Use of Probiotics and Prebiotics to Combat Antiparasitic Resistance

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Abstract

Parasitic infections pose a significant threat to both human and animal health worldwide, especially in tropical and subtropical regions, affecting millions of individuals and leading to huge economic losses. While several antiparasitic medications are being used to treat the parasitic infections but with the passage of time, efficacy of these synthetic drugs have decreased due to the development of resistance. To cope with this problem, there's need to employ a safe and environmental friendly alternative methods. The use of prebiotics and probiotics is gaining popularity due to its prophylactic nature. Prebiotics are the beneficial microbes that enhance the immunity and promote healthy gut microbiota whereas, prebiotics are indigestible food that nourish the gut microbes. Studies have shown that both prebiotics and probiotics possess antiparasitic potential via modulating gut flora, enhancing immunity, increasing beneficial bacteria and competing with pathogens for resources. This chapter explores the underlying mechanisms and relevant research studio investigating the potential of prebiotics and probiotics to combat antiparasitic resistance.

Keywords: Probiotics, Prebiotics, Antiparasitic resistance, Gut Microbiota, Bacteriocins, Competitive exclusion.

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Introduction

Parasitic diseases are a global health concern but more common in tropical and subtropical areas of the world (Nag & Kalita, 2022), climate change also promoting their prevalence (Dziduch et al., 2022). Approximately, 25% of the people around the world experience parasitic infections among them foodborne and zoonotic infections pose a great threat (Hossain et al., 2023). Moreover, more than 500 million ruminants are infected with parasitic infections globally causing huge economic losses (Dziduch et al., 2022). Parasitic infections threaten the survival of domestic (Rizwan et al., 2023), zoo and wild animals (Ferdous et al., 2023) leading to high morbidity and mortality rates (Ünal et al., 2020).

Various antiparasitic drugs such as fenbendazol, levamisole, ivermectin, pyrantel etc. are being employed in the world for the treatment of parasitic infections in humans as well as animals (Selzer & Epe, 2021) but with the passage of time antiparasitic resistance developed due to excessive use of drug, underdosing, parasitic genetic adaptation and mass treatment (Fissiha & Kinde, 2021). In addition, presence of drug residues in products of animals (milk, meat and eggs) poses significant threat to humans' health (Mesfin et al., 2024) and presence in faeces affects the population of dung beetles eventually disturbing the ecosystem (Tovar et al., 2023). Moreover, use of these drugs can show various side effects, such as headache, vomiting, allergic reactions, nausea, seizures, and even carcinogenic etc. (Tiwari et al., 2023). Thus to deal with this issue, a multifaceted approach is necessary, combining alternative methods including phytotherapy (Sarfaraz et al., 2025), use of vaccines, prebiotics, probiotics, proper nutrition and hygiene practices (Ribeiro & Vilela, 2023) need to be employed. In recent years, use of prebiotics and probiotics emerged as a promising sustainable approach in the healthcare, public and scientific domains (Cunningham et al., 2021)

Probiotics are the beneficial microorganisms that provide numerous health benefits both to humans and animals including antimicrobial, treating colon cancer, gastrointestinal infecions, and ulcer, aiding digestion, enhancing immunity, weight gain, increased milk production (Mazziotta et al., 2023). Probiotics such as bacteria (*Lactobacillus*, *Enterococcus*, *Streptococcus*), fungi and yeasts (Reda, 2018) are safe and nature-friendly alternatives (Vijayaram et al., 2024).

Whereas Prebiotics are the non-digestible food products that are degraded by gut microorganisms thus increasing the number of beneficial bacteria in the gastrointestinal system. These exhibit potential in alleviating various helath concerns such as constipation, vaginal infections, diarrhea, diabetes, obesity, improving bone health and immunity (Kaur et al., 2021). Prebiotics include resistant starch, polyphenols (tannins, falvinoids, Coumarin, phenolic acids), lactobionic acid, psyllium, oligosaccharides, fructans, polyunsaturated fattyacids, lactosucriose, galactomannan (Olaimat et al., 2020). The dietary sources of prebiotics include grains, chicory, seaweeds, greentea, mulberry, flaxseeds, blueberry, green algae, dragaon fruit, oats, agave, mushrooms, wheat, onions, honey, milk, beans, banana, tomato (Bamigbade et al., 2022).

