Probiotics for the Control of Helminth Zoonosis

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This paper is a comprehensive, concise, and an up to date review about probiotics effect and mechanisms against helminth infections of zoonotic importance. Zoonoses are diseases that can be transmitted from animals to humans in a reversible way. Despite zoonotic helminth diseases being still a challenge to the public health and the agriculture industries globally, they were still neglected in both human and veterinary medicine. Moreover, the increasing emergence of anthelmintic drug resistance constitutes failures of most disease control strategies, alarming for a quest to new alternative control approaches. Consequently, the use of beneficial microorganisms, probiotics, is becoming interesting for its prophylactic or therapeutic application against several diseases including helminths. Recent studies on probiotics against parasites and the interactions between bacteria, parasites, and the immune system in the gut draw much attention. However, the effects of these beneficial microorganisms in helminth infections remain largely unexplored. Therefore, the aim of the present review is to raise attention and to summarize recent findings on probiotics research against helminth parasites of zoonotic significance. State-of-the-art research on beneficial effect of bacteria on helminth infections and their proposed mechanisms of action is thoroughly discussed.

1. Introduction

Zoonosis is an infectious disease that can naturally be transmitted through direct or indirect means from animals to humans, or vice versa. These infections can be caused by bacteria, viruses, fungi, parasites, and prions. People may acquire these harmful agents from infected animals by several ways. For instance, infection can be via direct contact with feces, handling of pets, ticks, or mosquito bites, or via consumption of undercooked food of animal origin. Currently, more than 200 pathogens are being regarded as zoonoses. Possible driving factors for the emergence of zoonoses are global travel, international trades, and climate change, among others. As a result, the magnitude of these diseases may augment as long as these driving factors continue to amplify. Consequently, zoonotic diseases remain a global public health threat today [1, 2].

Nowadays, one of the most prevalent zoonotic diseases is infection with helminth parasites, which infect about one-third of the human population worldwide. Helminths are parasitic worms, an evolutionarily ancient and diverse group of metazoan organisms, which include cestode tapeworms, nematode roundworms, and trematode flukes. Infection with helminths usually tends to be chronic rather than acute infection, although there can be acute manifestations after initial infection in naive hosts. Mortality is low in healthy hosts, but is often life-threatening to individuals with poor immunity. However, morbidity can be quite high. Mental and growth stunting among children is also a big problem with helminth infections. Hence, helminth parasites are of significant concern to public health and food safety. Furthermore, helminths also infect a wide range of animal species and bring about direct and indirect economic losses to livestock production [3]. Prevention and control of helminth parasitic zoonosis is possible, from a simple application of hygiene and sanitation to regular deworming with anthelmintic drugs. However, due to the absence of effective vaccines and the emergence of anthelmintic drug resistance, eradication of parasitic infestation still lingers a challenge, which requires the development of new alternative strategies. Thus, the interest in exploiting probiotics as an alternative to drugs has increased considerably during the last couple of years.

Probiotics are exogenous living microorganisms, which are beneficial to the host’s health when administered in the digestive tract. The most widely used microorganisms for this purpose are bacteria of the genus *Lactobacillus* and...
Enterococcus, and some fungi and yeasts [4]. The protective effect of probiotics is by competitive exclusion or colonization resistance of pathogenic microorganisms in the gut. Another mechanism is their ability to produce antibacterial substances, like bacteriocins or oxygen peroxide, or by immunomodulation [5]. Likewise, probiotics may interfere with the physiology of parasites in the gut. Furthermore, their secretions may have anthelmintic effects and can reduce the virulence of many parasites. Hence, probiotics can be an integral part of helminth parasite control strategies [6].

Recent studies on probiotics against parasites and the interactions between bacteria, parasites, and the immune system in the gut draw much attention [7–10]. However, effects of probiotics on helminth infections remain largely unexplored. Thus, the aim of the present review is to compile recent research findings on probiotics against helminth parasites of zoonotic importance. In this review, state-of-the-art research on beneficial effects of bacteria on helminth infections and their proposed mechanisms of action will be thoroughly discussed.

2. Trends of Probiotics against Helminth Zoonosis

Zoonotic helminth infections are still remaining a challenge posing a significant impact on public health, food safety, and agriculture industries worldwide [11]. Despite many anthelmintic drugs being commercially available, resistance rates are increasing, alarming for a search for new alternate therapeutic strategies. As a result, the use of beneficial microorganisms, probiotics, is becoming interesting for its prophylactic or therapeutic application against several diseases including helminths. Recent studies on probiotics against parasites and the interactions between bacteria, parasites, and the immune system in the gut showed promising results. However, the effects and mechanism of these beneficial microorganisms in helminth infections remain incompletely understood. Therefore, it is imperative to recognize the current trends in probiotic research done on helminths thus far to better explore the mode of action and its beneficial effect on helminths. This review was developed based on state-of-the-art of beneficial bacteria research on helminths, mainly schistosomiasis, trichinellosis, toxocariasis, trichuriasis, ascariasis, hookworms, and Strongyloides, and discussed accordingly.

2.1. Probiotics against Schistosomiasis. Zoonotic schistosomiasis is caused by trematodes of the genus Schistosoma, mainly by S. mansoni, S. japonicum, and S. mekongi [11]. Other less prevalent species like S. haematobium, S. guineensis, and S. intercalatum can cause systemic diseases in people. However, most zoonotic cases of schistosomiasis are attributed to S. japonicum [12]. The parasite is widely distributed throughout tropical and subtropical areas. It is the third most devastating neglected tropical disease in the world with an overall disease burden of 3.31 million disability-adjusted life year (DALY) [3]. Despite only 14% of global schistosomiasis being of zoonotic origin, the global burden of zoonotic schistosomiasis is estimated to be over 10 million DALYs per annum [11]. More than 258 million people are infected in 78 endemic countries worldwide, of which 92% of them live in Africa [13]. A map showing the global distribution of human schistosomiasis due to S. mansoni, which were developed by the Schistosomiasis Research Group at Cambridge University, is depicted in Figure 1.

