Chapter 01

The Antiparasitic Effect of Botanicals with Special Reference to *Moringa* against *Cryptosporidium* Species

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ABSTRACT

Cryptosporidium (*C.*) belongs to the phylum Apicomplexa. There are different species of *Cryptosporidium* in which *C. parvum* is the main zoonotic agent. *C. parvum* causes gastrointestinal infections in animals. The transmission of *C. parvum* occurs through contaminated food and water. Its life cycle depends upon only a single host and sporozoites released attach to the epithelial lining of the small intestine. *Cryptosporidium* causes economic losses due to decreased milk productivity, mortality due to severe dehydration, and low reproductive performance. Different drugs are used for the treatment of *Cryptosporidium*. Nitazoxanide is the only FDA-approved that is used against *Cryptosporidium* infection. However, these drugs cause resistance in animals. Then alternative strategies are used for the treatment of infection. Plant extracts are used against *Cryptosporidium* that inhibit larvae migration and hatching of eggs. Bioactive compounds like flavonoids, alkaloids, tannins, and ascorbic acid, of different plants show their efficiency. Different extracts are present in plants that show their effect on the motility of larvae, and egg hatching. Of all medicinal plants, *Moringa oleifera* has great importance in the treatment of *Cryptosporidium*. It has antioxidant, anti-inflammatory, and antibiotic properties, and certain compounds treat intestinal lesions. *M. oleifera* is used for the treatment of parasitic infections in animals. Zinc, iron, and magnesium are also present in it. Zinc is used to increase metabolism, iron increases the growth of animals, and magnesium is used to increase milk production. *Cryptosporidium* can be prevented by treating the contaminated water with moringa seed extract.

KEYWORDS		
Cryptosporidium, Economic loss, Transmission, Resistance of drugs, Moringa	Received: 21-May-2024 Revised: 18-Jul-2024 Accepted: 15-Aug-2024	A Publication of Unique Scientific Publishers

Cite this Article as: Batool S**,** Ishtiaq A, Saeed K, Cheema K, Hussain A, Waris A, and Ashraf R 2024. The antiparasitic effect of botanicals with special reference to *Moringa* against *Cryptosporidium* species. In: Abbas RZ, Khan AMA, Qamar W, Arshad J and Mehnaz S (eds), Complementary and Alternative Medicine: Botanicals/Homeopathy/Herbal Medicine. Unique Scientific Publishers, Faisalabad, Pakistan, pp: 1-7. https://doi.org/10.47278/book.CAM/2024.008

INTRODUCTION

Cryptosporidium (C.) is a protozoal parasite that is present throughout the world (Galuppi et al., 2016), and it belongs to the phylum Apicomplexa (Hassan et al., 2021). It causes the gastrointestinal tract infection in domestic animals. Cryptosporidiosis causes intense diarrhea in ruminants and causes economic losses because of decreased growth, performance, and production of animals (Tomazic et al., 2018). *Cryptosporidium* species that infect the cattle are *C. parvum*, *C. anderson, C. bovis*, and *C. ryanae*. On the other hand, *C. parvum* is the only species that is linked to the characteristic symptoms of cryptosporidiosis in cattle and the primary source of infection in pre-weaned calves. *C. parvum* is the main zoonotic agent of cryptosporidiosis and may also infect several animal species (Pinto et al., 2021). *C. parvum* is the most pathogenic species in cattle and humans while other species have few cases. The zoonotic importance of *Cryptosporidium* is identified by knowing the effect of infection on public health (El-Alfy and Nishikawa, 2020). *C. parvum* is a vital species among all species of the genus *Cryptosporidium* and has zoonotic potential so it needs high consideration to be controlled (Sayed, Hamza, Galal, Sayed, & Gaber, 2016).

C. parvum is an obligate intracellular parasite that attaches to the epithelial lining of the gastrointestinal tract of the host and causes infection (Sayed et al., 2016). In cattle, *C. parvum* causes a severe gastrointestinal infection which also causes a decrease in the growth rate, and reduces milk production, anorexia, and weight loss. This parasite has a simple life cycle and depends on a single host species during its life cycle (Tarekegn et al., 2021). The oocyst of *Cryptosporidium* has two forms one is an environmental form which is a thick-walled oocyst. This oocyst gets ingested by the consumption of contaminated fodder or water. When thick-walled oocyst is ingested, it undergoes excystation due to changes in temperature, action of bile salt, and pH. The second form is sporozoites which are released from the oocyst. Sporozoites are released and attach to the epithelial lining of the gut (Pinto and Vinayak, 2021). The transmission of oocyst has critical importance in the life cycle of *Cryptosporidium spp* (Mohammed, Degefu, & Jilo, 2017).