This chapter provides an overview of the use of prebiotics and probiotics in mitigating antiparasitic resistance in both humans and animals.

1. Role of Probiotics to Combat Parasites

1.1. Mechanism of Probiotics

Probiotics exert their antimicrobial especially antiparasitic effects through variety of mechanisms including production of several biological molecules such as lactic acid, antibiotics, free fatty acids, lysozymes, acetic acid, butyric acid etc. that inhibit the growth of microbes. In addition, probiotics stimulate the dendritic cells to differentiate into T helper cells which produce cytokines that in turn regulate the antibodies (IgA & IgG) production conferring the anti-inflammatory action. Probiotics act as antioxidants by reducing the reactive oxygen species, enhancing the synthesis of antioxidant enzymes (catalase, peroxidase, glutathione, superoxide dismutase) and chelating the metal ions. Probiotics also work by intestinal modulation via increasing the beneficial microbes in the gut through competitive exclusion (adhering to the epithelial surface of the gut). Probiotics also compete for nutrients with the parasites (Saracino et al., 2021; Simon et al., 2021) as described in (figure 1).

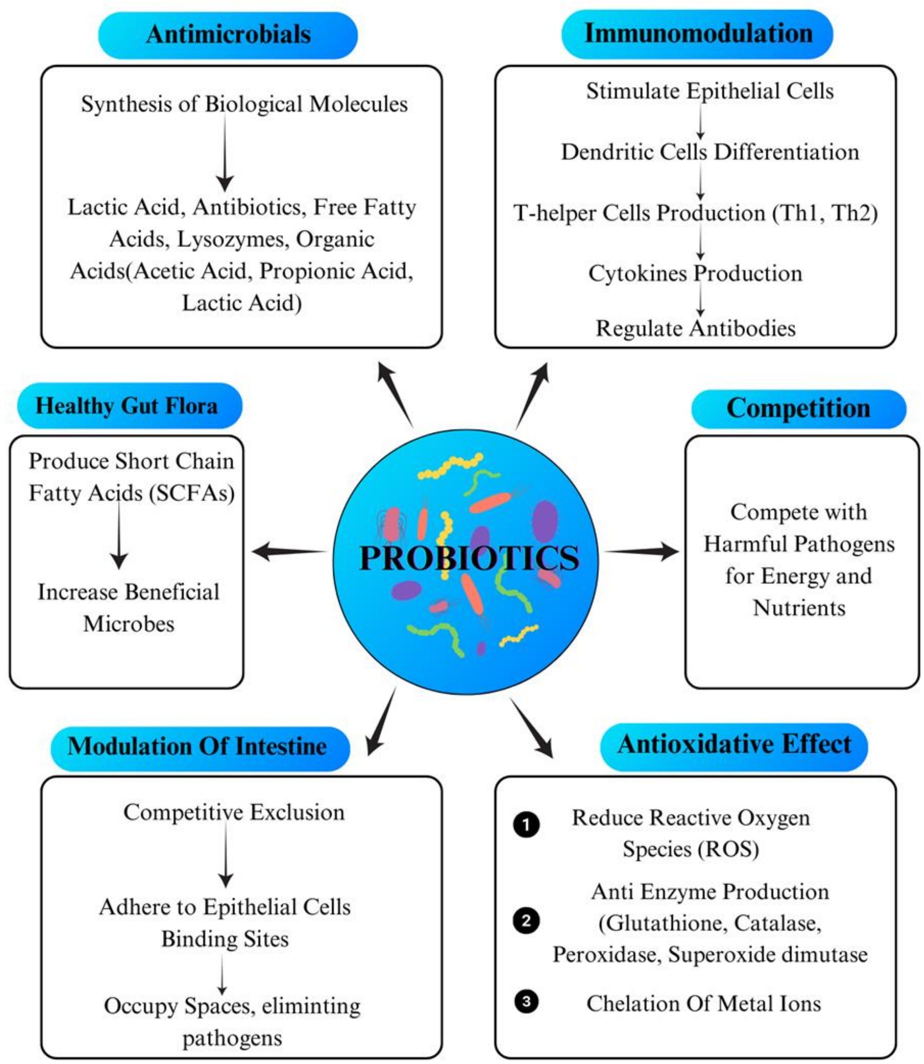

Fig. 1: Mechanism of Action of Probiotics (Saracino et al., 2021; Simon et al., 2021).

1.2. Use of Probiotics against Parasite Infections

Various probiotics including *Lactobacillus, Bacillus, Bifidobacterium, Saccharomyces, Escherichia* and *Pediococcus* have shown promising results in combating wide range of parasitic species of both humans and animals such as *Giardia lamblia, Eimeria species, cryptosporidium, Trichomonas vaginalis, Trypanosoma species, Leishmania species, Plasmodium, Schistosoma, Trichnella species, Toxocara, Asacaris, Trichuris, Haemonchus contortus, Hymenolepis* (Reda, 2018; Mandal et al., 2024) as described in the Table 1 and 2.

2. Role of Prebiotics to combat Parasites

2.1. Mechanism of Action of Prebiotics