Pathogenesis of human schistosomiasis begins after the larval stage of the parasite is transmitted via skin penetration when people are doing their routine activities in infested water areas. Thereafter, the larvae grow into adult stage and reside in the blood circulation, where female worms release eggs. The eggs that are not excreted spread and remain attached in body tissues thereby resulting in an immune system reaction and gradual damage to organs. Mental and growth stunting among children is a big problem with infections by this helminth. Also adults are as likely to become infected and can show a reduced ability to work. In chronic cases, the parasite can also damage the liver, intestine, spleen, lungs, and bladder [14]. Mass drug administration of praziquantel has been the main means of control so far, but there are complaints with this approach such as drug resistance. Furthermore, vaccines are in various stages of development today [15, 16]. Thus, considering the multifaceted socioeconomic impact of zoonotic schistosomiasis, the search for safe and more effective control remedies is required.

To date, various attempts have been made to investigate the protective and curative effects of beneficial bacteria in mice models for use in the control of S. mansoni [17–21]. Several probiotic strains, like Zymomonas mobilis, probiotic labneh containing Streptococcus salivarius subsp. thermophilus, Lactobacillus delbrueckii subsp. bulgaricus, and different Lactobacillus species, have been evaluated. Their anthelmintic and immunomodulatory effects on S. mansoni are summarized in Table 1. For instance, Lactobacillus sporogenes is among the most commonly studied [20, 21] probiotic strains that showed a significant antischistosome effect in egg and larval stages of the parasite. It has remarkably reduced the worm burden as well as egg count. Interestingly, both authors have reported that L. sporogenes reduced chromosomal aberrations and DNA damage induced by infection in the host.

2.2. Trichinellosis. Trichinellosis is among the top 10 global ranking of food borne parasitic infections, which pose a public health threat and economic losses in pig production
and food safety worldwide [22]. Globally, trichinellosis has been reported in over 55 countries, and an estimated 10,000 cases occur every year with 0.2% of these cases being lethal [23]. Humans can be infected by many species of parasites [24]. However, the most important etiological agent to cause disease in people worldwide is *T. spiralis*, the species most commonly found in pigs [25]. Other *Trichinella* species are less commonly reported and may be found in some parts of the world, usually infecting wild animals.

Ingestion of uncooked infected meat from pigs is the main source of infection in humans. Occasionally, horses and other domestic animals infected with larvae of *Trichinella* may also infect people [25]. The disease in humans is characterized by enteritis (intestinal phase) and tissue inflammation in the skeletal muscles with degenerative changes (tissue/muscular phase). The pathogenesis of *T. spiralis* infection is mainly attributed to the formation of larval capsules and host immunosuppression [26]. The latter could be regulated by a serine protease from adults and newborn larvae in the intestinal and in the muscular phases [27]. Moreover, the parasite can alter dendritic cell function and induce immunosuppression by regulatory T and B cells, stimulated macrophages, and cytokine production [28]. Nevertheless, the molecular mechanisms mediating these processes remain unknown.

Treatment of human trichinellosis with anthelmintics is not effective against all developmental stages of the parasite as it is only effective for adult worms. Furthermore, endeavors made thus far to produce vaccines against trichinellosis have not been successful due to the wide range of species-specific antigens and immunosuppressive effects of host responses [29]. Alternatively, the use of the immune stimulating probiotic bacteria has been suggested [7, 30].

In several studies *T. spiralis* has been used as a model parasite to validate anthelmintic and immunomodulatory properties of probiotic and bacteriocin-producing bacterial strains [7, 8, 30–32]. In all studies, the most widely explored bacteria are from the genus *Lactobacillus*, of which, *Lactobacillus casei* is the top ranked strain. It has anthelmintic effect with an efficacy range from 75% to 100% protection. Another bacterial strain within the genus *Lactobacillus*, which has showed a remarkable degree of protection around 90% against *T. spiralis*, is *Lactobacillus plantarum* P164 [7]. This suggested that these aforementioned Lactobacillus strains may be safe to use as prophylactic or curative probiotics against *T. spiralis*. Besides their anthelmintic effect, most of

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**Table 1: Probiotic strains used against Schistosoma mansoni infection in mice.**

| Probiotics strain                  | Dose/route                          | Mechanisms                                                                 | Antiparasitic effect                                                                 | References |
|------------------------------------|-------------------------------------|----------------------------------------------------------------------------|--------------------------------------------------------------------------------------|------------|
| *Zymomonas mobilis*                | 1 × 10⁹ CFU/mL orally, at a dose of 0.3 mL/day | Provoke a secondary immune response                                         | A 61% protection from the infection was observed in the treated group                | [17]       |
| Probiotic labneh containing *Streptococcus salivarius subsp. thermophilus*, *Lactobacillus delbrueckii subsp. Bulgaricus* and *DVS-ABT2* | Probiotic labneh and garlic and onions fed for 21 days before and 45 days after infection | Improving intestinal balance                                                      | 50%–66% reduction in worm burden; 70% and 56.44% egg count reduction in liver and intestine, respectively | [18]       |
| *Lactobacillus casei* B-44; *Lactobacillus plantarum* B-53; *Lactobacillus reuteri* B-1444 and *Lactobacillus acidophilus* | 1 × 10⁶ CFU each mixed with feed | A significant stimulation for IgM response against SWAP before and after infection | Increased IgM; A decrease in the activity of AST, LDH and γGT                         | [19]       |
| *Lactobacillus sporogenes*         | 12.5 million spores/mice/week for 8 weeks orally | Decreased cytokine-induced chromosomal aberrations and DNA damage          | Significant reduction in chromosomal aberrations                                     | [20]       |
| *Lactobacillus sporogenes*         | 12.5 million spores/mice/week for 8 weeks orally from the first day of infection | Reduced DNA damage; ameliorates the hepatic and intestinal damage         | Reduced worm and egg count                                                        | [21]       |

