [7, 8]. However, there is a major obstacle before the treatment efficiency of various diseases, which is the delivery of therapeutic agents to the target area. The application of conventional therapeutic agents has limitations such as non-selectivity, undesirable side effects,

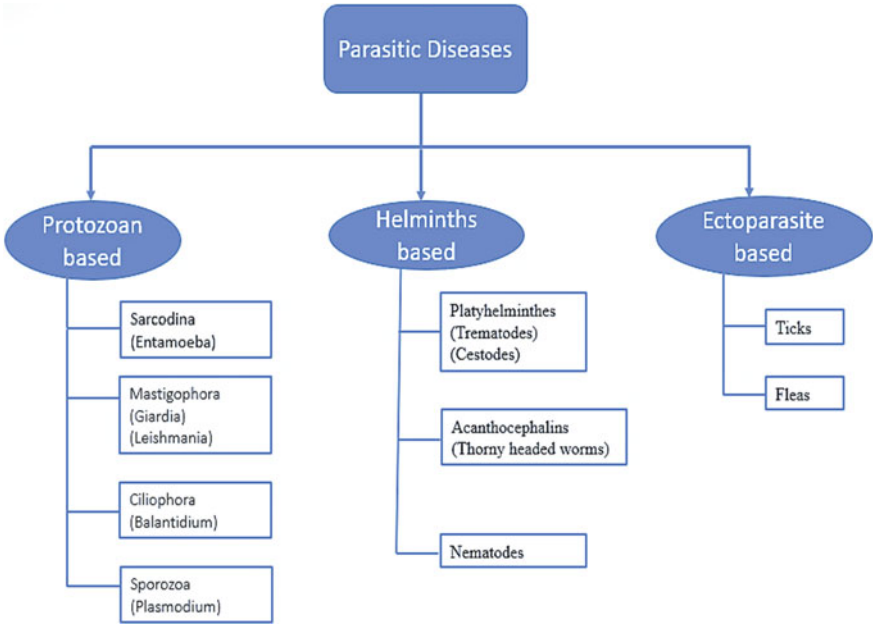

Fig. 1 Flowchart presenting types of parasites

low efficiency, and poor biodistribution [9]. Malaria is on the increase because of the development of drug resistance on the part of the parasites and insecticide resistance on the part of the mosquito vectors. Sleeping sickness is also on the increase, but there are no cheap and effective drugs or simple control measures to combat it. Despite a vast amount of effort, there are no vaccines against any human parasitic diseases [10]. Controlling the population of vector organisms, harboring these parasites has been considered to be a major approach to limiting the spread of parasitic diseases. The application of insecticide had proved to be highly successful, but due to the prolonged usage, resistance was developed by the vector against the insecticide. Similarly, a wide species of *Aedes, Culex,* and *Anopheles* have developed resistance against a wide variety of insecticides such as carbamates, pyrethroids, and organophosphates [11–13]. In the past few years, microbial agents like *Bacillus sphaericus* and *Bacillus thuringiensis* have received gained a lot of popularity in combating the vector population. These bacterial insecticides act as effective and eco-friendly mosquito larvicidal agents. They act as an ultimate substitute for chemical insecticides. However, presently a high level of resistance is observed in the vector population against them [14, 15]. Similarly, disease-causing fungi referred to as entomopathogenic are highly destructive pathogens that can help in keeping a check on the vector population. However, entomopathogenic fungi also have limitations such as difficulty in their mass production and the need for highly humid conditions makes entomopathogenic fungi slow killers [16].

These drawbacks have prompted the development of a novel strategy to control parasitic diseases. In this scenario, nanotechnology has been regarded as a boon. The use of nanotechnology and nanomaterials in medical research is growing rapidly. Nanotechnology makes use of materials and systems at atomic scales (1–100 nm). The size of nanoparticles (NPs) is alike to that of most biological structures and molecules; therefore, nanomaterials can be helpful for both in vivo and in vitro parasitical studies and applications [17]. Formation of stable interactions with ligands, variability in size and shape, high carrier capacity, and convenience of binding of both hydrophilic and hydrophobic substances makes NPs favorable platforms for the target-specific and controlled delivery of micro- and macromolecules in parasitic disease therapy [9]. Likewise, there has been an increase in the plant-based and microbial-based metal NPs in vector control, owing to their pupicidal and larvicidal activity. The underlying mechanism may be related to the ability of NPs to penetrate the exoskeleton and bind to the proteins and DNA. This leads to the denaturation of the cells and organelles [18–20]. Nowadays, nanovaccines are also gaining a lot of prominence as NPs can be utilized as adjuvants for generating long-lasting immunity through oral, intravenous, and transdermal administration [21, 22]. Therefore, the main focus of this chapter is to emphasize the growing importance of nanotechnology in controlling parasitic diseases. The chapter also throws light upon different kinds of parasitic diseases along with their vector species. Different strategies undertaken to date along with their drawbacks have also been discussed. Finally, the role of nanotechnology in controlling parasitic diseases through drug delivery as well as putting a check on vector populations has been explained. In the final section, the importance of designing nanovaccines for developing long-lasting immunity has been done for future prospects.

2 Nanotechnology-based Solutions (Targeted Drug Delivery) for the Treatment of Parasitic Diseases

Parasitic infections are one of the leading causes of death in tropical and subtropical locations across the world. Malaria, produced by the single-celled apicomplex *Plasmodium* protozoan, is still a major parasitic illness. *Plasmodium falciparum*, *Plasmodium vivax*, *Plasmodium malariae*, and *Plasmodium ovale* are four significant species of this protozoan that may infect humans [23]. In 2013, 198 million malaria cases were recorded globally, according to the World Health Malaria Report 2015. Malaria claimed the lives of 584,000 people worldwide (90% of the deaths were in Sub-Saharan Africa), with 78% of those under the age of five. The bulk of malaria cases in Africa is caused by the renowned *P. falciparum*, and the most common vector in transmitting malaria is *Anopheles gambiae*, one of the most efficient and difficult-to-manage vectors. In 2014, malaria was still being transmitted in 97 countries, putting 3.2 billion people at risk of illness, with 1.2 billion at high risk [24, 25]. Despite scientific progress, infectious diseases such as malaria continue

to be a global problem. The development of resistance to many of the currently available antimalarial medications is the fundamental reason why this illness still poses a threat in many areas throughout the world [26]. Enhanced solubility and bioavailability of hydrophobic pharmaceuticals, greater drug payload, extended drug half-life, improved therapeutic index, and controlled release of bioactive along with reduced immunogenicity and toxicity are all advantages of nanotechnology-based drug delivery systems [27–29].

NPs, especially liposomes, have gained considerable prominence in the field of drug delivery for the treatment of human diseases, particularly cancer; they provide several advantages, including controlled drug release, protection of the drug against degradation, improved pharmacokinetics, long circulation, and passive targeting to tumors and inflammatory sites due to the enhanced permeability and retention effect. The functionalization of liposomes with monoclonal antibodies or antibody fragments to generate immune liposomes has emerged as a promising strategy for targeted delivery to and uptake by cells overexpressing the antigens to these antibodies, with a consequent reduction in side effects [30].

