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An insight into the interaction between *Argulus siamensis* and *Labeo rohita* offers future therapeutic strategy to combat argulosis

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Abstract

Aquaculture and fisheries are salient flourishing sectors in the world but their sustainability is often afflicted by several pathogenic diseases. Among all the pathogenic diseases of fish, parasitic diseases are found to be a major cause of concern. Argulosis is one of the dominant parasitic problems encountered in Indian aquaculture practices. *Argulus siamensis* is the most prevalent argulid species harming the Indian major carp species including *Labeo rohita.* The major carps respond to parasitic infestation by elevating various immune relevant genes. The therapeutic chemicals, synthetic drugs and other plant extracts have made a progress in the fight against argulosis. However, there is no effective vaccine and drugs are available for this disease. Thus, designing efficient, cost-effective and eco-friendly control and treatment strategies for argulosis is presently needed. Keeping the aforementioned facts in mind, the current review elaborated the immunological interaction between *A. siamensis* and *L. rohita*, available combat tactics, highlighted the already identified vaccine candidates to design effective control measures and illustrated the use of omics technology in future to combat argulosis.

Keywords Argulosis · *Argulus siamensis* · *Labeo rohita* · Immunological interaction · Control · Omics

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Introduction

Fisheries and aquaculture are among the fastest-growing industries in the world. In 2018, global fish production was predicted to be around 179 million tonnes among which aquaculture contributes about 46%. Over the past two decades, Asia dominates fish farming contributing about 89% of the global catch. Asia also covered two-thirds of the global inland water production (FAO 2020). India accounts for 7.58% of the total global fish production, standing at rank 2nd in aquaculture and rank 3rd in fisheries production. Both fisheries and aquaculture contribute 1.24% to the national GVA(gross value added) and 7.28% to the agriculture GVAin India (data from https://nfdb.gov.in/about-indian-fisheries). However, several pathogenic diseases strike these sectors and cause immense loss. In Indian aquaculture practices, parasitic diseases are found major contributors to socio-economic losses (Sahoo et al. 2020). Parasites infect fishes of both wild and cultivated habitats. Shinn et al. (2015) estimated an annual global loss of 1.05 billion to 9.58 billion USD due to parasitic infection (Shinn et al. 2015). The majority of the fish parasites which belong to the class of protozoan, myxozoan, helminths and crustacean are depicted in Fig. 1, and a detailed description of the fish parasitic diseases has been listed in Table 1. The present review is focused on one of the major parasitic diseases "argulosis". *Argulus* is the most prevalent crustacean ectoparasite which infects Indian major carps (IMCs), causing argulosis and putting a major constraint on the Indian freshwater aquaculture system (Sahoo et al. 2013b, 2021). In India, *Labeo rohita* (*L. rohita*) is one of the preferred hosts for *Argulus siamensis* (*A. siamensis*) to cause argulosis. A loss of 29,524 INR (615 USD) per hectare each year has been estimated due to argulosis (Sahoo et al. 2013b, 2021). Indian major