In cattle, the transmission of *C. parvum* is through the fecal-oral route (Shaw et al., 2021). In the summer season, chances of infection are more due to the high intake of water and other activities like swimming but in winter these activities are decreased so the chance of infection is also reduced (Khan et al., 2022). In veterinary clinics, *Cryptosporidium* is diagnosed by fecal sample. Molecular methods are also used for species differentiation which include polymerase chain reaction (PCR) (Thomson et al., 2017). The *C. parvum* oocysts in food are detected by aptamers (Petersen et al., 2014). Different techniques are used for the detection of oocysts which include Allen and Ridley's formal method, centrifugation method, and sucrose flotation method. The most sensitive method between them is the formol-ether method. Detection in fecal samples is difficult due to the small size of the oocyst. For the identification of oocysts in stool samples different staining techniques are used including Nigrosine staining, safranin staining, Giemsa staining, and Ziehl staining (Siddique et al., 2021). Proper diagnosis of the *Cryptosporidium* is necessary to estimate the need for control of the disease (Gerace, Presti, & Biondo, 2019).

Different drugs are used to treat cryptosporidiosis. Nitazoxanide, clofazimine, glycopeptide occidiofungin, pyrazolopyridine derivates, paromomycin, and metronidazole, etc. are examples of some anti-cryptosporidium medicines. However, by use of these drugs except Nitazoxanide, shows no effective treatment. Clinical symptoms of cryptosporidiosis are only improved with paromomycin (Ali et al., 2024) (Namazi & Razavi, 2024). For the control of cryptosporidiosis in livestock, the drug Halofuginone lactate is used (Aboelsoued and Abdel Megeed, 2022). Nitazoxanide drug approved by the US Food and Drug Administration is used but this drug is ineffective in weak immune patients (Ranasinghe, Zahedi, Armson, Lymbery, & Ash, 2022). When these anti-parasitic drugs are used continuously against infection, resistance to the parasite may be developed (Ranasinghe et al., 2023). The oocyst which is the infective stage of *Cryptosporidium* has a thick outer shell that helps to live outside of the body. Oocysts can survive for a long period due to their outer thick shell causing resistance to different environmental conditions and disinfection of chlorine. When drugs cause resistance in animals, then as alternative strategies medicinal plants are being suggested as anti-parasitic drugs to cure parasitic infections (Nassar, 2022). As alternative approaches, some researchers used medicinal plants as new and effective drugs for the treatment of cryptosporidial infection (Namazi & Razavi, 2024).

Moringa oleifera is a medicinal plant that belongs to the family Moringaceae and it is widely distributed in north-eastern India, Pakistan, Afghanistan, and Bangladesh (Yerena-Prieto et al., 2022). There are some regional names for *M. oleifera* which include the drumstick tree, Kelor, mlonge, saijhan, benzolive, miracle tree, Marengo, mulangay, and Sanjana. It has an antioxidant property and consists of ascorbic acid, carotenoids, saponins, flavonoid, and phenolic content. These all have their role against oxidation. The extract of moringa leaves improves intestinal lesions and increases the level of antioxidants that defend against oxidative stress in the body (Namazi and Razavi, 2024).

It is used as a drug that has the potential to treat animals with infection of parasitic worms. This is commonly used for helminth parasites but has also shown some antiprotozoal activity. Due to the soluble lactin in its seed extract, it shows larvicidal properties. It stops the development of larvae due to their heamagglutinating activity (Fatima et al., 2014). Antibiotic and fungicidal activity is also present in the moringa plant due to their pterygosperium and related compounds. Every part of the moringa plant has different properties that are effective against infection (Haldar and Kosankar, 2017).