2.1 Recent Advances in Treating Leishmaniasis: Impact of Nanotechnology

Leishmaniasis is one of the fatal infectious diseases caused by an intracellular protozoan. There are three main types of leishmaniasis, viz., Visceral (VL), often known as kala-azar, cutaneous (CL), and mucocutaneous leishmaniasis [31]. According to Kalepu and Nekkanti et al., 40% of the novel compounds licensed for therapeutic development, including those for the treatment of leishmaniasis, have limited water solubility, and this proportion rises to 90% when medicines in the discovery pipeline are included [32]. Several studies have revealed the use of nanosystems for treating leishmaniasis in the recent decade, including metallic, polymeric, and lipid NPs, as well as liposomes and nanocrystals [33]. According to Nanomedicine and drug delivery Symposium (NanoDDS 2019), the efficacy of anti-leishmaniasis drugs can be increased by releasing the drugs in macrophage-rich organs like the liver, spleen, and bone marrow because in leishmaniasis infection macrophages are the main phagocytic cells involved (Fig. 2) [34]. The macrophage cells have receptors that can internalize and engulf drug-loaded nanoparticles in the range of 50–500 nm [35].

2.2 Techniques for Targeted Drug Delivery

Active and passive techniques are the two basic ways for targeted administration of drugs.

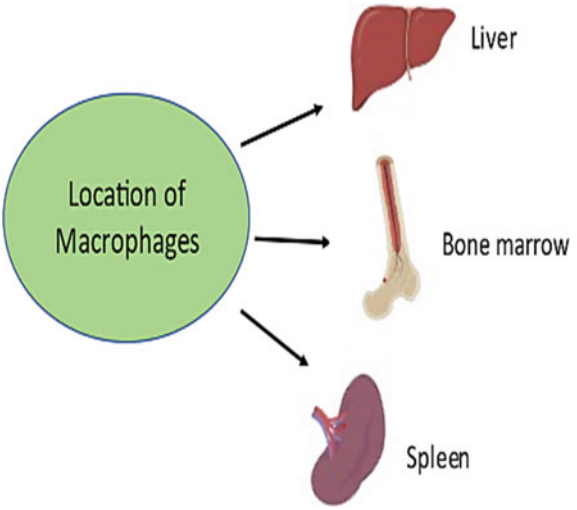

Fig. 2 Macrophage-rich organs targeted for Leishmania treatment

(a) Active targeting

Urban et al. [36] described an immunoliposomal nanovector capable of delivering its contents to *P. falciparum*-infected red blood cells (pRBCs). The scientists found that delivering chloroquine within pRBCs-specific monoclonal antibody BM1234-functionalized immunoliposomes increased the efficiency of the antimalarial medication. The antibody revealed a preference for pRBCs with parasites in the late stages of maturation. In cell culture, surface-functionalized liposomes with an average of five antibody molecules per liposome performed significantly better than non-functionalized liposomes. The results show that encapsulating chloroquine and fosmidomycin in immunoliposomes increased treatment efficacy ten-fold [36]. Using peptides and long-circulating liposomes, targeted therapy using liposomes has also been researched for malaria treatment. A 19-amino acid sequence from the N-terminal region of a protein synthesized by *P. berghei* circumsporozoite was used to surface functionalize PEGylated liposomes. Bioavailability studies of such a system revealed that surface-functionalized liposomes were 100-fold more selectively targeted to hepatocytes and non-parenchyma liver cells, and organs of the body revealed that 80% of the injected dose was found in the liver within fifteen minutes and that the uptake of peptide-bearing PEGylated liposomes by hepatocytes was over 600-fold higher than that of cardiac cells and over 200-fold higher than that in lungs or kidney cells. These findings imply that by employing peptide-targeted liposomes, antimalarial medications might be tailored to eliminate parasites from hepatocytes [37].

(b) Passive targeting

In malaria, passive targeting is neglected. When nanocarriers are administered intravenously, the mononuclear phagocyte system quickly absorbs them. As a result of the nanocarriers carrying medications inside macrophages, the

phagocyte uptake pathways are blocked, resulting in a two-fold increase in macrophage capacity. While this may delay the antimalarial drug's immediate action, it may also result in a depot-type release of medicines into the blood. This depot-type method might be useful for treating *P. vivax* infections in which the hypnozoites are latent within the hepatocytes. Because these hepatocytes reside in close proximity to the Kupffer cells, a depot release may be more therapeutically effective. Surface modification of the nanodrug delivery carrier with hydrophilic polymers such as poly (ethylene glycol) might potentially be used to accomplish passive targeting. Passive targeting is known to delay phagocytosis, resulting in a change in the drug's pharmacokinetic profile by lengthening the drug's plasma half-life. Malaria, which was once thought to be a problem only in impoverished countries, is now found in both industrialized and developing nations. The development of quick drug resistance, widespread presence, and limited private sector participation due to a lack of economic advantages are all important challenges in the fight against malaria. Furthermore, bringing a novel drug to market takes a long time and demands a significant expenditure [38]. To address this issue, it is critical to maximize the effectiveness of already available medications and improve their therapeutic efficiency. Combination therapy is preferred over monotherapy for the treatment of malaria, and artemisinin-based combination therapy is the most popular among the several options [39]. Despite the fact that artemether and lumefantrine are widely used as a combination therapy for uncomplicated malaria, the currently available formulation has various flaws, including drug breakdown in the gastrointestinal system, unpredictable absorption, and so on. Because of its nontoxicity, cost-effectiveness, and high success rate, the artemisinin combination therapy of artemether and lumefantrine is the first-line treatment for uncomplicated malaria [40]. The combination of artemether and lumefantrine is currently accessible as oral tablets. Even though this combination has a high success rate, the oral dosage form has several drawbacks, including; (a) the need to take these drugs with fat-fortified food to avoid low and/or erratic absorption, (b) the need to administer the drugs twice a day, and (c) drug degradation in acidic conditions [41]. These circumstances require the application of novel drug delivery approaches that have been previously successful in overcoming pharmacokinetic mismatches such as bioavailability, controlled release, and stability, in comparison to other drug molecules that are used to treat similar parasitic infections in general and malaria in particular [42–44]. As a result, the goal of this study is to develop an injectable (intraperitoneal; i.p.) co-loaded (artemether) nanolipid drug delivery system with the following advantages:

1. Method of administration: Fabricating injectable formulations avoids drug degradation in the gastrointestinal system, bioavailability dependence on fat intake, low patient compliance, and variable assimilation, among other issues [45].
2. Drug delivery systems: Due to the lipophilicity of the core materials (artemether and lumefantrine) and previous successes in using these lipids as

carrier materials in developing injectable delivery systems, lipid nanoparticles were chosen over other carrier materials in the current formulation [46].

Due to these issues, an injectable formulation of artemether and lumefantrine is required, which is currently unavailable. Recently, curcuminoids, a type of phytochemical, have been found to exhibit promising antimalarial activity. Curcuminoids are polyphenols obtained from the root of *Curcuma longa* Linn. Curcumin, desmethoxycurcumin, and bisdemethoxycurcumin are the three main active components; among them, curcuminoids are being researched for use in the treatment of inflammation, oxidative stress, hepatic diseases, diabetes, and cancer [47–50]. In vitro (chloroquine resistance and sensitive *P. falciparum* strains) and in vivo (*P. berghei*), curcuminoids have shown considerable antimalarial efficacy [39, 51]. These delivery systems have the advantages of being biodegradable and biocompatible, as well as allowing for regulated medication release. Drugs encapsulated within liposomes can also be protected from chemical degradation and have increased solubility. According to the researcher Owais, chloroquine was encapsulated into MAb F10-bearing liposomes and its efficiency was assessed in mice infected with chloroquine-susceptible or chloroquine-resistant *P. berghei* [52]. The chloroquine-loaded MAb F10-liposomes were able to remove both chloroquine-susceptible and chloroquine-resistant *P. berghei* infections. On days 4 and 6, chloroquine-resistant *P. berghei* was completely cured after intravenous injection of chloroquine-loaded MAb F10-liposomes at a dose of 5 mg/kg of body weight each day. This was attributable to the MAb F10-fragment's strong selectivity for *Plasmodium*-infected erythrocytes. For the past decade, a renewed attempt to identify next-generation antimalarials has been ongoing since resistance to all existing antimalarials has been reported [52].