SWAP: soluble worm antigen preparation, AST: aspartate transaminase, ALT: alanine transaminase, LDH: lactate dehydrogenase, γGT: gamma-glutamyl transferase, DVS-ABT2: containing *Streptococcus thermophilus*, *Lactobacillus acidophilus*, and *Bifidobacterium bifidum*, and CFU: colony forming units.
2.3. Toxocariasis. Toxocariasis is a neglected roundworm zoonotic infection distributed among many countries throughout the world [33]. It can be caused by *Toxocara canis* and *Toxocara cati*, which are the natural inhabitants of the intestines of dogs and cats, respectively. The most common *Toxocara* parasite of concern to humans is *T. canis*. It is associated with visceral larva migrans, which is characterized by the migration and permanence of larvae of helminths in humans [34]. The epidemiology of toxocariasis is worldwide, and prevalence rates can reach as high as 40% or more in parts of the world [35]. Humans can be infected either by accidentally ingesting infected eggs or eating undercooked or raw meat from an infected paratenic host like chicken's, ruminants, or pigs [36, 37]. Once inside the body, the eggs hatch in the small intestine and the larvae penetrate the wall and spillover to different organs and tissues via the blood circulation [38].

Even though toxocariasis in most human cases is asymptomatic, the migrated larvae can end up in the liver, lungs, heart, and brain causing severe complications. The two most common classical forms of the disease in people are visceral larva migrans (VLM) and ocular larva migrans (OLM) [39]. Besides, other forms like covert toxocariasis (CT) and neurological and asthmatic forms of toxocariasis have been documented [40]. However, the mechanism of how these roundworms invade the host and modulate their immune system is unknown. Thus, further studies on the interactions of this parasite with the immune system and gut flora in the host are needed to advance the knowledge about immune protection against *T. canis* [41]. The prevention and control of toxocariasis in the definitive host, that is, dogs and cats, will reduce the risk of infection for humans and other paratenic hosts. However, treatment is difficult due to the occurrence of different clinical forms of human toxocariasis [42]. Currently, new alternatives, like probiotics, are promising to control this zoonotic parasite.

Many studies have been attempted to evaluate the protective effects of probiotics against *T. canis* in mice experiments. Basualdo et al. [43] reported a significant reduction (75–100%) of worm burden in mice treated with a dose of 3 × 10⁸ (CFU/ml) of *Enterococcus faecalis*. Moreover, *E. faecalis CECT71219* at different doses of 7 × 10⁴ (CFU/g), 1.46 × 10⁴ CFU in culture and 1 × 10⁵ CFU fed in mice showed both in vitro and in vivo larvicidal activity [44]. In contrast, Avila et al. [45] reported that none of the *Saccharomyces boulardii* and *Bacillus cereus var. toyoi* showed in vitro effects against *T. canis* larvae. Interestingly, a recent study by de Avila et al. [46] has declared a definite efficacy of supplementation with the probiotic *S. boulardii* at a dose of 1 × 10⁷ (CFU/g), which reduced the intensity of infection in mouse studies. Besides the anthelmintic effect, *S. boulardii* modulates the mRNA expression levels of especially interleukin-12 (IL-12) and interferon gamma (IFN-γ) in mice. However, to understand the molecular mechanisms of probiotics in this nematode infection further study is needed.

The aforementioned probiotic strains influence the innate immune system such as phagocytosis (Table 2).

Other probiotic strains stimulate the production of IgG and IgA anti-*T. spiralis*, which help maintain intestinal humoral immunity by attaching to antigens, thus preventing attachment to the epithelium. Moreover, a more recent development by Dvoroňaková et al. [8] reported that the highest stimulatory effect on phagocytic activities of blood monocytes and leukocytes and their enzymatic activity was induced by strains *Enterococcus durans ED26E/7*, *Lactobacillus fermentum AD1* and *Lactobacillus plantarum 17L/1*. This may suggest how these probiotic strains act and the interactions between the parasites and the bacteria by stimulating the immune cells and their enzymatic activity.

| Probiotics strain | Dose/route | Mechanisms | Antiparasitic effect | References |
|-------------------|------------|------------|---------------------|------------|
| *Lactobacillus acidophilus* P110, *Lactobacillus plantarum* P164 and *Lactobacillus casei* ATCC 7469 | 1.0 ml/kg/day with a concentration of 1.9 × 10⁹ CFU/ml orally | Both showed higher levels of IFN-γ | 60.98%, 87.92% and 74.88% larval count reduction, respectively | [7] |
| *Enterococcus faecium* AL41, *Enterococcus durans* ED26E/7, *Lactobacillus fermentum* AD1 and *Lactobacillus plantarum* 17L/1 | 10⁹ CFU/ml in 100 μl orally | Stimulated phagocytosis and respiratory burst of blood PMNL and high intensity of enzymatic stimulation | Protective effect was induced by all strains, the highest reduction by *E. faecium* AL41 | [8] |
| *L. casei* strain ATCC 469 | 1.9 × 10⁹ CFU/ml orally | Reduced invasion of larvae into the host | Significant protective response | [31] |
| *Lactobacillus casei* | Intraperitoneal | Higher levels of IgG and IgA anti-*T. spiralis* and IL-4, but lower levels of IFN-γ | 78.6%–100% protection | [30] |
| *Lactobacillus casei* Shirota strain (LeS) | Intraperitoneal | IgA anti-*T. spiralis* levels were higher | Induces protection against *T. spiralis* | [32] |

PMNL: polymorphonuclear leukocytes.

**Table 2:** Effects of different strains of probiotics on *Trichinella spiralis* in mice model.
2.4. Trichuriasis. After ascariasis and hookworm infections, trichuriasis also called whipworm infestation is the world's third widespread nematode affecting around 800 million people and a range of mammalian hosts [47]. It remains a public health risk as it causes a huge economic burden and decreases the quality of life for many people in developing countries [48]. The causative agents of zoonotic trichuriasis are Trichurus vulpis and T. suis, which are whipworms of dogs and pigs, respectively. Whereas T. trichiura is a species that parasitizes humans, it can also be found in chimpanzees, monkeys, and lemurs. Despite its evolutionary relationship with T. suis found in pigs, there is no evidence that its transmission is zoonotic, except in unusual circumstances [49]. Most recent studies [50, 51] found no genetic difference between T. trichiura and T. suis from Trichuris samples collected in humans and pigs in Africa, Asia, Europe, and the New World and suggesting a common African origin of the parasite.