Transmission of *Cryptosporidium parvum* in Cattle

Transmission of *Cryptosporidium* in cattle is associated with zoonotic transmission. *C. parvum* is transmitted through food and water. *C. parvum* causes gastrointestinal infection and some species of *Cryptosporidium* are related to respiratory cryptosporidiosis. The infective stage is the oocyst stage that causes infection when it is excreted in the environment and transmission also occurs through the contaminated environment. When cattle ingest the infective stage (oocyst), its excystation occurs in the small intestine and releases the sporozoites. These sporozoites invade the wall of the intestine and asexual multiplication occurs. Sporozoites change into merozoites followed by sexual multiplication and formation of macrogamonts and macrogamonts. By following the fertilization of macrogamonts, oocysts are produced that sporulate within the host before being shed in host faces (Robertson et al., 2020). *C. parvum* is transmitted by ingestion of thick-walled oocyst from different sources. The main sources of transmission are contaminated water and food (Shafiq et al., 2015). Animals are often bathed with contaminated water and also drink this water that favour the transmission of *Cryptosporidium* (Abbas et al., 2022). The climatic conditions and weather fluctuations have an impact on the transmission of *Cryptosporidium* species. The role of climatic conditions is vital in the suspension of oocyst in water, contamination of water sources, and the temperature, and rainfall also affect transmission of this parasite (Fig. 1) (Golomazou et al., 2024)

Life cycle

Cryptosporidium is present everywhere in nature and it requires only a single host to complete its life cycle. Many stages are completed in its life cycle which include asexual and sexual replication. *Cryptosporidium* is an intestinal parasite which reproduce asexually and undergoes a cycle of merogony and sexual gamogony. It has a complicated life cycle. Three developmental stages occur in this parasite; meronts, gamonts, and oocyst. Multiple stages are present in an asexual division that follows the sexual division and development of the oocyst through fertilization. Oocysts come into the environment through faces. Because of the appropriate moisture and moderate temperature, oocysts bear the environmental conditions and live in the water and soil for several months. Due to their small size, oocysts transfer to another place through water sources and air. Two types of oocysts exist; thin-walled and thick-walled oocyst. Thin-walled oocysts present in the host intestine and cause intestinal lesions and thick-walled excreted in the environment and cause infection after ingestion of oocyst through oral uptake. After ingestion of oocyst, excystation occurs in the intestine and changes into sporozoites. Based on *Cryptosporidium* spp., sporozoites invade the gastric and intestinal epithelium. Inside the host, the next stage of asexual proliferation merogony occurs. The shape and size of merozoites and sporozoites are the same, only nucleus difference is present. In merozoites, the nucleus is located in the center than sporozoites. Merozoites attach to the epithelial cell and spread the infection to other intestinal sites (Abbas et al., 2022). Merozoites form two types of meronts. Gametogany is formed by merozoites and micro-macro gametes are formed by the division of Gametogany, followed by fertilization of gametes, which further fertilize to zygote. Thick and thin-walled oocysts are formed through the process of sporogony. The wall is created around the oocyst to tolerate the environmental conditions. In the next stage, the infection is transferred from one host to another. The final stage is the formation of infectious sporozoites through sporogony (Pumipuntu and Piratae, 2018; Mamedova and Karanis, 2020; Gururajan et al., 2021; Delling and Daugschies, 2022).