In recent decades, the use of nanomaterials in medicine for the diagnosis and treatment of parasitic disorders has acquired a lot of interest. Nanomaterials have shown diagnostic potential against malaria, toxoplasmosis, cryptosporidiosis, amebiasis, and leishmaniasis [53–56]. NPs have shown efficacy in targeting infected macrophages for the treatment of visceral leishmaniasis (VL) when used as a therapy option for parasitic infections [57]. Silver, alone or in conjunction with chitosan NPs, had anti-toxoplasma actions by increasing serum and decreasing parasite burden. Spiramycin-loaded chitosan NPs have been found to cure toxoplasmosis efficiently. Combination nanotherapy with silver, chitosan, and curcumin NPs has been demonstrated to successfully eliminate parasites from the intestine without causing any side effects in giardiasis.

NPs' biodegradability and non-immunogenic qualities make them ideal delivery vehicles for medicines and vaccines. Pfs25H, a nanoformulation of recombinant *P. falciparum* protein, was used as malaria transmission-stopping vaccine, preventing the parasite from infecting mosquitos. Similarly, antigen-specific immune responses against *P. vivax* were elicited by polymer poly (lactide-co-glycoside) acid (PLGA) NPs containing the malaria antigen VMP001 and immunostimulatory monophosphoryl A (MPL-A). Furthermore, macrophages and DCs successfully absorbed iron oxide nanoparticles coupled with recombinant merozoite surface protein 1

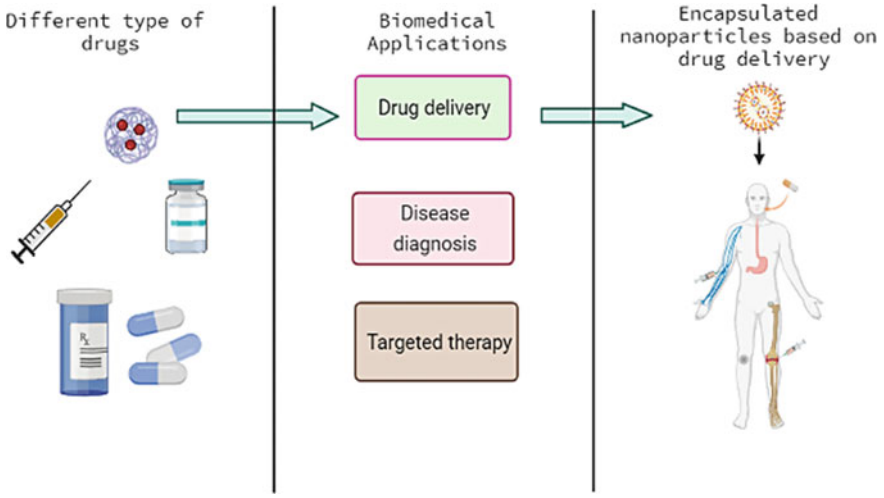

Fig. 3 Different types of drugs in the drug delivery system

(rMSP1), triggering pro-inflammatory responses. In the treatment of VL, quercetin–gold (Au) NP conjugation, doxorubicin–chitosan conjugation, amphotericin B as chitosan nanocapsule, and mannose–chitosan-based nanoformulation of rifampicin have functioned as effective delivery systems. Figure 3 depicts the different types of drugs used in the drug delivery process.

Drug developers are embracing a molecular medicine strategy that promises to deal with parasite diseases and improves the chances of successful therapy in a world where the expense of creating medicine for parasitic illnesses remains the greatest hurdle. Molecular medicine has changed drug discovery and development, yet there are enormous barriers to overcome before the promise can be realized. With the use of molecular platforms, better bioinformatics services, and better pharmacogenomics studies, the scientific community and stakeholders have considerably facilitated the scientific community and stakeholders to work together on a shared platform to battle parasitic illnesses.

3 Nano-based Strategies to Prevent the Transmission of Parasitic Diseases (Vector Control)

3.1 Different Parasitic Diseases and Their Vectors

Parasites and pathogens causing diseases are transmitted by arthropods such as mosquitoes, bugs, blackflies, tsetse flies, sand flies, lice, and ticks. These arthropods belonging to different orders Phthiraptera, Siphonaptera, Heteroptera, and Diptera

act as a vector for transmitting pathogens causing infectious diseases in humans [58, 59]. It has been estimated that vectors harbor parasites that cause approximately 17% of infectious diseases and about 700,000 deaths. The burden of these diseases is highest in the tropical and subtropical regions which affect the poorest population. In such areas, insects act as a predominant vector for parasites causing malaria, filariasis, chagas diseases, leishmaniasis, etc. [60]. Malaria is caused due to the infection of a protozoan parasite belonging to the genus *Plasmodium.* The parasite is vectored by the female *Anopheles* mosquito. *Anopheles* mosquitoes that pose a great threat are abundant and dwell in the proximity of people. They also have a long life and commonly feed on humans [61]. Likewise, lymphatic filariasis is a parasitic disease that is transmitted through *Culex* mosquitoes. *Brugia malayi*, *Brugia timori,* and *Wuchereria bancrofti* are mosquito-vectored filarial parasites causing human lymphatic filariasis. *Culex* species of mosquitoes are globally distributed due to which the probability of an outbreak of such diseases tends to increase. It has been stated that in the year 2018, approximately 893 million people were affected by this ailment [62–64].

Likewise, leishmaniases are also a vector-borne parasitic disease that infects approximately 1.4 million people every year worldwide. The vector responsible for the transmission of leishmaniases is the sandfly. It has been estimated that there are about thirty different species of sandfly that have been recognized as disease vectors. The protozoan parasite *Leishmania* is vectored predominantly by sandflies belonging to the genera *Phlebotomus* and *Lutzomyia.* These vectors are principally found in tropical and subtropical regions. They are highly prominent near human habitation and breed in organic wastes such as feces, manure, leaf litter, and in dark corners in the crevices of the walls having high humidity and temperature [65, 66]. Chagas disease, or American trypanosomiasis, is the result of infection by the parasite *Trypanosoma cruzi.* The parasite is transmitted by the blood-sucking triatomine vector also known as the kissing bug. It has been estimated that approximately six million people are found to be infected by this disease worldwide. The vector transmitting Chagas disease mainly occurs in poor rural areas. They nest mainly in the holes and cracks in walls and on roofs made of bamboo and sugarcane. They forage at night. Similarly, African trypanosomiasis or sleeping sickness is a dangerous, life-threatening, tropical parasitic disease triggered by trypanosomes belonging to protozoans. *Trypanosoma brucei gambiense* and *Trypanosoma brucei rhodesiense* are two species of trypanosomes that are responsible for the development of the disease in people. The vectors transmitting the parasites containing approximately 20 species of tsetse flies (*Glossina*) have inhabited tropical and subtropical Africa. Tsetse flies commonly inhabit fields and rural areas. It has been estimated that sleeping sickness has been detected in 36 different countries of Central and South America [67, 68]. Likewise, Babesiosis is a parasitic enzootic disease triggered by the protozoan *Babesia* parasitizing erythrocytes of vertebrates, including humans. The parasite is vectored by Ixodid ticks. *Ixodes ricinus* has been identified as the primary vector for the parasite in Europe. According to surveillance conducted in the USA, there has been an increase in cases of Babesiosis by 11% in the year 2018 [69, 70]. Figure 4