Dogs and other wild canids and, possibly, pigs are the major reservoirs of zoonotic species of Trichuris. The parasites spread from person to person via the ingestion of eggs via food or water, or via hands contaminated with infective eggs [49]. Most cases of human infection with zoonotic Trichuris have been asymptomatic or may show moderate diarrhea. Ingestion of T. suis eggs results in short term self-limited colonization of humans [52]. Regular deworming with anthelminthic drugs such as albendazole and mebendazole and high-standard hygienic measures may lessen infections. Nevertheless, Trichuris could persist in the animal host and soil due to their egg being highly resistant and long lifespan of adult worms. Moreover, mass drug administration (MDA) of suboptimal drug dosage is the perfect “breeding ground” for drug resistance. Thus, eradication of trichuriasis requires a specific treatment strategy such as immune stimulant probiotics.

Several studies in mice have revealed the effects of beneficial bacteria and associated interactions in a model of enteric nematode infection with the intestinal whipworm T. muris [53–55]. Oral supplementation with live Lactobacillus rhamnosus (JB-1) at a dose of 1 × 10^9 CFU/day has significantly accelerated larvae removal in T. muris resistant C57BL/6 mice. This was accompanied by upregulation of anti-inflammatory cytokine IL-10 levels and mucus secreting epithelial cell numbers. These findings revealed that probiotics such as L. rhamnosus (JB-1) modulate the number of mucus secreting epithelial cells and enhance worm removal through an interleukin (IL-10)–goblet cells-mediated pathway [54].

In contrast, a report by Dea-Ayuela et al. [53] showed that oral consumption of L. casei ATCC7469 increased susceptibility to infection with T. muris. This finding was associated with down-regulation of Th immune response with low levels of gamma interferon (IFN-γ) and Th2 response characterized by decline levels of IL-4 and IL-13 [53]. Furthermore, Holm et al. [55] reported that persistent T. muris infection remarkably enhances the population of the genus Lactobacillus, but causes a reduction in the population of other bacterial species in the gut. Thus, the effects of interactions between T. muris and the microbiome in the host can be aimed at promoting mutual benefit, or elimination of one another [56, 57]. Studies showing helminth infection increasing gut diversity would be interesting if helminths can in fact be commensal and promote growth of “good” gut bacteria. Currently, there have been a few trials with human infections of Trichuris to treat various inflammatory bowel diseases (IBD). Nowadays, experimental and clinical trials with T. suis both in vitro and in vivo showed various immune regulatory strategies and promoted host immune responses. This property of the parasite may help to counteract many diseases like Crohn's disease [52] and multiple sclerosis [58, 59].

2.5. Ascariasis. Ascariasis is the most common soil-transmitted roundworm zoonotic infection. A. lumbricoides and A. suum are phylogenetically related species that infect people and swine, respectively [60]. A. lumbricoides has a prevalence rate of 25% and usually affects humans worldwide, but most frequently occurs in tropical and subtropical areas [61, 62]. Whereas A. suum commonly infects pigs globally and causes huge economic losses to the pig industry. Humans can be infected by ingestion of infective A. suum eggs present in soil especially where pig manure is widely used as fertilizer [63–67]. Most recently, incidence rates of 13.2% of A. suum-specific antibodies in humans were reported [67]. Taking into account its global distribution and huge impact on public health and economy, appropriate invasive control strategies are required to control ascariasis.

Regarding probiotics on A. suum, Bifidobacterium lactis subspecies animalis [68] and Lactobacillus rhamnosus [69, 70] have been reported so far. Both bacterial strains have reduced Ascaris suum-induced eosinophil activity and decreased the severity of allergic skin and lung responses in pig models (Table 3). Thus, these study protocols could be used to validate the effect of different probiotic strains on responses to different pathogens to reduce drug resistance of Ascaris species.

2.6. Other Helminths. In addition to the aforementioned helminth infections, other roundworms, like hookworms and Strongyloides, are more prevalent helminth zoonotic infections causing huge morbidity and economic burdens worldwide. Globally, around 576–740 million and 30–100 million people are infected by hookworms and Strongyloides, respectively [71]. Among hookworms, Ancylostoma braziliense is regarded as the most common cause of cutaneous larva migrans in humans. Other species including A. caninum, A. ceylanicum, Uncinaria stenocephala, and Bunostomum phlebotomum are involved less frequently. Moreover, A. ceylanicum is the only zoonotic hookworm known to produce patent intestinal infections in humans. More recently, a number of studies have been reported looking at molecular diagnosis of zoonotic A. ceylanicum in humans and dogs in different parts of the world [72–77]. Despite A. caninum being the most widely distributed among hookworms, it infrequently causes eosinophilic enteritis in humans [78]. Regular deworming of dogs and cats with a range of antihelminth drugs can reduce the risk of infection in humans [71]. Nevertheless, resistance has been observed in some of the currently used drugs such as pyrantel in dogs [78]. Hence, novel control approaches such as probiotics may confer sustainable protection against hookworms.
A “pool” of $1 \times 10^6$ CFU of each strain of *L. acidophilus*, *L. plantarum*, and *L. delbrueckii* have shown a significant effect on *A. caninum* infection with around 90% efficacy in naturally infected dogs. Moreover, an increase in leukocyte and lymphocyte counts was reported [79], suggesting the immune activation effects of probiotics. On the other hand, *Bifidobacterium animalis* strain 04450B revealed a much lower response with 33% reduction of adult worms and 21% reduction of egg production in *Strongyloides venezuelensis* infected mice [80].