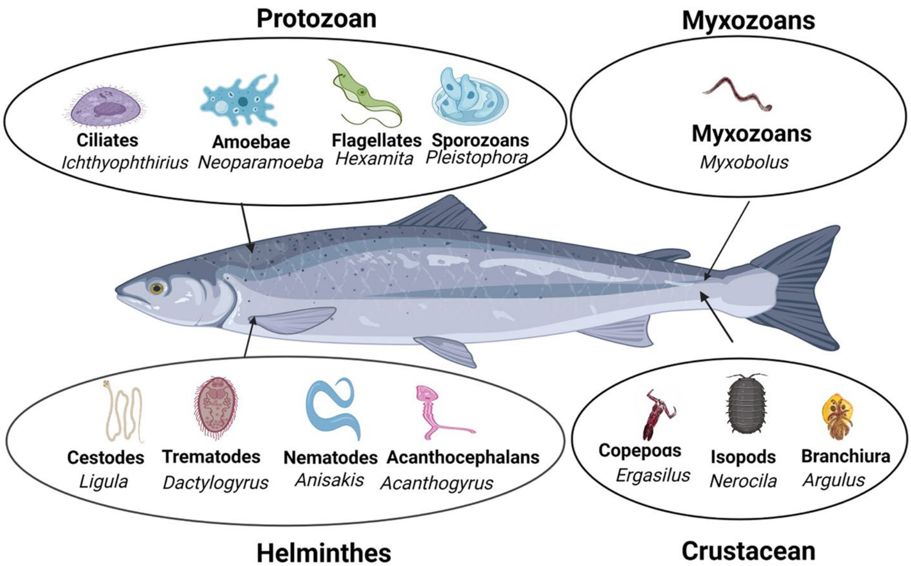

Fig. 1 Common protozoan and metazoan parasites of fish. Fish parasites correspond to both protozoa and metazoan. In protozoa, parasites from different groups including ciliates, e.g. *Ichthyophthirius*; amoebae, e.g. *Neoparamoeba*; flagellates, e.g. *Hexamita*; and sporozoans, e.g. *Pleistophora* harm fishes. Metazoan parasites that infect fishes embrace myxozoans, e.g. *Myxobolus*; trematodes, e.g. *Dactylogyrus*; cestodes, e.g. *Ligula*; nematodes, e.g. *Anisakis*; acanthocephalans, e.g. *Acanthogyrus*; crustaceans, e.g. *Argulus*; etc.

Table 1 A selective list of parasitic diseases of fish

Disease	Pathogen	Symptoms	References
Ichthyophthiriasis	*Ichthyophthirius multifiliis*	Infected fish exhibit tiny white spots on the fins and skin and mucus production; foci of infection become thickened and necrotic; falling of necrotic skin and scales off the surface often occurs	Wei et al. (2013)
Trichodiniasis	*Trichodina*, *Trichodinella* and *Tripartiella*	Irritation, hyperplasia of the epithelial cells, clubbing of the gill filaments and even fusion of the gill filaments, red lesion on body, fin root, exophthalmos, darken body colour, dislodged scales	Ihwan et al. (2016), Mitra et al. (2013)
Cryptocaryonosis (marine ich/marine white spot disease)	*Cryptocaryon irritans*	Whitish or greyish spots on the body surface and gills, mucus hyperproduction, skin discoloration, anorexia and respiratory distress, behavioural changes like fin tremors, hyperactivity and sudden darting movements	Colorni and Burgess (1997)
Chilodonellosis	*Chilodonella hexasticha*, *Chilodonella piscicola*	Higher production of mucus and disturbances in the respiratory function of the skin, entire body is covered with the bluish-white coating, skin depigmentation, ulceration, scale loss, hyperplasia of gill epithelium and necrosis in the gill and skin of fishes	Bastos Gomes et al. (2017)
Brooklynelliosis	*Brooklynella* spp.	Extensive skin damage and subcutaneous haemorrhage after parasite attachment to the skin and gills	Nagasawa and Cruz-Lacierda (2004)
Ichthyobodosis/Costiasis	*Ichthyobodo* spp.	Infection on skin and gill, excess mucus production form a blue- grey or white film over body surface and gill, lethargic behaviour, loss of appetite, Gill hyperplasia and lamellar fusion	Meyers et al. (2019)
Hexamitasis	*Hexamita* spp.	Anorexia, dark coloration of the skin, reduced growth, excessive nervousness, disease become systematic with fish becomes anaemic with swollen kidney, abdominal distension and exophthalmos	Timur et al. (2009)

Table 1 (continued)