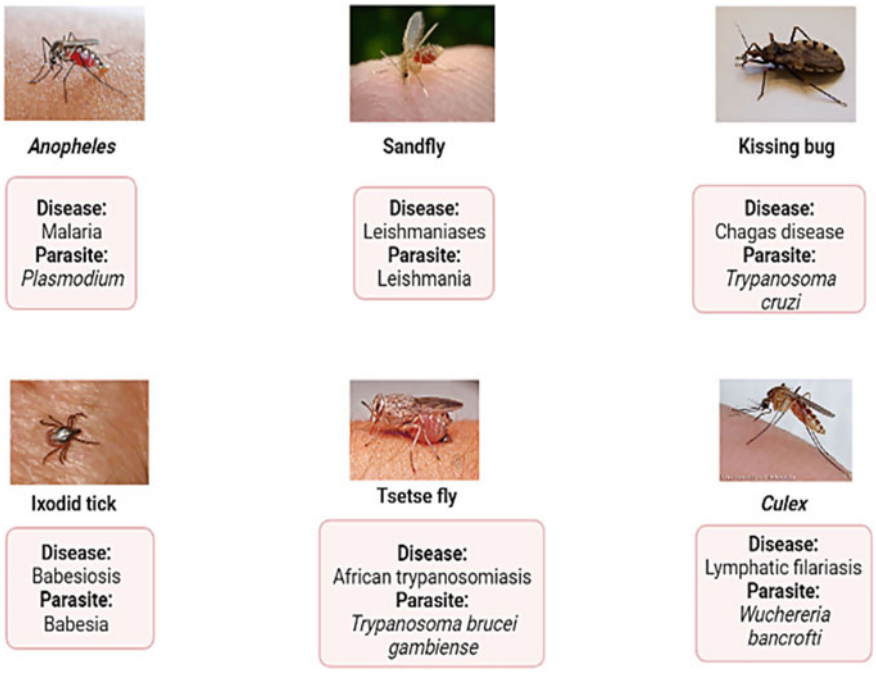

Fig. 4 Different vector species harboring a variety of parasites responsible for severing parasitic diseases

illustrates different kinds of insect vector that carry deadly parasites which causes deadly diseases.

The above-described parasitic diseases have rooted themselves throughout the globe, especially in Asia, Africa, and South America. They are continuously spreading at a fast pace due to a lack of awareness, education, and hygiene. People migrating to the natural environments of parasite occurrence also increase the likelihood of spreading infection. Destruction of the natural environment of vectors transmitting parasites also results in vectors moving to new areas to spread diseases. These insects occur in huge numbers, reproduce rapidly, and move quietly. They can very quickly and efficiently transmit a parasite to us, often painlessly and often during our sleep. Therefore, it becomes highly essential to combat the insect vector so that the chances of the disease spreading are minimized [67].

3.2 *Strategies Undertaken to Control Vector-Borne Parasitic Diseases*

The principal method for the control of parasitic diseases is through vector control strategy. Since the eighteenth century, vector control programs have been highly effective in the eradication of vector-borne parasitic diseases. Vector control aims to limit the transmission of parasites and pathogens by reducing or eliminating human contact with the vector. Various chemical and non-chemical-based methods that target the immature and adult stages of the vector have been undertaken to date [59]. Chemical insecticides like dichloro-diphenyl-trichloroethane (DDT) gained a lot of prominence during the nineteenth century. The DDT spray operation significantly reduced the mosquito and sandfly populations. However, in the later years, vector population developed resistance against DDT [12, 71]. Likewise, other chemical insecticides such as pyrethroids have been used for a long period to control the Triatomine vector, despite that pyrethroid resistance has been developed by the vector population. Control of tick vectors using acaricides had been highly effective in controlling the tick population, although recently resistance has also been developed by these vector species against the acaricides. Along with that, toxicity posed by the acaricides toward the environment also limits their utilization. Furthermore, the development of new acaricides is a long and expensive process, which reinforces the need for alternative approaches to control tick infestations [72–74].

In the past few years, microbial agents such as *B. sphaericus*, and *B. thuringiensis* have gained a lot of popularity in combating the mosquito vector population. They act as an ultimate substitute for chemical insecticides. However, presently, a high level of resistance has been observed in the vector population against them [15]. Likewise, entomopathogenic fungi have also been utilized for the eradication of the mosquito vector population. Although apart from being highly effective, entomopathogenic fungi [16]. Natural enemies of the vector such as tadpoles and larvivorous fishes act as potential predators of mosquito larvae. However, the introduction of larvivorous fishes belonging to the genus *Gambusia* and *Poecilia* is a threat to the native species. Along with this, though tadpoles and salamanders are efficient in putting a check on the mosquito larvae population, still they cannot be used alone as an independent intervention. More detailed knowledge is required to use them effectively. Other disadvantages such as the low survival rate of tadpoles and caution needed at the time of introduction of invasive species limit their applications [18, 75, 76].

Nowadays, nanobiotechnology is gaining a lot of prominence in vector control. Several nanopesticides and nanoformulations serve as important strategies for vector control. The specific utilization of nanoscience and polymer science that specifically affects vector physiology has been regarded as an efficient approach to vector eradication [77, 78]. Over the past decade, NPs have also been used as an alternative to minimize vector populations. NPs synthesized from microbes and plant parts have contributed to the area of public health in combating the vectors such as mosquitoes. Therefore, it can be stated that nanotechnology is the most promising

branch of the twenty-first century which facilitates vector control and reduces the rate of transmission of infection [79–81].

3.3 Nanotechnology in Vector Control

(a) Nanoemulsion

The emulsion system which comprises droplet size on the nanometer scale (20–200 nm) is often termed miniemulsions and nanoemulsions [82, 83]. As the nanoemulsion has an appropriate size, they appear transparent or translucent to the naked eye and therefore attains stability against sedimentation or creaming [84]. Due to these properties, this system is being practically applied in various fields such as pharmaceuticals and cosmetics. Currently, few studies have described possible applications of these nanoemulsions in the field of insect vector control strategies [77]. Nanoemulsion of essential oils is highly effective against insects. The underlying mechanism behind the toxicity is the deregulation of the growth hormone that ultimately stops insect shedding which finally leads to death. Recent studies have also reported the biological activity of nanoemulsified essential oils on etiological agents of parasitic origin. This potentially increases the diversification of the use of these nanoemulsions in the control of infectious/parasitic diseases [85]. Table 1 describes a variety of plant species utilized for the synthesis of nanoemulsion which has shown good efficacy against vector species. Eucalyptus oil nanoemulsion formulated using water, tween 80, and eucalyptus oil has been found to have mosquito larvicidal activity. Eucalyptus oil acts as a natural pesticide due to its allelopathic property. After exposing the larvae to nanoemulsion, it was concluded that at a concentration of 250 ppm, nanoemulsion caused 98% mortality of *Culex* larvae. Along with this, the histopathological studies reveal that the midgut of the larvae was completely damaged which led to death [93]. Tarragon essential oil has also been found to be highly effective against malarial vector *An. stephensi*. It was stated that the decrease in the droplet size of the nanoemulsion caused an increase in larvicidal activity. It was concluded in the study that the nanoemulsion can be suggested as a low-cost, environment-friendly mosquito larvicide [94]. *Pelargonium roseum* essential oil has been a potent larvicidal agent as it caused more than 90% mortality above 40 ppm in the Anopheles vector. The major components such as citronellol, L-menthone, linalool, and geraniol present in *P. roseum* essential oil were responsible for the mosquitocidal property. Therefore, essential oil-based nanoformulation has been considered a potent candidate for mosquito larvae control [95].