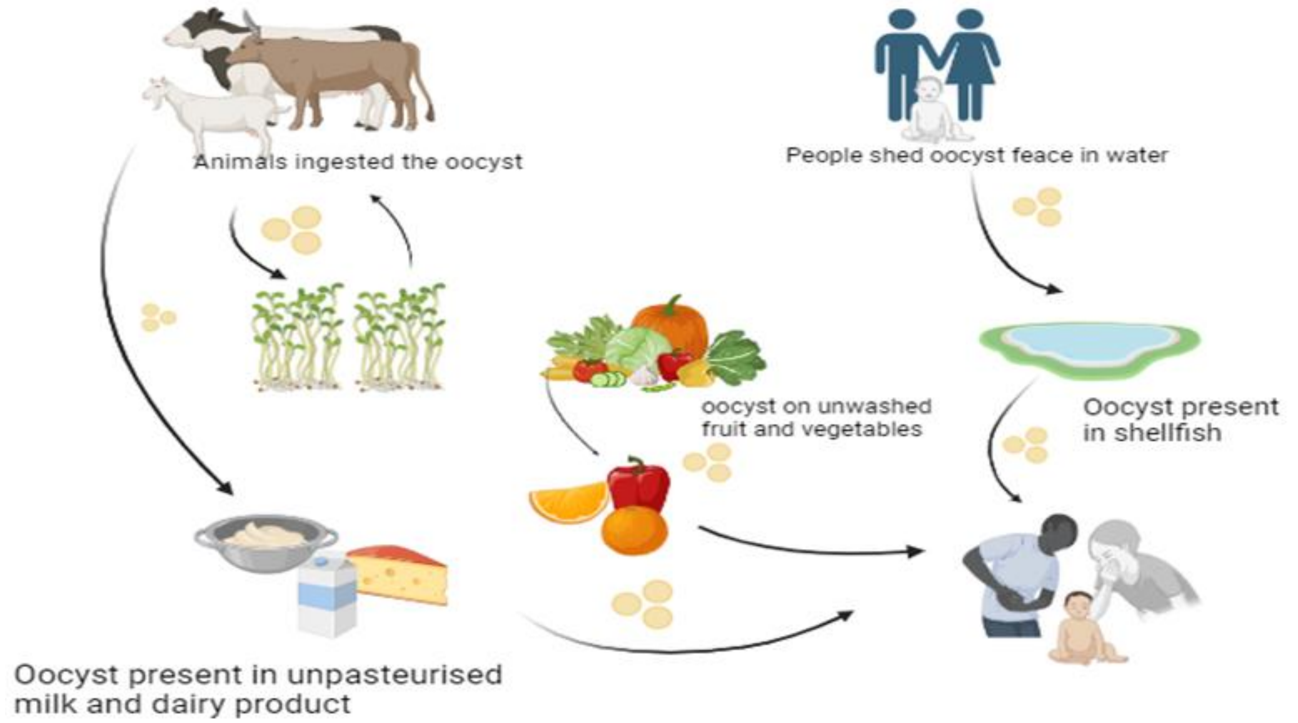

Fig. 1: Transmission of *Cryptosporidium*

Economic Losses

Livestock plays an important role in the development of country economy. However, some factors that pose a threat to livestock production include the different strategies that are used for animal breeding, poor veterinary service, and parasitic diseases. In the world, Pakistan is a milk-producing country, and it fulfills domestic needs. However, the population of Pakistan increased and milk production does not meet the demand of people. Increase the population demand for food and put stress on the price of dairy products. In Pakistan, different factors inhibit the growth of the sector of livestock. Low production of milk and income of farms are the main losses due to livestock diseases (Ashfaq et al., 2015). Parasites that are present in and outside the body of the host get their food. These parasites include helminths, protozoa, lice, and flies that cause gastrointestinal diseases. These diseases cause economic loss in cattle. For the identification of economic loss in cattle due to parasitic disease, different models are used (Rashid et al., 2019). Parasitic disease inhibits the growth and causes disease of blackleg in young cattle. Treatment of reproductive disorders and mastitis is expensive, which also causes major economic loss. Mortality in cattle is due to hemorrhagic septicemia (Ghafar et al., 2020). *Cryptosporidium* causes diarrhea in animals that cause death due to severe dehydration (Khan et al., 2022).

Benefits of Moringa Leaves

Plants have great importance in human life through their medicinal properties and dietary supplements. *Moringa oleifera* is one of the fast-growing, small trees that grow on sandy arid soil and this tress has aesthetically attractive properties (Sujatha and Patel, 2017). This tree may be pollinated by both self-pollination and cross-pollination. There are 13 species of the Moringaceae family. These are dispersed over the globe according to their geography and environment

(Umbreen Shahzad et al., 2019). *M. oleifera* is prevalent in the tropical region of the world sub-Himalayan tract and countries including Pakistan, India, Asia, Africa, Arabia, Philippines, Central America, and Cambodia (Shahzad, Khan, Jaskani, Khan, & Korban, 2013). All parts of this plant contain amino acids, beta-carotene, and phenolic compounds (Gupta and Ahmed, 2020). *M. oleifera* has significant nutritional values and is a rich source of protein, vitamins, and micronutrients that complete the nutritional deficiency of the KPK rural region. The vitamins included in this tree, are vitamin AandC and the micronutrients are Ca, Fe, and K (Haroon et al., 2023). The locally known name of moringa in Pakistan is "Sohanjna" and it is distributed in Punjab, Sindh, and Khyber Pakhtunkhwa (KPK). It is also called a miracle tree due to its nutritional, and medicinal properties (Faisal et al., 2020). *Moringa* is used as an animal feed. During the winter season, with the help of moringa leaves urea-molasses block is made that overcomes the nutritional deficiencies in cattle (Malik et al., 2019). Anti-inflammatory, antibiotics, and antioxidant characteristics are present in moringa leaves. In cattle, *M. oleifera* is used as a protein diet (Mahmood et al., 2022). It shows a great impact on the control of parasites and hinders the disease associated with parasites (Soltan et al., 2017). Magnesium is present in it which increases milk production and the level of iron is also high which increases the growth of animals. Zinc increases the metabolism of protein, fats, and sugar and plays a role in tissue respiration (Su and Chen, 2020).