Disease	Pathogen	Symptoms	References
Amyloodiniosis (velvet)	*Amyloodinium ocellatum*	Increased respiratory rate, white or brown coloration ("velvet") or cloudy appearance (If the infection is confined to the gill, the "velvet" appearance will not be present), skin can seem hazy	Francis-Floyd and Floyd (2011)
Amoebic gill disease (AGD)	*Neoparamoeba perurans/Paramoeba perurans*	Affected fish become lethargic, increased ventilation rate, a gathering near the water's edge. White mucoid patches present on gill, epithelial hyperplasia and lamellar fusion	Oldham et al. (2016)
Microsporidiosis	*Glugea* spp. and *Pleistophora* spp.	Swollen abdomen, brown to black nodules of various sizes has been observed in fat tissue and internal organs	Cruz-Lacierda and Erazo-Pagador (2004)
Heterosporosis	*Heterosporis* sp.	Infect the skeletal muscles, Gross lesions and necrosis of skeletal muscle tissue	Phelps et al. (2015)
Whirling disease	*Myxobolus cerebralis*	Characteristic symptoms include destruction of ossification, skeletal deformation and blackening of the caudal part of the fish body	Sarker et al. (2015)
Gyrodactylosis	*Gyrodactylus* spp. (skin flukes)	Characterized by the destruction of the skin or rarely the gills, increased mucus production, frayed fins, skin ulcers and damaged gills. The lesions are caused by the feeding activity of the parasites	Ali and Faruk (2018)
Dactylogyrosis	*Dactylogyrus* spp. (gill flukes)	Mostly affect gill, so increased frequency of breathing, telangiectasis (gill blood blisters), over stimulated mucus production, discoloured and swollen gill	Ali and Faruk (2018)

Table 1 (continued)

Disease	Pathogen	Symptoms	References
Diplostomiasis/diplostomatosis (parasite cataract or eye fluke disease)	*Diplostomum* spp. and *Tylodelphys* spp.	Metacercariae counts in the eyes affect fish survival, Total blindness when metacercariae counts exceed 40 individuals per eye, the harmed host may lose its ability to feed, resulting in delayed growth, weight loss and either direct mortality due to malnutrition or indirect mortality due to increased vulnerability to predation	Violante-González et al. (2009)
Ergasilosis	*Ergasilus* spp. (gill maggot)	Asphyxia in heavy gill infestations, excessive blood-tinged gill mucus, high mortality in heavy infestations	Ibrahim (2019)
Lernaeasis	*Lernaea* spp. (anchor worm)	Skin irritation with excessive mucus secretion, abnormal swimming behaviour, haemorrhagic and ulcerated lesions with potential for secondary infections as anaemia, retarded growth, loss of weight and balance of body	Abbas et al. (2014); Ibrahim (2019)
Argulosis	*Argulus* spp. (fish lice)	Physical injury and abnormal swimming, causes skin irritations, localized swelling, skin lesion, haemorrhagic reaction, anaemia, thin and darkened soft body, red and black spots all over the pelvic to the anal fin region, the fins look frayed and eyes appear sunken	Rahman et al. (2019)

carps (IMCs) farming accounts for more than 90% of overall aquaculture output (Maharajan et al. 2019), and hence, carp culture is referred to as the backbone of Indian aquaculture. *L. rohita* is one of the dominant carp species for aquaculture in India which share more than 60% of total carp production. *L. rohita* contribute 3.7% of the major species yield in world aquaculture (FAO 2020).