(b) Nanoparticles

NPs have been considered the most eligible candidate for the control of insect vectors. The insects have a hydrophobic and porous external surface. This waxy cuticular surface has orifices ranging from 0.5 to 2 μm, which is larger than the nanometer size scale. This allows the NPs to penetrate through

Table 1 Different kinds of plant species engaged in the synthesis of nanoemulsion which is found to be highly effective against vectors

Plant species	Vector species	Droplet size (nm)	Effective LC_{50} concentration	References
Neem *(Azadirachta indica)* oil	*Culex quinquefasciatus*	31.03–251.43	11.75 mg L^{-1}	[86]
Anethum graveolens	*Anopheles stephensi*	10.7–1880.0	_	[87]
Ocimum basilicum	*Culex quinquefasciatus*	200	36.53–38.89 ppm	[88]
Ocimum basilicum	*Culex quinquefasciatus*	28	3 mg/L^{-1}	[89]
Ricinus communis	*Anopheles culicifacies*	114	3.4 ppm	[90]
Mentha spicata	*Culex pipiens*	97.8	43.57 μg/mL	[91]
Schinus terebinthifolius	*Culex pipiens*	41.3	6.8–40.6 μl L^{-1}	[92]

the exoskeleton and bind to the proteins and DNA. This leads to the denaturation of the cells and organelles, which leads to death [18, 96]. Currently, several NPs include aluminium oxide (Al_2O_3), titanium dioxide (TiO_2), zinc oxide (ZnO), gold (Au), and silver (Ag) have been widely studied for the evaluation of their insecticidal and acaricidal properties [97–99]. Nanosilica is considered to be ideal for the control of *Anopheles* and *Culex* mosquitoes. Larvicidal bioassay reveals that 50% mortality was observed when *Anopheles* and *Culex* were exposed to hydrophobic nanosilica at the concentration of 32.3 and 128.9 ppm. Along with this, hydrophobic nanosilica has also pupicidal and ovideterrence activity against both species of mosquitoes [100]. Nowadays, biosynthesized NPs are gaining popularity. Plants' metabolites and microbial cultures are being extensively used for the synthesis of NPs. The advantages of this green synthesis include cost-effectiveness, single-step process, and eco-friendly. Although bio-fabricated metal NPs are found to be highly effective against a wide variety of insects, to date majority of the studies are being carried out on mosquitoes [12, 98].

Vinca rosea leaf extract-based Ag NPs are suitable for controlling malarial vector *An. stephensi. V. rosea* leaf extract when mixed with silver nitrate ($AgNO_3$) produces brownish-colored nanosilver particles. The synthesized particles were tested against *An. stephensi* larvae for a period of 24, 48, and 72 h. It was observed that more than 90% mortality was seen at the concentration of 68.62 mg/mL after 72 h, thereby making phytofabricated nanosilver a potent candidate for malarial vector control [101]. Likewise, Au NPs synthesized using flower extract of *Couroupita guianensis* were highly effective in controlling pesticide-resistant *Anopheles* vectors. The Au NPs synthesized were oval, spherical, and triangular in shapes of 29.2–43.8 nm

dimensions. A field study conducted concludes that a single treatment with *C. guianensis* flower extract-fabricated Au NP had led to complete larval mortality after 72 h [97]. Entomopathogenic fungi like *Fusarium oxysporum* have also been involved in the synthesis of NPs. Fungus-based Ag NPs exhibit mosquito larvicidal properties. The characterization of the fungi-mediated nanosilver reveals the presence of functional groups present in the fungal extract that assisted in the formation of Ag NPs. This myco-synthesized nanosilver tested for larvicidal activity against *A. stephensi* has shown strong mortality at the concentration range of 69.985–401.639 lg/ml. Thereby, the study confirmed that *F. oxysporum* cultures filtrate-mediated synthesized Ag NPs as a very effective green pesticide for the control of mosquitoes. *B. marisflavi* has also been considered suitable for the synthesis of NPs [102]. Ag NPs synthesized using *B. marisflavi* culture was elucidated to evaluate their efficacy against the immature stages of *An. stephensi.* The study illustrates that the LC_{90} value for the ovicidal and pupicidal activity was attained at 65.84 ppm and 58.41 ppm concentrations of *B. marisflavi*-mediated Ag NPs. The larvicidal activity was also possessed by the nanosilver, which led to more than 90% mortality at the concentration of 55.90 ppm. Therefore, it was concluded that the marine *Bacillus* proves to be appropriate for NPs' synthesis which can control malarial vectors [103].

Soil fungi such as *Chrysosporium keratinophilum* and *Verticillium lecanii* have been considered ideal for Au and Ag NPs formation. NPs based on soil fungus were studied to evaluate their larvicidal efficacy against *Culex quinquefasciatus.* After conducting the larvicidal bioassay according to the guidelines of the WHO, the results were analyzed. It was observed that the larvae of *Cx. quinquefasciatus* were found highly susceptible to the synthesized Ag NPs than the Au NPs [104]. Likewise, Ag NPs synthesized using the aqueous extract of the seaweed *Sargassum muticum* was studied to investigate their field efficacy against *Cx. quinquefasciatus.* The biosynthesized Ag NPs are mostly spherical in shape, crystalline in nature, with face-centered cubic geometry, and with a mean size of 43–79 nm. In the field, a single treatment of Ag NP in water storage reservoirs was effective against the *Culex* vector, allowing the complete elimination of larval populations after 72 h. In ovicidal experiments, egg hatchability was reduced by 100% after treatment with 30 ppm of Ag NP. Ovideterrence assays highlighted that 10 ppm of Ag NP reduced the oviposition rate by more than 70% [105]. Similarly, Ag NP synthesized using *Cassia fistula* (fruit pulp), *B. amyloliquefaciens,* and *B. subtilis* has also been studied for their larvicidal and pupicidal property against *Cx. pipiens.* It has been concluded that the exposure of larvae to the biosynthesized Ag NP led to a decrease in protein content. Along with this, there was an alteration in the activity of different biochemical constituents that affected the nervous system of the larvae ultimately leading to death [106, 107]. Marine sponge *Spongia officinalis*-synthesized ZnO-NPs were found to be an excellent insecticidal agent against *Cx. pipens* larvae. The synthesized NPs were subjected to characterization techniques such as FT-IR which confirmed the presence of different chemical functional groups such as polysaccharides, hydrocarbons, phenols, amines, amides, and carboxylates that helped in the formation of ZnO NPs. ZnO NPs of very small size of 11.5 nm were obtained that were exposed to the mosquito larvae. It was observed that the tested ZnO-NPs severely induced

larvicidal activity with LC_{50} and LC_{90} of 31.823 and 80.09 ppm for *Cx. pipiens*. The study thus concluded the possibility of using *S. officinalis*-mediated ZnO-NPs for vector control [108].

NPs are highly effective in controlling tick vectors. Studies are being carried out to prove that NPs synthesized through chemical and green fabricated routes have high acaricidal properties. Most of the studies assessed the toxicity of Ag NPs against ticks, followed by TiO_2 NPs, and to a minor extent by ZnO, nickel (Ni) NPs, and copper (Cu) NPs. However, most of these studies have been carried out on the effect of NPs in controlling economically important ticks that parasite a variety of livestock species [99]. A study was undertaken by Avinash et al. [109] to investigate the acaricidal property of neem-coated Ag NPs on the deltamethrin-resistant strain of *Rhipicephalus (Boophilus) microplus*. It was observed in the study that after 24 h of exposure, maximum mortality of 93.3% was seen at the concentration of 50 ppm of neem-coated nanosilver [109]. According to a very recent study, the acaricidal activity of green-synthesized nickel oxide (NiO) NPs using an aqueous extract of *Melia azedarach* ripened fruits was investigated against different developmental stages of the camel tick *Hyalomma dromedarii*. The synthesized NPs were exposed to the egg, nymph, larvae, and adult stages of the tick. NiO NPs of size ranging from 21 to 35 nm were able to cause more than 50% mortality at the concentrations of 5.00, 7.15, and 1.90 mg/mL in embryonated eggs, larvae, and engorged nymphs, respectively, whereas the egg productive index (EPI), egg number, and hatchability (%) were lower in females treated with the NiO NPs [110]. Table 2 summarizes the efficacy of biologically synthesized NPs against different developmental stages of the vector.