Prebiotics pass undigested through upper gastrointestinal tract and are fermented by gut microbiota in the colon. This fermentation process produces short chain fatty acids (SCFAs) such as butyric acid, propionic acid and acetic acid which play a pivotal role in maintain the gut health. SCFAs creates the gut environment acidic by lowering the pH that inhibits the harmful microbes. SCFAs strengthen the gut barrier by increasing epithelial cells of colon and the mucus production. In addition, SCFAs compete with pathogens for binding sites on gut surface (competitive exclusion), regulate programmed cell death and metabolism, acts as an antioxidant by neutralizing the reactive oxygen species. modulates immunity by increasing the production of immune cells, lowering the inflammatory responses via inhibiting cytokines production (You et al., 2022; Chen et al., 2024). Furthermore, Prebiotics are also involved in directly enhancing the beneficial microbes and lowering the harmful microbes by producing the antimicrobial substances such as bacteriocins, organic acids, etc. (Elshaghabee & Rokana, 2022). thus being an excellent alternative in lowering the parasitic burden (figure 2).

2.2. Use of Prebiotics against Parasitic Infections

Variety of prebiotics including inulin, β-glucans, lactoferrin, Sugarcane molasses Mannan-oligosaccharide have demonstrated promising results against parasitic species of both humans and animals. These parasites encompass giardia, *Trichinella spiralis* (Javaid et al., 2024), *Eimeria* species (Abd El Monsef et al., 2024; Matthew et al., 2022) and ectopararsites (Nagrampa et al., 2018) as described in the Table 3 and 4.

3. Addressing Antiparasitic Resistance with Prebiotics and Probiotics

3.1. Reduction of drug Dependency

Prebiotics and probiotics can lessen the reliance on the conventional antimicrobial drugs by decreasing the required dosage and frequency. Antimicrobial substances produced by probiotics could serve as potential alternative to antimicrobial drugs thereby slowing the development of antimicrobial resistance (Li et al., 2022). The probiotics (*Lactobacillus* and *Enterococcus*) eliminated the adults and larvae *of Trichinella spiralis* and also decreased the reproductive capacity of the parasite thus being an excellent alternative against to antiparasitic drugs (Bucková et al., 2018).