### 3. Mechanisms of Action of Probiotics

The efficacy of beneficial bacteria on the host often depends on the mechanism by which they exert their activity. They may involve one or multiple modes of action including production of antimicrobial substances, modulation of the mucosal immune system, alteration of the intestinal microbiota, and enhancement of enzymatic activity [81]. The primary mode of action of probiotics against parasites might be by enhancing the intestinal barrier and modulation of the microflora in the gut [8, 9, 44–46, 55]. They may augment the number of beneficial microorganisms, like lacto-bacilli and bifidobacteria, which then inhibit growth of harmful pathogens by competing for attachment site in the intestinal mucosa. The second proposed mechanism may involve secretion of antimicrobial substances, like bacteriocins, and organic acids such as lactic, acetic, and butyric acid, mainly secreted by *Lactobacillus* species and may have a larvicidal effect on parasites [82].

Immunostimulation and immunomodulation of either innate or adaptive immune system components [7, 8, 30, 46] are among the leading proposed elucidations for how probiotics exert their action against helminths. For example, probiotic *S. boulardii* promoted a reduction in intensity of infection by *T. canis* by modulating cytokine mRNA expression, especially IL-12, in experimentally infected mice [46]. Furthermore, *L. sporogenes* act against cytokine induced apoptosis by decreased chromosomal aberrations and DNA damage in *S. mansoni* infected mice [20, 21]. Nevertheless, modes of action of specific probiotics are generally not understood. Interestingly, effects of probiotics are the product of cross-talk between host and probiotic agent. Thus, more research on host-microbes or pathogen-pathogen interactions using state-of-the-art immunogenetic technologies may perhaps illuminate our knowledge of probiotics mode of action on helminths [81].

### 4. Conclusions

Considering the multifaceted socioeconomic consequences of zoonotic helminth infections and increasing rates of anthelmintic drug resistance, a quest to new alternative control strategies, like probiotics, is urgently needed to mitigate infection. The efficacy of probiotics strains, mainly bacteria in the genera *Lactobacillus*, *Enterococcus*, and *Bifidobacterium*, has been largely evaluated mainly for the control of schistosomiasis, trichinellosis, and toxocariasis. A difference in the efficacy of these strains, which might be attributed to the variability in study design, experimental animals used, dose ranges, and route of administration, was discerned. Results from these experiments indicated that some bacterial strains in the genera *Lactobacillus* and *Enterococcus* could be used as prophylactic or curative probiotics against helminths after validating it in repeated human and animal clinical trials. Their mode of action can be strain-specific or by a combination of different mechanisms. Furthermore, most effects of probiotics on helminths have been conducted in animal experiments and in vitro culture. Studies involving human trials were scarcely reported. In some cases, helminth-microbe interactions were also assessed. Nevertheless, the molecular mechanisms whereby these beneficial microorganisms act remain poorly understood. Hence, further investigations on host-microbe or pathogen-pathogen interactions using modern molecular techniques could enlighten our knowledge of the mechanism of action of probiotics.

### Conflicts of Interest

The author has declared that no conflicts of interest exist regarding the publication of this paper.
References

[1] CDC, "Animals (Zoonotic)," URL http://www.cdc.gov/parasites/animals.html retrieved on Nov 8, 2016.

[2] WHO, "Zoonosis," http://www.who.int/zoonoses/en/, 8 Nov, 2016.

[3] P. J. Hotez, M. Alvarado, M. G. Basáñez et al., “The global burden of disease study 2010: interpretation and implications for the neglected tropical diseases,” PLoS Neglected Tropical Diseases, vol. 8, Article ID e2865, no. 7, 2014.

[4] C. Hill, F. Guarnier, G. Reid et al., “Expert consensus document: the international scientific association for probiotics and prebiotics consenus statement on the scope and appropriate use of the term probiotic,” Nature Reviews Gastroenterology & Hepatology, vol. 11, no. 8, pp. 506–514, 2014.

[5] M.-J. Butel, “Probiotics, gut microbiota and health,” Médecine et Maladies Infectieuses, vol. 44, no. 1, pp. 1–8, 2014.

[6] F. Berrilli, D. Di Cave, S. Cavallero, and S. D’Amelio, “Interactions between parasites and microbial communities in the human gut,” Frontiers in Cellular and Infection Microbiology, vol. 2, p. 141, 2012.

[7] M. M. E. Temsahy, I. R. Ibrahim, S. F. Mossallam, M. H. Mours, A. A. Bary, and S. A. A. Salam, “Evaluation of newly isolated probiotics in the protection against experimental intestinal trichinellosis,” Veterinary Parasitology, vol. 214, no. 3–4, pp. 303–314, 2015.

[8] E. Dvořáňáková, B. Bucková, Z. Hurníková, V. Revajová, and A. Lauková, “Effect of probiotic bacteria on phagocytosis and respiratory burst activity of blood polymorphonuclear leukocytes (PMNL) in mice infected with trichinella spiralis,” Veterinary Parasitology, vol. 231, pp. 69–76, 2016.

[9] V. F. Del Cocco, M. D. Sparo, A. Sidoti, M. Santín, J. A. Basualdo, and M. A. Córdoba, “Effects of Enterococcus faecalis CECT 7121 on Cryptosporidium parvum infection in mice,” Parasitology Research, vol. 115, no. 8, pp. 3239–3244, 2016.

[10] L. A. Reynolds, B. B. Finlay, and R. M. Maizels, “Cohabitation in the intestine: interactions among helminth parasites, bacterial microbiota, and host immunity,” The Journal of Immunology, vol. 195, no. 9, pp. 4059–4066, 2015.

[11] P. R. Torgerson and C. N. L. Macpherson, “The socioeconomic burden of parasitic zoonoses: global trends,” Veterinary Parasitology, vol. 182, no. 1, pp. 79–91, 2011.

[12] J. L. Finkelstein, M. D. Schleinitz, H. Carabin, and S. T. McGarvey, “Decision-model estimation of the age-specific disability weight for schistosomiasis japonica: a systematic review of the literature,” PLOS Neglected Tropical Diseases, vol. 2, no. 3, article e238, 2008.

[13] WHO, “Neglected diseases schistosomiasis,” http://www.who.int/gho/neglected_diseases/schistosomiasis/en/ retrieved on Nov 25, 2016.