Argulosis: a dominant parasite of Indian aquaculture

Argulosis is one of the major parasitic problems encountered in Indian aquaculture practices. Morphologically, *Argulus* has a dorsoventrally flattened body, an oval or rounded carapace, two compound eyes, a stylet and a sucker (Steckler and Yanong 2013). Because of obligatory parasitic nature of *Argulus*, it cannot complete its lifecycle without the host, and therefore frequently encountered swimming freely in search of new hosts or mates and to lay eggs. *Argulus* often sparsely distributed on their host in natural water, and hence appears to be less problematic in natural reservoirs. However, in aquaculture practices, its aggregation increases on the host which exerts a strong detrimental effect. *Argulus* firstly firm on fins and then shifted to head or body surface of fish species. The highest parasite load is generally seen on the body surfaces as the infection proceeded (Kar et al. 2016). To infect host, *Argulus* punctures the host skin, injects toxin and feeds on mucus and blood that cause a skin lesion (Saurabh and Sahoo 2010; Saha et al. 2011). Further argulosis leads to causing cutaneous ulceration, immunological suppression, osmotic imbalance, abnormal swimming, haemorrhages, lowered growth rate, anaemia, growth impairment and secondary infection in freshwater fish (Sahoo et al. 2012; Rahman et al. 2019; Datta et al. 2022a). There are approximately 129 valid species of *Argulus* distributed worldwide in both freshwater (85) and marine water (44), except in Antarctica (Poly 2008). Among various species, *Argulus coregoni*, *A. japonicas* and *A. foliaceus* are the 3 most studied species worldwide in freshwater (Steckler and Yanong 2013). So far, 10 species of *Argulus* have been identified in India (Sahoo et al. 2012). The genetic diversity of *Argulus* species collected from various freshwater aquacultures shows the dominance of *A. japonicas* and *A. siamensis* (Sahoo et al. 2013c).

Host-parasite interactions during argulosis

The host-parasite relationship is a complex phenomenon in which the parasite strives to establish itself in the host while the later resists through its defence mechanisms (Kar et al. 2016). The susceptibility and resistance of the host will decide whether the disease spreads or not. The host physiological and immunological state may influence the interaction. Parasite's capacity to avoid its host's defence is a major factor that influences susceptibility and infectivity (Khan 2012). Teleost fishes are the earliest jawed vertebrates to trigger both innate and adaptive immune responses against the pathogen (Whyte 2007). Innate immunity of fishes is comparable to mammals although the adaptive response is slower than mammals because of its lower body temperature (Woo 2007). Hence, in fish defence, the innate immune system serves as the first line of defence as well as an important component in combating diseases. Furthermore, innate immune system also provides the signal that initiates adaptive immune system to develop a defensive response (Whyte 2007; Smith et al. 2019).

Immune response of *L. rohita* against *A. siamensis*

Recently, various researchers have focused their research on *A. siamensis* to understand the immune response of *L. rohita* toward its infection (Fig. 2). Although *A. siamensis* infect a wide range of host but there is variability in susceptibility pattern of fishes. In ectoparasitic infections, skin seems to be an initial target organ. Therefore, local and systemic inflammatory responses in the host skin are believed to affect a host's susceptibility or resistance to infection. *L. rohita* is more susceptible to *A. siamensis* infection followed by *L. fimbriatus*. *Ctenopharyngodon idella* finds to be the most resistant species for *A. siamensis* infection in carp culture (Kar et al. 2016). The immune response of susceptible and resistant fish species shows a variation. The resistant fish species skin has the higher expression of MHC class IIb (major histocompatibility class) and MMP2 (matrix metalloproteinase 2) as compared to susceptible fish. This indicates that MMP2 and MHC class II immune relevant genes are involved in protective response against *A. siamensis.* The expression of MMP2 and MHCII remains systematic as the parasite has freedom to move. The differential responses are shown in *L. rohita* and *C. idella* which suggests that the presence of early immunological mechanisms could be responsible for host susceptibility and resistance (Kar et al. 2016).

Earlier, it is documented that non-specific immune response of *L. rohita* infested with *A. siamensis* shows the lower activity of complement and α-2-macroglobulin and a higher level of glucose and antiprotease activity of serum (Saurabh and Sahoo 2010), i.e. higher glucose level indicates ectoparasite as a stressor for fish (Datta et al. 2022b).