3.2. Restoration of gut Microbiota

Parasitic infections lead to dysbiosis in the microbial community of alimentary canal by increasing harmful bacteria and decreasing beneficial bacteria, due to immune suppression *(Su et al., 2018)*. Probiotics contribute to a healthy microbial population of the gut by introducing good bacteria and eradicating harmful bacteria via detoxification, a strong gut barrier and an acidic environment, while prebiotics provide nourishment for these beneficial microbes (Somal et al., 2024). In a study, inulin supplementation enhanced the growth of beneficial bacteria such as *Actinobacteria* and *Akkermansia muciniphila* (Javaid et al., 2024). A study in pigs confirmed these results, showing that inulin administration increases the concentration of beneficial microbes such as *Actinobacteria* and *Bacteroidetes* (Myhill et al., 2018).

Table 1: Studies exploring the use of probiotics in controlling parasitic species of humans.

Sr. No.	Parasite	Probiotic	Model Animal	Effects	Reference
1	*Giardia duodenalis*	*Saccharomyces*, *Bifidobacterium* and *Lactobacillus*	*In-vitro*	Restored the intestinal damage by balancing microbiota, regulating gut mucus barrier enhancing production of antioxidant enzymes, regulating systemic and mucosal immunity, directly inhibiting parasite through secretion of deconjugated bile salts	(Dashti & Zarebavani, 2021)
2	*Ancylostoma ceylanicum* and *Heligmosomoides polygyrus bakeri*	*Bacillus thuringiensis* crystal protein	Hamsters	Exhibited 175 times more anthelminthic effectiveness than albendazole, worked by disrupting the intestinal cells of parasites ultimately leading to their death	(Li et al., 2021)
3	*Schistosoma mansoni*	*Bacillus cereus*	Mice	Decreased the worm burden and liver enzymes (Alkaline Phosphatase & Aspartate Transaminase), increased production of cytokines (IFN-γ, TNF-α, IL-17)	(Dos Santos et al., 2024)
4	*Giardia* sp. and *Ascaris* sp.	*Saccharomyces bouvardias*	Humans	Enhanced the beneficial bacteria numbers & decreased harmful bacteria in the gut, restored the microbial community of gut	(Pryshliak et al., 2022)
5	*Plasmodium berghei*	*Lactobacillus sakei*	Mice	Completely inhibited the growth of parasite, prevented weight loss, maintained the normal hematological parameters	(Toukam et al., 2021)
6	*Echinococcus granulosus*	*Lactobacillus acidophilus*	Mice	Reduced the parasitic burden upto 98%, improved the immunity	(Yousif & Ali, 2020)
7	*Cryptosporidium parvum*	*Lactobacillus plantarum* and *Lactobacillus acidophilus*	Mice	Decreased the worm load, showed the immunomodulatory effect by enhancing the mucosal immunity & cytokines production, repaired the intestinal damage	(Al-khaliq et al., 2021)
8	Blastocystis	*Lactobacillus rhamnosus*, *Lactococcus lactis* and *Enterococcus faecium*	In vitro	Suppressed the parasitic growth either directly or indirectly by producing antimicrobials (lactic acid), competition for nutrients Also reduced parasitic numbers by producing toxins (lipopolysaccharide)	(Lepczyńska & Dzika, 2019)

3.3. Synergistic Effects

Early studies showed that combined therapy of probiotics and conventional antiparasitic drugs results in more effective parasitic reduction than monotherapy. Moreover, combined therapy lessens the severity of drug side effects, promotes quicker recovery and lowers the required dosage (Almallah et al., 2023). Combination of *Lactobacillus acidophilus* and drug albendazole against *Trichnella spiralis* in mice completely degenerated the parasite via strong immune response (BOCKTOR et al., 2022).