[14] CDC, “Schistosomiasis,” http://www.cdc.gov/parasites/schistosomiasis/disease.html retrieved on Nov 15, 2016.

[15] M. T. Inobaya, R. M. Olveda, T. N. P. Chau, D. U. Olveda, and A. G. P. Ross, “Prevention and control of schistosomiasis: a current perspective,” Research and Reports in Tropical Medicine, vol. 5, pp. 65–75, 2014.

[16] P. J. Hotez and A. Fenwick, “Schistosomiasis in Africa: an emerging tragedy in our new global health decade,” PLOS Neglected Tropical Diseases, vol. 3, no. 9, article e485, 2009.

[17] J. De Fátima Macedo Santos, J. Vasconcelos, J. R. De Souza, E. De Medeiros Coutinho, S. M. L. Montenegro, and E. Azevedo-Ximenes, “The effect of zymomonas mobilis culture on experimental schistosoma mansoni infection,” Journal of the Brazilian Society of Tropical Medicine, vol. 37, no. 6, pp. 502–504, 2004.

[18] A. M. Abdel-Salam, N. Ammar, and A. Z. Abdel-Hamid, “Effectiveness of probiotic labneh supplemented with garlic or onion oil against schistosoma mansoni in infected mice,” International Journal of Dairy Science, vol. 3, no. 2, pp. 97–104, 2008.

[19] K. Z. Ghanem, A. M. Abdel-Salam, and A. S. Magharya, “Immunoprophylactic effect of probiotic yoghurt feeding on schistosoma mansoni-infected mice,” Polish Journal of Food and Nutrition Science, vol. 14, pp. 123–126, 2005.

[20] M. E. M. Zowail, G. Y. Osman, A. H. Mohamed, and H. M. I. El-Esawy, “Protective role of lactobacillus sporogenes (probiotic) on chromosomal aberrations and DNA fragmentation in schistosoma mansoni infected mice,” Egyptian Journal of Experimental Biology (Zoology), vol. 8, pp. 121–130, 2012.

[21] A. H. Mohamed, G. Y. Osman, M. E. M. Zowail, and H. M. I. El-Esawy, “Effect of Lactobacillus sporogenes (probiotic) on certain parasitological and molecular aspects in Schistosoma mansoni infected mice,” Journal of Parasitic Diseases, vol. 40, no. 3, pp. 823–832, 2016.

[22] B. Gottstein, E. Pozio, and K. Nöckler, “Epidemiology, diagnosis, treatment, and control of trichinellosis,” Clinical Microbiology Reviews, vol. 22, no. 1, pp. 127–145, 2009.

[23] K. Darwin Murrell and E. Pozio, “Worldwide occurrence and impact of human trichinellosis, 1986–2009,” Emerging Infectious Diseases, vol. 17, no. 12, pp. 2194–2202, 2011.

[24] E. Pozio and D. S. Zarlenga, “Recent advances on the taxonomy, systematics and epidemiology of Trichinella,” International Journal for Parasitology, vol. 35, no. 11–12, pp. 1191–1204, 2005.

[25] E. Pozio and K. Darwin Murrell, “Systematics and epidemiology of trichinella,” Advances in Parasitology, vol. 63, pp. 367–439, 2006.

[26] F. Bruschi and L. Chiumontio, “Trichinella inflammatory myopathy: host or parasite strategy?” Parasites & Vectors, vol. 4, no. 1, article no. 42, 2011.

[27] X. P. Wu, X. L. Liu, X. L. Wang et al., “Unique antigenic gene expression at different developmental stages of Trichinella pseudospiralis,” Veterinary Parasitology, vol. 194, no. 2–4, pp. 198–201, 2013.

[28] C. Aranzamendi, L. Sofronic-Milosavljevic, and E. Pinelli, “Helminths: immunoregulation and inflammatory diseases—which side are Trichinella spp. and Toxocara spp. on?” Journal of Parasitology Research, vol. 2013, Article ID 329438, 11 pages, 2013.

[29] G. Ortega-Pierrés, A. Vaquero-Vera, R. Fonseca-Liñán, R. M. Bermúdez-Cruz, and R. Argüello-García, “Induction of protection in murine experimental models against trichinella spiralis: an up-to-date review,” Journal of Helminthology, vol. 89, no. 5, pp. 526–539, 2015.

[30] F. Martinez-Gomez, B. E. Fuentes-Castro, and C. R. Bautista-Garfias, “The intraperitoneal inoculation of lactobacillus casei and bifidobacterium animalis subsp. animalis against schistosoma mansoni infection at low challenge doses,” Parasitology Research, vol. 109, no. 6, pp. 1609–1617, 2011.

[31] V. Randazzo and S. R. Costamagna, “Effect of oral administration of probiotic agents on trichinella spiralis-infected mice,” Revista de Patologia Tropical, vol. 34, no. 2, pp. 129–135, 2005.

[32] F. Martinez-Gomez, R. Santiago-Rosales, and C. Ramón Bautista-Garfias, “Effect of lactobacillus casei shirotia strain

Journal of Veterinary Medicine
intrapерitoneal administration in CD1 mice on the establishment of trichinella spiralis adult worms and on IgA anti-T. spiralis production,” Veterinary Parasitology, vol. 162, no. 1-2, pp. 171–175, 2009.

[33] P. A. M. Overgaauw and F. van Knapen, “Veterinary and public health aspects of Toxocara spp,” Veterinary Parasitology, vol. 193, no. 4, pp. 398–403, 2013.

[34] D. Despommier, “Toxocariasis: clinical aspects, epidemiology, medical ecology, and molecular aspects,” Clinical Microbiology Reviews, vol. 16, no. 2, pp. 265–272, 2003.

[35] CDC, “Parasites - Toxocariasis (also known as Roundworm Infection),” http://www.cdc.gov/parasites/toxocariasis/epi.html retrieved on Nov 20, 2016.