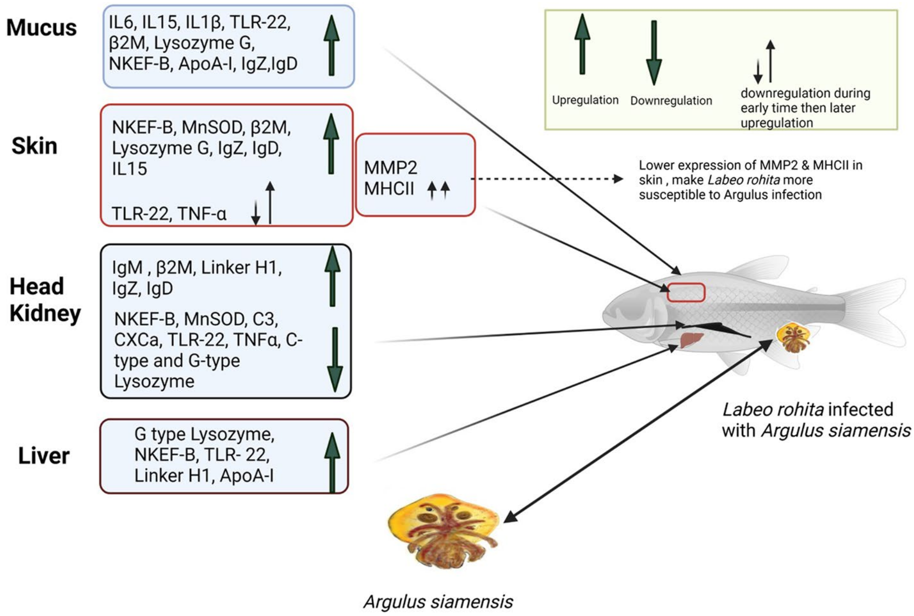

Fig. 2 Expression of various immune relevant genes in *A. siamensis*-infested *L. rohita.* Several innate and adaptive immune genes show elevated expression in the mucus, skin and other organs of *L. rohita* during *A. siamensis* infection. Assorted immune gene covers interleukins, Toll-like receptors, lysozyme, antioxidant gene, MMP2, MHCII, β2M, IgD, IgM and IgZ

Moreover, the immune response and immune gene expression in the skin and head kidney of *L. rohita* infested with *A. siamensis* infection were also reported previously (Kar et al. 2015a). Kar et al (2015a, b) measured and analysed the expression kinetics of immune relevant genes (acute phase protein (C3, CXCa, lysozyme G, lysozyme C and TNFα), Toll-like receptor (TLR 22), antioxidant gene (Mn SOD and NKEF-B) and adaptive immunity gene (β2M and IgM)) relative to the β actin gene (Kar et al. 2015a). In the skin of infected fish, most genes such as β2M (β2-microglobulin), NKEF-B (natural killer cell enhancing factor B), Mn SOD (superoxide dismutase) and g-type lysozyme were found to be significantly upregulated. The TLR-22 and TNF-α genes were considerably downregulated at first but afterwards showed upregulation, whereas C3 gene shows no change in their expression. In the head kidney, the majority of the genes were significantly downregulated except IgM (immunoglobulin) and β2M.

In recent years, research into the molecular characterization of fish immune genes has gained momentum. Mucus on the fish's skin acts as the first line of protection against pathogens. The molecular events in the mucosal immune response of *L. rohita* to *A. siamensis* infection were also identified (Parida et al. 2018). Interleukins (IL 6, IL 15 and IL 1β), TLR 22, β2M, lysozyme G and NKEF-B were found to be upregulated in fish mucus in a cascading fashion. This upregulated gene expression in mucus cell regulates infection-induced inflammation. The elevated gene expression also demonstrates the relevance of mucosal immunity in parasitic infection. Interleukins 15 and g-type (goose type) lysozyme in *L. rohita* reflect enhanced expression during parasite infection. During *A. siamensis* infection, interleukin 15 showed upregulation in fish kidney and skin tissue (Das et al. 2015), while g-type lysozyme showed elevated expression in liver tissue (Mohapatra et al. 2019).