Table 2: Studies exploring the use of probiotics in controlling parasitic species of animals

Sr. No.	Parasite	Probiotic	Host	Effects	Reference
1	*Eimeria tenella*	*Lactobacillus*	Chicken	Decreased fecal egg counts, enhanced immunity and antioxidants, decreased intestinal sores, weight gain and improved hematology	(Mohsin et al., 2021).
2	*Toxopalsma gondii*	*Lactobacillus delbrueckii* and *Lactobacillus fermentum*	Mice	Improved the survival rate upto 95%, reduced tachyzoites upto 82%, enhanced immune response by increasing interferon-gamma (IF-γ) and protected liver from severe damage by decreasing infiltration of inflammatory cells	(Almallah et al., 2023)
3	*Ichthyophthirius multifiliis*, *Clonorchis sinensis paramyosin* and *Myxobolus*.	*Aeromonas sobria*, *Brochothrix thermosphacta*, *Bacillus* spp., *Lactobacillus* sp. and *Nitrosomonas*	Fish	probiotics exert their beneficial effects through diverse mechanism like bacteriocins production, competitive exclusion, nutrients competitions, providing nutrients and host immunomodulation	(Simon et al., 2021).
4	*Trichinella britovi*	*Lactobacillus casei* and *Lactobacillus paracasei*	Mice	Inhibited larvae and adult parasites via immunomodulation by increasing number of gut associated lymphoid tissue cell, also negatively impacted the reproductive ability of the parasite	(Boros et al., 2022)
5	Nematodes (*Strongyles* & *Eimeria*)	*Enterococcus faecium*	Horses	Reduced the fecal egg counts, increased phagocytic activity	(Lauková et al., 2023)
6	*Ascaris suum*	Inactivated bacterial strain of *Bacillus thuringiensis*	In vitro (Pigs, foals)	Inhibited both parasitic eggs,	(Urban et al., 2021)
7	*Eimeria* species	Combination of coccidiosis vaccine & BLES (*Bacillus animalis*, *Lactobacillus casei*, *Enterococcus faecalis*, *Saccharomyces cerevisiae*)	Broilers	Reduced oocysts shedding. Improved feed efficiency, decreased intestinal sores, enhanced beneficial bacteria, increased production of N-glycans (immune response),	(Cai et al., 2023)
8	*Toxocara canis*	*Lactobacillus acidophilus*	Mice	Reduced the larval numbers upto 58%, exerted the immunomodulatory effect	(Cadore et al., 2021)
9	*Trichinella spiralis*	*Lactobacillus acidophilus*	Mice	Reduced the adults upto 62% and larvae upto 74%, altered the cytokines level	(Farrag et al., 2021)
10	*Cryptosporidium parvum* and *Giardia duodenali*	*Lactobacillus* sp.	Calves	Decreased diarrheal symptoms and worm burden, increased growth by improving the mucosal, antimicrobials production Combination of Probiotic and phytobiotic (rosmarinic acid) proved to be more effective	(Stefańska et al., 2021)

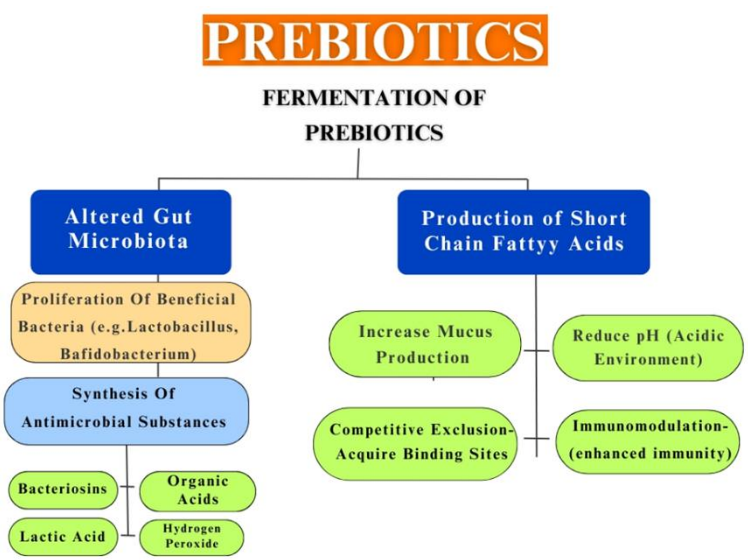

Fig. 2: Mechanism of action of Prebiotics (You et al., 2022; Chen et al., 2024).