It can be concluded that nanotechnology is a science that is being widely employed for controlling a wide variety of pest and vector species such as mosquitoes and ticks [120–122]. In spite of that to date, maximum studies and research work have been done to control mosquito adults, pupae, and larvae [116, 123–125]. Several works have also been carried out to investigate the efficacy of NPs in controlling tick vector species causing parasitic diseases in livestock. However, the field application of NPs is still a major research gap in this field. In addition to this, further challenges for future research should be focused on broadening the number of studied tick species as this field is completely unexplored [17, 99, 111]. These NPs have also played an important role in controlling parasitic diseases such as Chagas disease, Leishmanial diseases, and African trypanosomiasis through various nanoformulations and via nanoparticulate drug delivery. No such study for controlling these vector populations through NPs has been performed to date. Therefore, it becomes highly essential to carry out further research work so that steps can be undertaken to put a check on vectors causing deadly parasitic diseases [126]. Figure 5 shows the diagrammatic representation of nanoemulsions and metal NPs fabricated through plants and microbes such as bacteria, algae, and fungi. The synthesized nano-based particles and emulsions have been considered eligible candidates for controlling the vector population.

Likewise, essential oils obtained from plants assist in nanoemulsion formation which also helps in the vector control strategy.

Table 2 Plant extract and microbial culture used for the synthesis of NPs which are found to cause more than 50% mortality in different vector species

Plant/microbial extract	Metal nanoparticle	Vector species	Stage	LC50	References
Mimosa pudica	Ag	*Rhipicephalus microplus*	Larvae	8.98 mg/l	[111]
Euphorbia hirta (plant leaf extract)	Ag	*Anopheles stephensi*	Pupa Larvae	34.52 ppm 10.14–27.89 ppm	[112]
Vinca rosea leaf extract	Ag	*Anopheles stephensi Liston* *Culex quinquefasciatus*	Larvae	16.84 mg/mL (after 72 h) 43.80 mg/mL (after 72 h)	[101]
Calotropis gigantea	TiO_2	*Rhipicephalus microplus*	Larva	24.63 mg/l	[113]
Solanum trilobatum	TiO_2	*Hyalomma anatolicum*	Larva	25.85 mg/l	[114]
Bacillus megaterium	Ag	*Culex quinquefasciatus*	Larvae	0.567–8.269 ppm	[115]
Caulerpa scalpelliformis (frond extract)	Ag	*Culex quinquefasciatus*	Pupa Larvae	7.33 ppm 3.08–586 ppm	[116]
Lobelia leschenaultiana	ZnO	*Rhipicephalus microplus*	Adult	1.7 mg/ml	[18]
Citrus limon leaf extract	Pd (Palladium nanoparticles)	*Anopheles stephensi*	Larvae	7.215%	[117]
Sargassum myriocystum	Ag	*Culex quinquefasciatus*	Larvae	5.59 mg/L	[118]
Penicillium corylophilum	Se (Selenium)	*Anopheles stephensi*	Larvae	25 ppm	[119]
Penicillium chrysogenum	MgO	*Anopheles stephensi*	Larvae	12.5–15.5 ppm	[20]

4 Recent Advancements in the Development of Nanovaccines

Control of parasitic diseases necessitates a complex combination of public health, education, political will, and medical science efforts. As the key components vary widely, the nature of the interplay differs for each parasitic disease [127]. The following key points explain the limitations of drugs and vaccines that prompted the development of nanotechnology in controlling parasitic diseases.

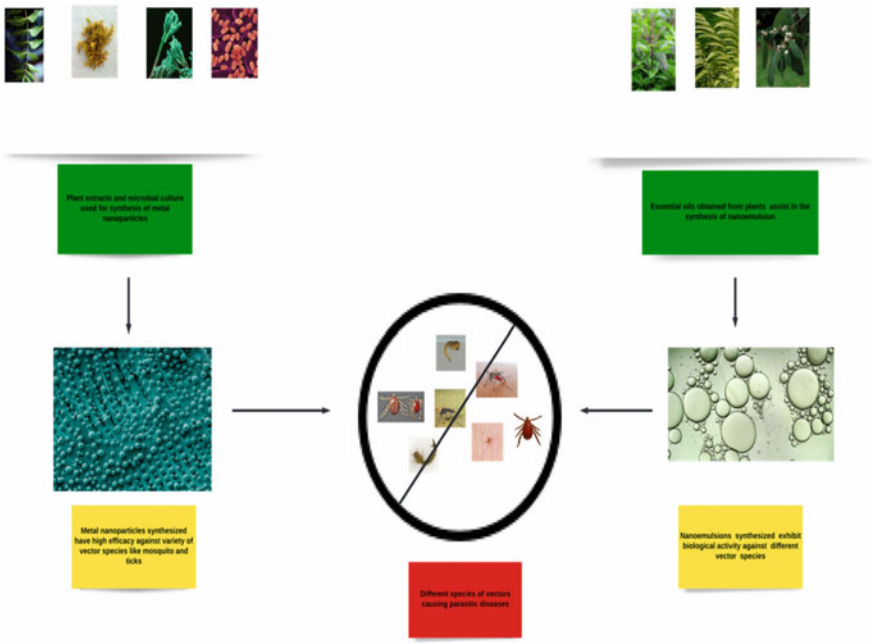

Fig. 5 Plants' extract and microbial culture have been used for the synthesis of metal NPs which have the potential for controlling mosquito larvae, pupae, and tick population

4.1 Available Drug-Related Problems

Antiparasitic drugs are still the best option for managing parasitic infections. Most of the available antiparasitic drugs by their insolubility are poorly absorbed and excreted out of the body. Additionally, the low gastrointestinal absorption profile and variable bioavailability of poorly soluble medicines pose a considerable challenge in developing appropriate dose forms [128]. Antiparasitic drug resistance as a result of widespread and irrational use is one of the major threats around the globe and is responsible for the mortality of millions per year [129]. Satisfactory effects often necessitate high and multiple doses, which are prone to drug resistance, low efficacy, reinfection, and hazardous side effects. Several ways to develop nano-sized medication delivery devices have been researched in recent years. Particularly, in the case of novel antiprotozoal, the lack of effective vaccinations, safe and affordable medications, increased drug resistance, and lack of novel drugs for the prevention and treatment of human protozoan infections have amplified the disease's impact manifold [130].

4.2 Drug Resistance and Lack of Vaccines

Resistance to various antiparasitic drugs remains a major threat to global efforts to control and eliminate parasitic diseases. Vaccination has long been considered the most long-term approach for parasite disease control in humans and animals. The parasites share complex biology by the virtue of which their life cycle proceeds through various developmental stages in different hosts and the harvesting of vaccines from these animal hosts is a daunting task in terms of cost, quality control, standardization, and shelf life [131]. A substantial impediment in vaccine development is the absence of in vitro methods required to culture different stages of parasites. The capacity of many parasites to modify host immune responses in order to postpone or prevent parasite clearance complicates vaccine development even more. Additionally, the maintenance of parasite populations necessitates passage through or formation of persistent infections in their specific animal host.