Toll-like receptor 22 (TLR22) is uniquely found in teleosts and the role of TLR22 during *A. siamensis* infection was investigated both in *L. rohita* and *Catla catla*. *C. catla* shows higher resistance level than *L. rohita.* The mRNA expression patterns of TLR22 in *L. rohita* upregulated in the skin, intestine, kidney, brain, spleen and liver. On the other side, higher TLR22 transcript levels were found only in the liver, kidney and spleen of *C. catla* (Panda et al. 2014). Uma et al. (2012) studied the tissue-specific expression of TLRs in gold fish (*Carassius auratus*) infested with *Argulus* sp. The TLR 2, 4 and 7 were upregulated in the skin, gut, liver and kidney, whereas TLR 9 was found to be downregulated in all of these tissues. The TLR 22 showed upregulation only in the skin and liver tissue (Uma et al. 2012). The expression of other important innate immune molecules *Labeo rohita* NKEF-β (*Lr*NKEF-β) was found to be upregulated in the liver, kidney and skin during *A. siamensis* infection which indicates its role in innate immunity against biotic stress and oxidative damage (Parida et al. 2020b).

Furthermore, the antimicrobial small peptides and proteins also play an eloquent role during ectoparasite infection. Earlier, the elevated expression of a high density lipoprotein, i.e. apolipoprotein A-I (ApoA-I), was noticed in the skin, mucous, liver and kidney of *L. rohita* (Mohapatra et al. 2016). The uplifted expression of linker histone H1 in the kidney and liver tissue of infected *L. rohita* indicates its antimicrobial role during ectoparasitic infection (Parida et al. 2020a). Besides small peptides and proteins, parasite invasion also alters immunoglobulin expression in *L. rohita*. Previous study on three immunoglobulins (IgD, IgM and IgZ) in parasitized *L. rohita* assessed the higher expression of IgM in the kidney (although it was undetectable in the skin and liver) and elevated level of IgZ and in kidney, mucus and skin tissue (Kar et al. 2015b).

Available combating strategies of argulosis

Argulus infestation in Indian carp farming has been estimated to cause a loss of 3000 million INR (625,000 USD) each year (Sahoo et al. 2019). Worldwide, little progress has been made in the control and treatment of argulosis caused by *Argulus* spp. in both freshwater and brackish water fish (Fig. 3). Traditional ways of controlling *Argulus* spp. continue to rely on the use of toxic chemicals and anti-parasitic drugs (Hakalahti-Sirén et al. 2008; Hemaprasanth et al. 2012; Raja et al. 2022). Several chemicals like common salt, potassium permanganate, organophosphate and deltamethrin are commonly in use for the treatment of argulosis (Sahoo et al. 2012; Das et al. 2018a). Doramectin and ivermectin were found to be effective in suppressing *A. siamensis* infestation in *L. rohita* (Hemaprasanth et al. 2012). However, the usage of these chemotherapeutics can sometimes result in drug resistance (Sevatdal et al. 2005) as well as a harmful influence on the environment (Johnson et al. 2008).

Anti-parasitic medicinal plant extracts can also be used as an environmentally friendly treatment for parasite infestation as they are decomposable, eco-friendly and economical. Kumar et al. (2012) use *Piper longum* extract (piperine), against the infestation of *Argulus* spp. on goldfish, and find piperine has the potential to become a novel medication for the