Table 3: Studies investigating the efficacy of prebiotics against human parasitic species.

Sr. No.	Parasite	Prebiotic	Model Animal	Effects	Reference
1	*Giardia duodenalis*	Polysaccharides (Inulin, homogalacturonan, arabinogalactan, xylan)	In vitro	Inhibits the growth & binding to gut lining	(Sabatke et al., 2022)
2	*Trcihnella spiralis*	Galactomannan	In vitro	Adheres to rTsgal protein inhibiting the parasitic invasion into epithelial cells of intestine, enhances the immunity	(Zhang et al., 2024)
3	*Toxoplasma gondii*	Omega 3 polyunsaturated fatty acids	Mice	Lowered the survival rate of parasite by stimulating the autophagus process	(Choi et al., 2019)
4	*Schistosoma mansoni*	Omega 3 polyunsaturated fatty acids	Mice	Decreased the number worms especially females and eggs, enhanced the liver and spleen condition	(El-Beshbishi et al., 2019)
5	*Trypanosoma brucei*	Oligosaccharides (glucosamine, acetylglucosamine)	In vitro	Inhibits the proliferation of the parasite via disrupting its metabolic activity	(Silva et al., 2019)
6	*Leishmania species*	Oligosaccharides	In vitro	Directly inhibits the parasite by concentrating in parasites vacuole	(Silva et al., 2019)
7	*Entamoeba histolytica*	Polyphenols	Mice	Decreased the parasitic burden, also strengthened the mucus barrier of the gut	(Shaker et al., 2018)
8	*Plasmodium falciparum*	Mulberry	In vitro	Reduced the proliferation of the pararsite by targeting the dihydrofolate reductase	(Pradhan et al., 2023)

Table 4: Studies investigating the efficacy of prebiotics against animal parasitic species.

Sr. No.	Parasite	Prebiotic	Host	Effects	Reference
1	*Nosema ceranae*	Acacia gum, inulin, and fructooligosaccharides	Honey bees	Acacia showed the highest efficacy followed by fructooligosaccharide while inulin was ineffective Acacia's efficacy stem from its anti-inflammatory and antioxidative properties	(Borges et al., 2021)
2	*Eimeria tenella*	Sugarcane molasses	Broilers	Improved the hematology, immunity & nutrient absorption, reduced eggs shedding	(Matthew et al., 2022)
		Lactoferrin		Lowered the intestinal lesions and fecal egg count, enhanced the immunity and histopathology of chickens, also proved to be an antioxidant, accelerated growth	(Abd El Monsef et al., 2024)
3	Ectoparasite	Inulin	Fish	Enhanced growth, immunity & blood parameters of fish, also increased antioxidative enzymes, lowered worm burden, improved the structure of liver and spleen	(Yones et al., 2020)
4	*Neobenedenia girellae* (Ectoparasite)	cMOS (conditioned mannan-oligosaccharides)	Fish	Lowered the size and burden of ectoparasites, increased the immunity via increasing inflammation, producing antimicrobials Enhanced the activity of lysozyme in skin mucus	(Fernández-Montero, et al., 2019)
5	Coccidia	Mannan-oligosaccharide	Chicken	Promoted growth and weight gain, lowered the eggs shedding, improved the immunity & gut health by increasing the beneficial microbes	(Nagrampa et al., 2018)
6	*Eimeria perforans*, *E. magna*, *E. media*, and *E. irresidua*	Bio-Mos (mnnan oligosaccharide)	Rabbits	Increased weight, lowered th parasitic burden, improved the gut health ()	(El-Ashram et al., 2019)
7	Gastriinetsinal helminths	Chicory	Livestock	Loered the parasitic burden, Showe dmor ethan 70% efficacy,	(Peña-Espinoza et al., 2018)
8	*Dactylogyrus* specie (Fluke)	Fructans (*Allium sativum* & *Allium cepa*)	Fish	Increased the hematology and immunity of fish, exhibited potential antiparasitic effects both in vitro and in vivo	(Reda et al., 2024)
9	*Cryptosporidium parvum*	Chitosan oligosaccharide	Lambs	Lowered the fecal egg counts, increased weight	(Aydogdu et al., 2019)