4.3 Lack of Novel Drugs

Increasing drug resistance among animal parasites along with the high cost of drugs, limited availability, and food safety concerns over drug resistance are the few notable limitations that have facilitated the need for the development and implementation of alternative management techniques [132]. Antigenic variation, sequestration, and immunosuppression are examples of adaptive strategies used by protozoan and metazoan parasites to evade immunity. Many parasites use these strategies to extend their survival in the mammalian host to compensate for their low transmissibility to the arthropod vector on which their cyclical development depends. Parasites can delay sterilizing immunity which leads to their chronicity in the host cell. Many parasites have the ability to modify host immune responses in order to postpone or prevent parasite clearance.

4.4 Nanotechnology as a Solution

NPs are at the forefront of the rapidly developing field of nanotechnology with several potential applications. NPs with exceptional biodegradability and biocompatibility are regarded as the most effective vehicle for delivering drug compounds in the biomedical field. Nano-based drug delivery systems improve the bioavailability and therapeutic efficiency of drugs while lowering the side effect profile [133]. Reduction in particle size leads to higher dissolution rates due to increased surface area, which is one of the most effective strategies to solve these issues [134]. NPs, as an innovative novel drug carrier, offer a promising technique to treat parasitic infections effectively by addressing the constraints of limited bioavailability, poor cellular permeability,

nonspecific distribution, and quick removal of antiparasitic medications from the body [135].

4.5 Availability of Different Nano-based Delivery Systems

Over the years, nanomaterials have emerged as potable drug carriers. Nanotechnology-based drug delivery systems have included biodegradable nanoparticles, dendrimers, polymeric micelles, liposomes, microcapsules, solid lipid nanoparticles, and solid core–shell nanoparticles.

(a) Nanocapsules

Nanocapsules consist of one or more active materials (core) and a protective matrix (shell) in which the therapeutic composition can be encapsulated (Fig. 6) [136]. The protective layer of nanocapsules is normally pyrophoric (liable to ignite spontaneously on exposure to air) and easily oxidized [137]. Nanocapsules are a class of polymer-based nanoparticles other than nanospheres that can penetrate the basal membranes due to their small size, making them suitable carriers for drug delivery. Their shape has a low aspect ratio, making them easier to penetrate cells than capsules with a high aspect ratio, such as rods. Antibodies and cell-surface receptors can be added to their surfaces to detect biomolecules for targeted administration. Nanocapsules are of biological relevance because they can be utilized for controlled drug release and targeting while protecting enzymes, proteins, and foreign cells, among other cellular components [138, 139]. Sustained release, improved drug selectivity and effectiveness, enhanced therapeutic bioavailability, and reduced drug toxicity are some of the key advantages of nanocapsules. Polymer-based NPs are being investigated as a means of delivering chloroquine and artemisinin against intracellular Plasmodium and amphotericin B against Leishmania [140–142].

(b) Nanosphere

Nanospheres of inorganic materials are used as lubricants with the help of nano-sized "ball bearings." By virtue of particle size, nanospheres are ideal to be administered orally, locally, and systematically. Nanospheres have small particle sizes; thus, they are suitable to be administered orally, locally, and systemically. Usually, most nanospheres are prepared using polymers that are biodegradable and biocompatible. They are used as a delivery system in order to enhance the entrapment and release of the drug (Fig. 7).

(c) Solid lipid nanoparticles

Solid lipid nanoparticles (SLN) have emerged as a versatile alternative to polymer-based nanoparticles as the paucity of safe polymers with regulatory approval, as well as their exorbitant cost, have restricted the use of polymer-based NPs in clinical practice. SLN contains aqueous surfactant dispersions with a matrix composed of solid lipids which is biodegradable [143, 144]. Generally, the lipids that are well metabolized by the body can be employed. Large-scale

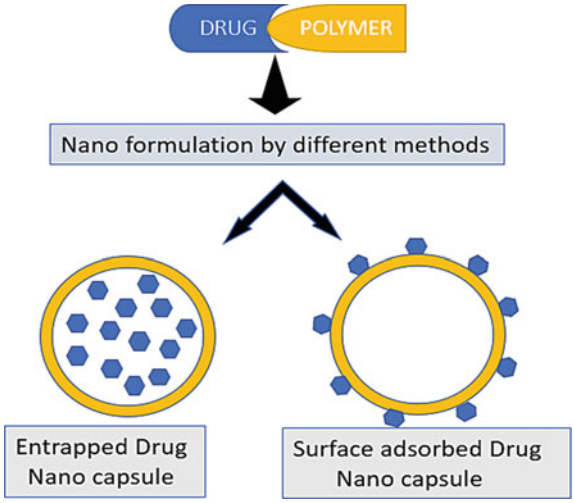

Fig. 6 Drug association with nanocapsules

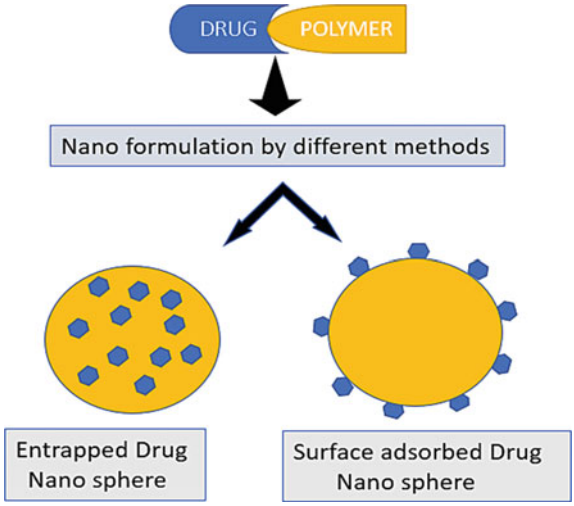

Fig. 7 Drug association with nanosphere

production can be performed in a cost-effective and relatively simple way using high-pressure homogenization leading to SLN (Fig. 8) [145].

(d) Liposomes

Liposomes are a well-known formulation technique for enhancing drug delivery and boosting therapeutic results in a variety of medications, and vaccines. Liposomes are structurally related to the lipid membrane of viable cells. Liposomes are tiny artificial aqueous vesicles encircled by phospholipid bilayers that encapsulate hydrophilic, hydrophobic, and amphiphilic compounds [146]. Liposomes are biocompatible, shielding the encapsulated drugs from metabolic processes, enabling them for a bigger pharmacological payload per

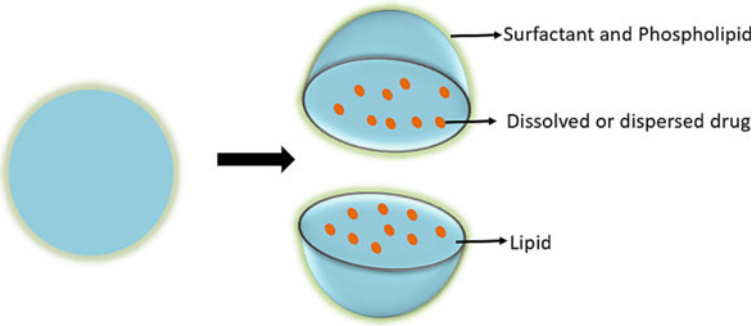

Fig. 8 Solid liquid nanoparticles loaded with drug

particle as well as increasing chemical biodistribution to the targeted regions in vivo [147].

(e) Dendrimers

The presence of a well-defined nanoscale polymeric framework with a low polydispersity index and high functionality is evolving dendrimers as viable drug delivery vehicles [148]. 'The term dendrimer' is derived from the Greek word 'dendron,' which means 'tree/branch,' due to its similarity to a tree, and meros, which means portion. A dendrimer consists of a symmetrical core, multiple branches emanating from the core referred to as generations (first generation, second generation, and third generation subsequently), and the periphery functional groups [149]. Dendrimers are nano-sized polymers of a regular structure and a high density of end groups that are heavily branched fractal-like macromolecules with well-defined three-dimensional structures, shapes, and topology [150]. Recently, dendrimers have been employed for the management of malaria, leishmaniasis, toxoplasmosis, and acanthamebiasis (Fig. 9) [151].