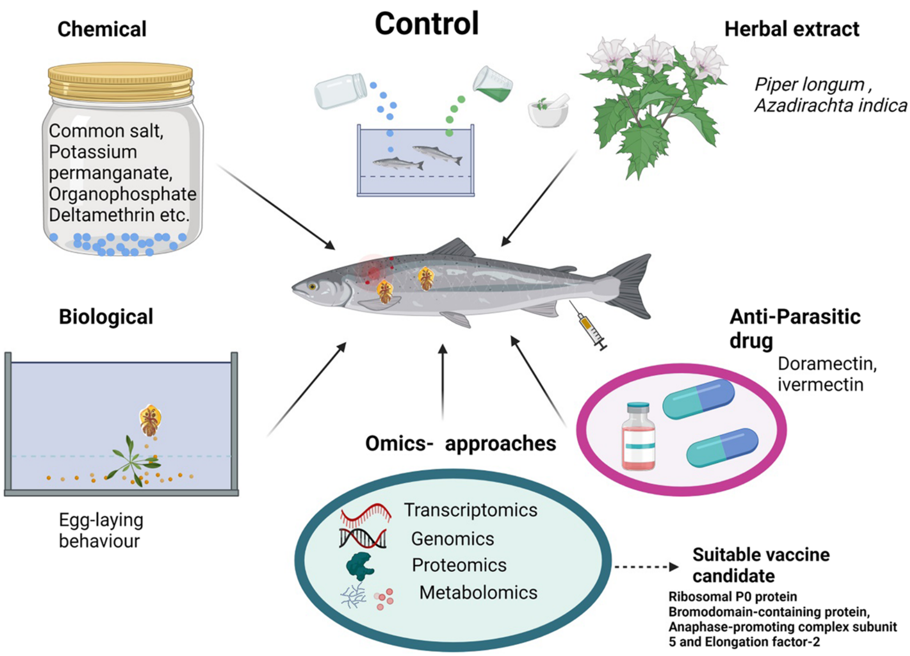

Fig. 3 Different control strategies for *A. siamensis* infection. Control strategies for *A. siamensis* cover chemical, biological and anti-parasitic drugs; herbal extract; and through omic approaches. Various chemical uses for argulosis treatment include common salt, potassium permanganate, organophosphate and deltamethrin. Common anti-parasitic drugs, e.g. doramectin and ivermectin, were found to be effective in suppressing *A. siamensis* infestation. Biological method involves egg-laying behaviour of *A. siamensis*. *A. siamensis* deposits their egg on any solid substratum, water plants and weeds. Other methods presume the use of medicinal plant extract, e.g. neem, as they are decomposable and eco-friendly. Omic approaches which include genomic transcriptomics, proteomics and metabonomics also help to identify suitable vaccine candidates

treatment of *Argulus* spp. (Kumar et al. 2012). Azadirachtin, an extract from *Azadirachta indica*, also shows anti-parasitic properties against *Argulus* spp. in *Carassius auratus* (Kumar et al. 2013; Banerjee et al. 2014). Real-time PCR is a crucial technology in drug development. EF-1 (elongation factor-1 alpha) was also discovered as the most stably expressed reference gene in *A. siamensis* utilizing real-time PCR for evaluating the anti-parasitic component's efficiency. These anti-parasitic drugs and anti-parasitical herbal extracts interfere with the ion channel of parasite's nervous system. Anti-parasitic medications work by modifying the action of several ion channel genes, which kill the parasite. Neem leaf extract was also found to be a better alternative for the development of an effective drug against *A. siamensis* (Sahoo et al. 2019). Nicotine present in the tobacco leaf is potentially active against the adult parasite at a LC of about 8 ppm which in turn is sublethal and to the host fish (Banerjee and Saha 2013).

Biological control is another viable option for controlling any parasitic disease; however, its effectiveness relies on the ecology and behaviour of parasite species. The knowledge of egg-laying behaviour can be used to control the parasite by supplying artificial substrate and strategically positioning it in the host's habitat zone to finally remove the deposited eggs. Gravid *A. siamensis* deposits their egg on any solid substratum, water plants and weeds. *A. siamensis* prefer wood and dark colour substratum for egg deposition. The hard shell of snails also provides a substratum for deposition (Sahoo et al. 2013d). Previously, egg-laying behaviour was used for the control of *A. foliaceus* in rainbow trout fishery (Gault et al. 2002). Interruption of symbiotic association of *Argulus* with other organisms may be another strategy of biological control (Banerjee et al. 2016).