Prior studies have proven that combined use of prebiotics (Inulin, homogalacturonan, arabinogalactan, xylan) with conventional antiparasitic drug (nitazoxanide) in the treatment of giardia intestinalis may exhibit synergistic effect. This synergy results in lower required dosage and achieving more enhanced treatment efficacy (Sabatke et al., 2022). Moreover, combination of lactoferrin with an anticoccidial drug (diclazuril), yielded superior results in improving gut health and mitigating disease severity (Abd El Monsef et al., 2024).

4. Synbiotics

Synbiotics are the simultaneous combined therapy of prebiotics and probiotics, where prebiotics act as source of nutrients and provide ideal environment for the growth and proliferation of probiotic microbes (Javanmiri et al., 2024) thus enhancing the efficacy of the treatment. Evidence from various studies suggests that combined use of prebiotics and probiotics can be more effective in controlling parasites compared to using them individually (Shaaban et al., 2021). Synbiotics supplementation demonstrated higher efficacy in improving the blood health and also lowered the mortality rates as compared to individual treatment (Matthew et al., 2022). Combined administration of *Lactobacillus casei* and inulin proved to be effective against murine's giardiasis leading to increased weight, decreased the parasitic burden, boosted beneficial microbes and enhanced immunity (Shukla et al., 2019).

5. Safety and Limitations of using Probiotics and Prebiotics

Probiotics, while being promising for various health but present certain limitations. These include potential of life threatening side effects of certain strains, failure of colonization in the gut of certain individuals and risk of genetic mutations impacting their efficacy. Furthermore, the challenges associated with probiotics include risk of harmful metabolites production, transfer of antibiotic resistant genes to harmful bacteria, degradation susceptibility due to environmental factors, possibility of systemic infections, inaccurate labeling and products contamination. Individual variations in the health and genetics can also influence the efficacy (Liang et al., 2024).

Prebiotics such as inulin, galactose, and fructans are generally considered safe, as long as they are used in appropriate dosages. Prebiotics are often used to relieve the diarrhea but high doses of fructooligosaccharides, inulin, and oligofructose and fructans can induce diarrhea, abdominal pain, constipation and allergic reactions. Furthermore, excessive butyrate (a beneficial metabolite) can promote the proliferation of harmful bacteria. To mitigate these concerns, it is highly recommended that prebiotics should be properly labeled with concentration, source, storage guidelines and possible allergic reactions, moreover, new prebiotics must undergo extensive clinical trials on humans (Anadon et al., 2021; Abia, 2023).

Conclusion and Future Recommendations

This chapter has summarized the current understanding of the potential of prebiotics and probiotics in mitigating parasitic infections in both humans and animals. Evidence from both in vitro and in vivo studies suggests that these can help reduce the development of antiparasitic resistance by enhancing immunity and balancing gut flora. Prebiotics such as inulin, ooligofructose, polyphenols, polysaccharides, free fatty acids and probiotics including *Lactobacillus*, *bacillus* and *Saccharomyces* species exhibited the potential in inhibiting various parasites such as *Trichnella*, *Eimeria*, *Trypanosoma*, *Trichuris* etc. Future research should focus on elucidating the exact mechanisms of both prebiotics and probiotics in regulating the host immunity and intestinal mcirobes to mitigate the pararsitic infections. Long term clinical trials are needed to determine the optimal concentration, frequency and duration of both prebiotics and probiotics.

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