[36] H. Smith and R. Noordin, “Diagnostic limitations and future trends in the serodiagnosis of human toxocariasis,” in Toxocara: The Enigmatic Parasite, C. V. Holland and H. V. Smith, Eds., pp. 89–112, CABI Publishing, CAB International, Wallingford, Oxfordshire, UK, 2006.

[37] C. Fan, H. Lan, C. Hung, W. Chung, and C. Liao, “Sero-epidemiology of Toxocara canis infection among mountain aboriginal adults in Taiwan,” The American Journal of Tropical Medicine and Hygiene, vol. 71, pp. 216–221, 2004.

[38] N. R. Pecinalli, R. N. Gomes, F. C. Amendoeira et al., “Influence of murine toxocara canis infection on plasma and bronchoalveolar lavage fluid eosinophil numbers and its correlation with cytokine levels,” Veterinary Parasitology, vol. 134, no. 1-2, pp. 121–130, 2005.

[39] P. Chiodo and J. Basualdo, “Toxocariasis,” de zoonosis IV, Asociación Argentina de Zoonosis, Buenos Aires, pp. 349–354, 2008.

[40] R. M. Maizels, “Toxocara canis: molecular basis of immune recognition and evasion,” Veterinary Parasitology, vol. 193, no. 4, pp. 365–374, 2013.

[41] H. Smith, C. Holland, M. Taylor, J.-F. Magnanval, P. Schantz, and R. Maizels, “How common is human toxocariasis? towards standardizing our knowledge,” Trends in Parasitology, vol. 25, no. 4, pp. 182–188, 2009.

[42] J. Basualdo, M. Spero, P. Chiodo, M. Ciarinella, and M. Minvielle, “Oral treatment with a potential probiotic (Enterococcus faecalis CECT 7121) appears to reduce the parasite burden of mice infected with Toxocara canis,” Annals of Tropical Medicine and Parasitology, vol. 101, no. 6, pp. 559–562, 2007.

[43] L. F. D. C. de Avila, P. D. L. Telmo, L. H. R. Martins et al., “Protective effect of the probiotic saccharomyces boulardii in toxocara canis infection is not due to direct action on the larvae,” Revista do Instituto de Medicina Tropical de São Paulo, vol. 55, no. 5, pp. 363–365, 2013.

[44] L. F. D. C. de Avila, P. M. M. de Leon, M. Q. de Moura, M. E. A. Berne, C. J. Scanni, and F. P. Leivas Leite, “Modulation of IL-12 and IFNy by probiotic supplementation promotes protection against Toxocara canis infection in mice,” Parasite Immunology, vol. 38, no. 5, pp. 326–330, 2016.

[45] CDC, “Trichuriasis (also known as Whipworm Infection),” https://www.cdc.gov/parasites/whipworm/ retrieved on Nov 22, 2016.

[46] R. L. Pullan, J. L. Smith, R. Jasrasaria, and S. J. Brooker, “Global numbers of infection and disease burden of soil transmitted helminth infections in 2010,” Parasites & Vectors, vol. 7, no. 1, article 37, 2014.

[47] Pan American Health Organization (PAHO), “Zoonoses and communicable diseases common to man and animals,” in Parasitoses, p. 580, Scientific and Technical Publication, 3rd edition, 2003.

[48] H. Meekums, M. B. F. Hawash, A. M. Sparks et al., “A genetic analysis of trichuris trichiura and trichuris suis from ecuador,” Parasites Vectors, vol. 8, Article ID Article no. 168, 2015.

[49] A. B. Berne, C. J. Scaini, and F. P. Leivas Leite, “Modulation of IL-12 and IFNy by probiotic supplementation promotes protection against Toxocara canis infection in mice,” Parasite Immunology, vol. 38, no. 5, pp. 363–365, 2013.

[50] M. B. F. Hawash, M. Betson, A. Al-Jubury et al., “Whipworms in humans and pigs: origins and demography,” Parasites & Vectors, vol. 9, no. 1, article no. 1325, 2016.

[51] R. W. Summers, D. E. Elliot, J. F. Urban Jr., R. Thompson, and J. V. Weinstock, “Trichuris suis therapy in Crohn’s disease,” Gut, vol. 54, no. 1, pp. 87–90, 2005.

[52] M. A. Dea-Ayuela, S. Rama-Iñiguez, and F. Bolás-Fernandez, “Enhanced susceptibility to Trichuris muris infection of B10Br mice treated with the probiotic Lactobacillus casei,” International Immunopharmacology, vol. 8, no. 1, pp. 28–35, 2008.

[53] J. McClements, J. J. Kim, H. Wang et al., “Lactobacillus rhamnosus ingestion promotes innate host defense in an enteric parasitic infection,” Clinical and vaccine immunology: CVI, vol. 20, no. 6, pp. 818–826, 2013.

[54] J. B. Holm, D. Sorobeta, P. Killierich et al., “Chronic Trichuris muris infection decreases diversity of the intestinal microbiota and concomitantly increases the abundance of lactobacilli,” PLoS ONE, vol. 10, no. 5, Article ID e0125495, 2015.

[55] M. Meekums, M. B. F. Hawash, A. M. Sparks et al., “A genetic analysis of trichuris trichiura and trichuris suis from ecuador,” Parasites Vectors, vol. 8, Article ID Article no. 168, 2015.

[56] M. B. F. Hawash, M. Betson, A. Al-Jubury et al., “Whipworms in humans and pigs: origins and demography,” Parasites & Vectors, vol. 9, no. 1, article no. 1325, 2016.

[57] R. W. Summers, D. E. Elliot, J. F. Urban Jr., R. Thompson, and J. V. Weinstock, “Trichuris suis therapy in Crohn’s disease,” Gut, vol. 54, no. 1, pp. 87–90, 2005.

[58] A.-K. Bär, N. Phukan, J. Pinheiro, and A. Simoes-Barbosa, “The Interplay of Host Microbiota and Protozoan Parasites at Mucosal Interfaces: Implications for the Outcomes of Infections and Diseases,” PLOS Neglected Tropical Diseases, vol. 9, no. 12, Article ID e0004716, 2015.