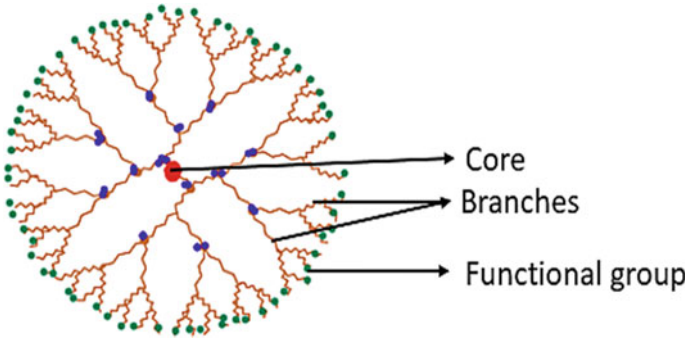

Fig. 9 Structure of dendrimer showing the core, branches, and periphery groups

4.6 Brief Introduction of the History and Evolution of Vaccines

Vaccination is the most effective and realistic strategy for eradicating infections since Edward Jenner's pioneering work 200 years ago. Vaccination has made a huge difference in terms of human and animal health by eradicating two major infections, smallpox and rinderpest [152]. Polio has nearly been eradicated, and the success in combating measles makes it another possible eradication target. The disciple of vaccination is emerging rapidly and many new vaccines, including those for non-infectious disorders, are likely to be produced in the next decade. Presently, seventy different types of vaccines are approved against thirty infectious diseases around the globe [153]. In recent times, SARS-CoV-2 vaccines are the most promising approach for curtailing the pandemic, and they have been an extraordinary success. Vaccines have got an upper hand when compared to conventional drugs because the enhanced drug resistance along with low efficacy, low shelf life, surging toxic effects, and drug incompetence to latch on to the site of infection are a few of the undesirable effects of traditional conventional drugs [126]. To design an optimal vaccine, there are some key facets to be kept under consideration like safety, stability, cost-effectiveness, and the property to show adequate and lasting immunity with the least number of doses [154, 155]. With the advent of science and technology, there was a breakthrough in the types of vaccines to boost the immune response and prevent life-threatening diseases. Currently, four types of vaccines including live attenuated vaccines, inactivated or dead vaccines, subunit vaccines [protein vaccines, polysaccharide vaccines, nucleic acid-based vaccines], and toxoid vaccines are widely known [156]. There are obvious challenges associated with vaccines in terms of safety with live attenuated vaccines, the inefficiency of dead vaccines to evoke an immune response, the need for prime-boost vaccination regimens as well as cold storage for preservation [157, 158]. These shortcomings demand an alternative that can prevent these challenges.

4.7 Need for Nanovaccines

Nanotechnology advancements and their applications in medicine and pharmaceutical fields have transformed the twentieth century [159]. In the realm of vaccination, nanotechnology can aid in the improvement of existing vaccines [160]. Nanovaccines contain nanoparticles that specifically target the site where the infection arises, as opposed to conventional medicines that impact the entire body [161]. Caused by small tailored effects, nanotechnology is gaining prominence in biology [162, 163]. Nanoparticles have the properties like unique particle shape, size as well as hydrophobicity to manifest self-adjuvant effects, hydrophobicity and release kinetics [164]. The administration of particles from 20–100 nm in size can directly enter the lymphatic system while the larger particles need to be internalized by antigen-presenting cells prior to reaching the lymphatic system which signifies the

relevance of size in the biodistribution of nanoparticles efficiently [165]. The rod-shaped nanoparticles are found to be circulating more efficiently in the blood and gastrointestinal tract when compared to their spherical counterparts. As opposed to hydrophilic formulations, particles synthesized from hydrophobic polymers are more efficiently phagocytosed [166]. Nanovaccines are new-generation vaccines in which NPs are utilized as carriers and/or adjuvants and can elicit cellular and humoral immunity which is both immediate and long-lasting [21, 161, 167]. Nanovaccines can be designed to mimic the size and shape of pathogens to promote easy uptake by immune cells [168]. Materials at the nanoscale level can incorporate into membrane-bound endosomes, hence never getting access to the cytosol and cell machinery in contrast to other synthetic drugs which disrupt the integrity of biological barriers. Nanotechnology-based vaccines can also be delivered via a variety of routes, including intranasal, intravenous, transdermal, and oral administration, and can be functionalized to breach the blood-brain barrier [22, 169].

5 Challenges and Future Perspectives

Based on the elaborated literature explained in this chapter, it can be concluded that nanotechnology can play an important role in controlling parasites causing deadly diseases along with their respective vector species. Nanotechnology provides unlimited opportunities for improving the efficacy of the currently used antiparasitic drugs by overcoming the drawbacks such as short half-life and low bioavailability of the medicines. NPs loaded with drugs can be applied either orally or could be directly injected for drug delivery. Despite all these, still research carried out on this is in its infancy and requires further studies. Likewise, controlling the vector population through nanotechnology is another strategy undertaken for the eradication of parasitic diseases. Nowadays, NPs synthesized using plants and microbes are gaining a lot of importance due to their insecticidal and acaricidal property against different vector species. To date, maximum research has been done to evaluate the mosquitocidal and acaricidal effect of metal NPs on different vectors. However, apart from these, there are other vectors such as bugs and sandflies that cause deadly parasitic diseases. Until now, no such study has been done to control these vectors using nanotechnology. Recently, NPs-based vaccine platforms (nanovaccines) have emerged as promising alternatives to more traditional vaccine platforms. Nanovaccines offer several benefits over traditional adjuvants by offering stability outside the cold chain, strengthening immunogenicity, activating humoral and cellular immune responses, and facilitating long-lived responses without the need for booster doses. However, further studies investigating the use of nanovaccines for disease prevention or therapies are urgently needed, so that the large-scale manufacturing of nanovaccines could be practiced.

6 Conclusions

Through the reformulation of conventional medications into site-specific targeted administration of drugs, nanomaterials-based drug delivery systems provide an upgraded and effective alternative therapy. The combination of nanotechnology and pharmaceutical sciences research is promising and has increased fast in recent years. They are frequently nanoscaled in size because nanoengineering-enabled drug delivery materials are intended at the atomic or molecular level. As a result, unlike larger materials or traditional medications, they can freely circulate throughout the human body. The development of novel medications for the control and treatment of neglected tropical diseases (NTDs) is a big problem that will require significant funding. Despite the fast proliferation of parasite infections throughout the world, novel therapeutic options are urgently needed to combat them. According to the findings, the nanoparticulate-mediated drug delivery method improves efficacy by allowing for site-specific administration, improved targeting efficiency, and greater drug bioavailability at the illness site. Disease causing parasites are vectored by arthropods, out of which mosquitoes, sandflies, and bugs are highly prominent. Putting a check over these vector populations has also been one of the most important strategies for controlling parasitic diseases. Several methods have been undertaken in the past to eradicate vectors, but the drawbacks of these traditional methods prompted the development of a novel approach. In such a scenario, nanotechnology can be considered an effective way to eliminate parasitic infection. Metal NPs are highly efficient in suppressing the insect vector population. Nanotechnology-enabled vaccinations are also a novel technique for successfully eliminating NTDs; there are currently no vaccines against NTDs, but research is underway to develop effective nanovaccines. Several reported outcomes in this research revealed that reformulation of conventional medications using nanoparticles can improve drug quality, efficacy, and minimize toxicity. Nano-based vaccinations, on the other hand, are required to enhance investigations and research to generate effective, safe, and low-cost medications to combat NTDs.

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