None of the existing control strategies has been effective in addressing the problem of argulosis. In order to completely eradicate, biphasic treatments must be administered precisely on time concerning temperature-dependent hatching patterns (Banerjee and Saha 2013). Vaccines are claimed as the "sole green and effective solution" for protecting fish from diseases. At present, there is now only one commercial parasite injectable vaccine (Providean Aquatec Sea Lice) available for ectoparasite sea lice (Villegas 2015; Shivam et al. 2021). The most important criterion for any vaccine development is the identification of suitable protective antigens of parasites. Omic approaches provide a significant tool for this purpose by identifying suitable vaccine candidates (Shivam et al. 2021). Interaction between *A. siamensis* and gut microbiome of *L. rohita* is also a future candidate for *Argulus* infection control strategy as *Argulus* infection could significantly influence the diversity and richness of the gut microbiota (Mondal et al. 2022).

Preliminary research has been conducted in this direction. The protective response in *L. rohita* elicited by *A. siamensis* whole antigen was investigated. Immunized fish showed lower parasitic load and reduced haemorrhagic patches on the skin as well as higher antibodies presence, which provide insight for vaccine development against *A. siamensis* in *L. rohita* (Das et al. 2018b). Two immunodominant protein fractions were identified as candidate antigens in *A. siamensis*, which could be employed as potential targets for immunoprophylaxis development (Saurabh et al. 2012). The ribosomal P0 protein is also suggested as a protective antigen for vaccine development against this parasite in *L. rohita.* Immunized fish confirmed the increased production of antibodies during parasitic infection but there was no change in parasitic load (Kar et al. 2017). Immunoproteomic emerged as popular techniques that help in the identification of suitable immunoreactive antigens. Using 2D electrophoresis and western blot technique, 14 immunogenic spots were identified from *A. siamensis* from which bromodomain-containing protein, anaphase-promoting complex subunit 5 and elongation factor-2 were suggested as a suitable vaccine candidates (Das et al. 2021). A western blot system has been developed using immunized fish, rohu serum and other reagents to analyse the immunoreactive proteins in *A. siamensis* antigens (Das et al. 2018a).

In the era of post-genomic sequencing, whole genome sequence of *A. siamensis* is not available yet. However, there is a recent finding on gut microbiota analysis of *Argulus*-infected rohu (*L. rohita*) through 16 s rRNA amplicon sequencing (Mondal et al. 2022). The transcriptome analysis of *A. siamensis* generated 75,126,957 reads and 46,352 transcripts contigs on Illumina HiSeq 2000 Sequencing Platform. The assembled contigs yielded a total of 19,290 coding DNA sequences (CDS), including 184 novel CDS and 59,019 open reading frames (ORFs) (Sahoo et al. 2013a). Transcriptome investigations can provide preliminary information about genes involved in parasite physiological activities that could be targeted for vaccine development. Transcriptome shotgun assembly (TSA) sequences were also searched for *A. siamensis* for peptide discovery. A total of 27 transcripts encoding potential neuropeptide precursors were discovered and inferred for their pre/preprohormone using bioinformatics. From the deduced precursor protein, the structure of 105 distinct peptides was predicted (Christie 2014). The predicted peptides open up new avenues for research into peptidergic control of physiology and behaviour in *A. siamensis*.

Conclusion

A. siamensis is the most prevalent parasite causing argulosis in *L. rohita*. *L. rohita* seems to be more susceptible to *A. siamensis* infection. *A. siamensis* infestation usually combats by several therapeutic chemicals, anti-parasitic drugs, herbal extracts and biological control. Much progress has been achieved in phytotherapy, but till now, there is no vaccine against this disease. Various approaches such as western blotting, ELISA, immunoproteomic techniques and high-throughput sequencing were employed for vaccine development strategy. Omic approaches which include genomic transcriptomics, proteomics and metabonomics provide a significant role in such types of problems by identifying potential vaccine candidates. In the future, integrated approaches can be used to combat the disease caused by *A. siamensis*. Hence, this review provides a platform to design an effective control strategy against this parasite.

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Declarations

Ethical approval Not applicable.

Consent to participate Taken.

Consent for publication Yes.

Competing interests The authors declare no completing interests.

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