[59] M. M. Zais and N. L. Harris, “Interactions between the intestinal microbiome and helminth parasites,” Parasite Immunology, vol. 38, no. 1, pp. 5–11, 2016.

[60] F. Benzel, H. Erdur, S. Kohler et al., “Immune monitoring of Trichuris suis egg therapy in multiple sclerosis patients,” Journal of Helminthology, vol. 86, no. 3, pp. 339–347, 2012.

[61] B. Rosche, K.-D. Wernecke, S. Ohlrnau, J.-M. Dörr, and F. Paul, “Trichuris suis ova in relapsing-remitting multiple sclerosis and clinically isolated syndrome (TRIOMS): study protocol for a randomized controlled trial,” Trials, vol. 14, article no. 112, 2013.

[62] W. Peng, K. Yuan, M. Hu, and R. B. Gasser, “Recent insights into the epidemiology and genetics of ascaris in china using molecular tools,” Parasitology, vol. 134, no. 3, pp. 325–330, 2007.

[63] J. Bethony, S. Brooker, M. Albonico et al., “Soil-transmitted helminth infections: ascaris, trichuriasis, and hookworm,” The Lancet, vol. 367, no. 9521, pp. 1521–1532, 2006.

[64] M. Walker, A. Hall, and M.-G. Basañez, “Individual predisposition, household clustering and risk factors for human infection with Ascaris lumbricoides: new epidemiological insights,” PLOS Neglected Tropical Diseases, vol. 5, no. 4, Article ID e007, 2011.

[65] P. Nejsum, E. D. Parker et al., “Ascariasis is a zoonosis in denmark,” Journal of Clinical Microbiology, vol. 43, no. 3, pp. 1142–1148, 2005.
[64] N. Arizono, Y. Yoshimura, N. Tohzaka et al., "Ascariasis in Japan: Is pig-derived Ascaris infecting humans?" *Japanese Journal of Infectious Diseases*, vol. 63, no. 6, pp. 447-448, 2010.

[65] R. P. Bendall, M. Barlow, M. Betson, J. R. Stothard, and P. Nejsum, "Zoonotic ascariasis, United Kingdom.," *Emerging Infectious Diseases*, vol. 17, no. 10, pp. 1964–1966, 2011.

[66] M. Hoenigl, K. Seeba, T. Valentijn, I. Zollner-Schwetz, and R. Krause, "Pulmonary ascariasis in patients from wealthy countries: Shift in epidemiology?" *International Journal of Infectious Diseases*, vol. 16, no. 12, p. e888, 2012.

[67] R. Schneider and H. Auer, "Incidence of Ascaris suum-specific antibodies in Austrian patients with suspected larva migrans visceralis (VLM) syndrome," *Parasitology Research*, vol. 115, no. 3, pp. 1213–1219, 2016.

[68] G. Solano-Aguilar, T. Shea-Donohue, K. Madden et al., "Feeding probiotic bacteria to swine enhances immunity to Ascaris suum," *Veterinary Immunology and Immunopathology*, vol. 128, no. 1-3, pp. 293-294, 2009.

[69] D. I. Thomas, R. J. Husmann, M. Villamar, T. R. Winship, R. H. Buck, and F. A. Zuckermann, "Lactobacillus rhamnosus HN001 attenuates allergy development in a pig model," *PLoS ONE*, vol. 6, no. 2, Article ID e16577, 2011.

[70] S. Jang, S. Lakshman, A. Molokin et al., "Lactobacillus rhamnosus and Flavanol-enriched Cocoa Powder Altered the Immune Response to Infection with the Parasitic Nematode Ascaris suum in a Pig Model," *The FASEB Journal*, vol. 30, no. 1, 2016.

[71] CDC, "Parasites-Hookworm," http://www.cdc.gov/parasites/hookworm/index.html Nov 28, 2016.

[72] R. J. Traub, "Ancylostoma ceylanicum, a re-emerging but neglected parasitic zoonosis," *International Journal for Parasitology*, vol. 43, no. 12-13, pp. 1009–1015, 2013.

[73] R. J. Traub, T. Inpankaew, C. Suthikornchai, Y. Sukthana, and R. C. A. Thompson, "PCR-based coprodiagnostic tools reveal dogs as reservoirs of zoonotic ancylostomiasis caused by Ancylostoma ceylanicum in temple communities in Bangkok," *Veterinary Parasitology*, vol. 155, no. 1-2, pp. 67–73, 2008.

[74] T. Inpankaew, F. Schär, A. Dalsgaard et al., "High prevalence of Ancylostoma ceylanicum hookworm infections in humans, Cambodia, 2012," *Emerging Infectious Diseases*, vol. 20, no. 6, pp. 976–982, 2014.

[75] R. J. Traub, R. P. Pednekar, L. Cuttell, R. B. Porter, P. A. Abd Megat Rani, and M. L. Gatne, “The prevalence and distribution of gastrointestinal parasites of stray and refuge dogs in four locations in India,” *Veterinary Parasitology*, vol. 205, no. 1-2, pp. 233–238, 2014.

[76] C. Gordon, J. Kurscheid, M. Jones, D. Gray, and D. McManus, "Soil-transmitted helminths in tropical australia and asia," *Tropical Medicine and Infectious Disease*, vol. 2, no. 4, p. 56, 2017.

[77] F. A. Smout, L. F. Skerratt, J. R. Butler, C. N. Johnson, B. C. Congdon, and R. A. Thompson, "The hookworm Ancylostoma ceylanicum: an emerging public health risk in Australian tropical rainforests and Indigenous communities," *One Health*, vol. 3, pp. 66–69, 2017.

[78] M. D. Murphy and A. R. Spickler, *Zoonotic hookworms*, November 2013, http://www.cfsph.iastate.edu/Factsheets/pdfs/hookworms.pdf.

[79] M. D. G. Coelho, F. A. D. S. Coelho, and I. M. D. Mancilha, "Probiotic therapy: A promising strategy for the control of canine hookworm," *Journal of Parasitology Research*, vol. 2013, Article ID 430413, 6 pages, 2013.