Plant Bioactive Compound for Control of Gastrointestinal Parasite

The excessive use of chemicals and drugs against gastrointestinal parasites causes anthelminthic resistance, then an alternative method is used for the treatment of infection. These alternative approaches play an important role in the control of GIT parasites in cattle (Zeineldin et al., 2020). The drug resistance is developed against *Cryptosporidium*, then medicinal plants are used as alternative strategies. Drug metronidazole that causes resistance in *Cryptosporidium* (Ojuromi and Ashafa, 2020). Much literature revealed that 139 plants are used for the treatment of diarrhea and abdominal pain, and 30 species are used against protozoal infections (Calzada and Bautista, 2020). Many natural compounds are present in plants that have great efficiency against parasites. These compounds are variable due to their growth environment, and condition, and their harvesting method also plays an important role in the preservation of compounds (Hoste et al., 2015). The effect of plant extract and compounds on anthelmintic activity can be detected by adding them to animals' diet during their infection period (Chagas, 2015).

Different bioactive substances are present in medicinal plants such as flavonoids, alkaloids, and tannins that show their properties against anthelminthic activities. Tannins hinder the hatching of eggs and migration of larvae. It binds with cuticles and causes changes in the movement of larvae, reproduction, absorption, and nutrition. Different parameters are used for showing the effect of plant extract on the GIT parasite from which is part of the species, the dose and type of extract are used. Different types of extract are used; methanolic extract, ethanolic extract, aqueous extract, and acetone extract (Blomstrand et al., 2021). A study by (Akouedegni et al., 2019) revealed that compared to methanolic extract, ethanolic extract of *S. monbin* leaves has a greater influence on larvae motility. Observation of researchers reported that for larvae the aqueous extract shows a greater impact than the ethanolic extract. For larvae migration, the acetone extract of *P. biglobossa* shows a greater effect than methanolic extract, on egg hatching the acetonic extract of plant *cassia alata* plays an important role than aqueous extract. The presence or lack of secondary metabolite in one extract relative to another might be the cause of the variation in activity across the extract of the same plant (Degla et al., 2022). According to a report by Farooq et al. (2008), in the Cholistan desert veterinarians use traditional medicine for the treatment of parasitic disease in cattle. However, the study by Khan (2009) revealed that 35 species of plants were collected from the Cholistan desert of Pakistan and showed the efficiency against parasitic disease in cattle. Tipu et al. (2006) described the efficiency of the anti-coccoidal and anti-parasitic activities, present in leaves and fruits of *Azadirachta indica.* Plant extract is used for the treatment of tick-borne protozoal disease and mastitis in cattle. Different plant species are useful for livestock diseases like gastrointestinal disease, healing of wounds, cough, fever, urinary tract infection, and placental removal (Ahmed and Murtaza, 2015).

Effect of *Moringa* against *Cryptosporidium*

Cryptosporidium is transmitted through contaminated water. When contaminated water along with feces and oocyst of parasites is given to crops, health issues are raised. Water is treated with inorganic and organic chemicals, but this treatment of water is expensive and the emergence of many diseases occurs in animals. The natural way is used for the treatment of water. Among water, *M. oleifera* seeds are used for the treatment of water (Petersen, Petersen, Enemark, Olsen, & Dalsgaard, 2016). The bioactive compound of moringa phenol and alkaloids shows an antiparasitic effect (Elghandour et al., 2023). According to a study, *M. oleifera* extract is used in poor countries as a water purifier and to avoid people with waterborne disease (Mariane de Souza, Beltran, Bergamasco, & Cusioli, 2024).

Conclusion

Cryptosporidium is a gastrointestinal parasite that causes intense diarrhea, lesions in the intestine, blacklegs, mastitis, and dehydration in animals. From *Cryptosporidium* species, *C. parvum* is a main zoonotic agent that causes transmission of infection from animal to human and vice versa. *C. parvum* causes economic loss due to the low production of milk and inhibits the growth of animals. Drugs that are used against infection in animals cause resistance. Medicinal plants are used for the treatment of gastrointestinal infections. Bioactive compounds are present in these plants that show their effect. Of all these plants, *Moringa oleifera* is the plant that is known as a miracle tree due to its magical properties. This plant tolerates adverse climatic conditions. Bioactive compounds like flavonoids, tannins, vitamins, and alkaloids are present in it that show antiparasitic activity. By using these bioactive compounds new drugs are made for the treatment of *Cryptosporidium* in animals. The contaminated water is also treated with moringa seed extract for the prevention of *Cryptosporidium*. However, more research is required to know the benefits of moringa and the application of moringa in animals against *Cryptosporidium*.

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