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REVİEW **DERLEME**

Effective herbal therapeutics against the protozoan parasites in aquaculture

Su ürünleri yetiştiriciliğinde protozoan parazitlerine karşı etkili bitkisel ilaçlar

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Abstract: In industrial aquaculture, producing at high stock densities is inevitable to maximize efficiency and harvest per unit volume. Antibiotics, disinfectants, and other chemicals have become necessary to prevent and control disease outbreaks in intensive fish farming practices. However, the negative impacts of the use of synthetic chemical drugs on environmental health have sparked discussions, making research into alternative treatments inevitable. Medicinal plants offer promising solutions for disease control due to their natural, biodegradable, and antimicrobial properties. The therapeutic properties of plants have been known and safely used in traditional medicine for a long time. The idea that medicinal plants can be utilized in aquaculture as a safer, sustainable, and environmentally friendly practice has begun to be embraced. Although numerous treatment protocols have been developed against metazoan parasites in aquaculture, managing protozoan parasites still poses a significant challenge. A detailed literature review has identified that more than 30 plant species have the potential to control many protozoan pathogens in fish, including *Ichthyophthirius multifiliis* and *Cryptocaryon irritans*. Studies highlight the effectiveness of plant-derived compounds in combating parasites and promoting growth, supporting immunity, serving as antibacterial agents, and even as anaesthetics. Since research on medicinal plants predominantly targets commercially valuable fish farming, there is a recognized need for expanded studies on their application in shellfish farming. Collaboration among researchers, institutions, and farmers is crucial in increasing awareness of local medicinal plants and promoting their use. The use of plants with medicinal properties in aquaculture represents a promising path for disease control and sustainable production. Adopting these natural alternatives could align with responsible agricultural practices and meet the urgent need to mitigate the environmental impacts of traditional treatments in the aquaculture industry.

Keywords: Medicinal plants, herbal therapeutics, protozoan, antiparasitic, aquaculture

INTRODUCTION

In industrial aquaculture, high stock densities and specially formulated feeds are essential to achieve better yield advantages per unit volume. It is an international reality that fish farmers must use large quantities of antibiotics, disinfectants, and other chemical preparations to control mortality rates and prevent significant financial losses from disease outbreaks. Moreover, the use of artificial drugs and chemical therapies, which can damage the natural ecological structures in both water and soil, has been the subject of global and local debates for the past twenty years due to their potential to create adverse effects on the environment and human health. Many alternative methods are being developed to minimize the negative impacts of current treatment practices in aquaculture. While studies on the development and widespread adoption of vaccines and immune enhancers, particularly Specific Pathogen Free (SPF) varieties, continue, developing therapeutic natural alternatives to combat common disease agents has become necessary under increasing environmental sensitivity.

The therapeutic effects of medicinal plants have been known for many years in traditional medicine and pharmacology. It is also reported that this knowledge has been experimentally used in small enterprises against various infections in terrestrial animals and sometimes fish. Medicinal plants are considered safe and highly potent due to their natural, biodegradable, and antimicrobial properties (Valladão et al., 2015). At the same time, more information is available on the identification and treatment of viral, bacterial, and fungal diseases, as well as metazoan parasites, than on protozoan parasites. Pathological tissue changes such as hyperplasia, hypertrophy, or necrosis in protozoan infections can be confused with pathologies caused by many other pathogens. Protozoan parasites can cause acute and chronic detrimental effects in the aquaculture of fish and shellfish (Buchmann, 2015).

Responsible agricultural practices prioritize an ethical approach that avoids using substances harmful to humans and the environment during cultivation stages. In the fight against climate crisis and strategies to reduce water and environmental pollution, limiting the use of harmful substances and synthetic chemicals forms the basis of the transition to good agricultural practices. The approach that medicinal plants can also be utilized to combat diseases in good agricultural practices has started to be adopted.

To date, the potential of phytochemicals (plant derived chemicals) derived from over 30 different plant species to prevent and control unicellular parasites such as Ichthyophthirius *multifiliis*, *Cryptocaryon irritans*, *Piscinoodinium pillulare*, *Ichthyobodo necator*, *Trichodina* sp., *Scuticociliates* sp., and *Hexamita* sp. in freshwater and marine organisms has been researched (Bulfon et al., 2015).

The primary purpose of this review is to raise awareness among decision-makers about medicinal plants as alternative treatment methods in the industrial aquaculture sector and to encourage future research within the scope of responsible aquaculture and agricultural ethics. In this context, medicinal plants proven effective in aquaculture and experimental infections, along with their application protocols, have been listed, and a reference has been prepared for those interested in use.

Application of herbal supplements in aquaculture as anti-protozoan therapeutics agents

Numerous studies have been conducted against unique unicellular pathogenic parasitic agents commonly causing diseases in aquaculture environments. The effectiveness of various plant extracts has been extensively listed against pathogenic protozoan parasites (*in vivo* and *in vitro*), including *I. multifiliis*, *C. irritans*, *P. pillulare*, *I. necator*, *Trichodina* sp., *Gregarines sporozoites*, *Scuticociliates*, and *Hexamita* sp. agents. Previous studies offering environmentally sensitive alternative treatment methods in aquaculture have primarily focused on mitigating serious protozoan infections (Table 1).

Ichthyophthiriasis is among the most significant protozoan diseases, especially in freshwater fish. A study on the antiparasitic efficacy of Magnolol, extracted from plants of the *Magnolia* genus (*M. officinalis* and *M. grandiflora*) used in traditional Chinese and Japanese medicine, reported 100% effectiveness against *I. multifiliis* theronts under in vitro experimental conditions. It was reported to inhibit protomont and tomont cyst development at concentrations of 0.6 mg/L or higher and for 6 hours at 0.8 mg/L and 1.0 mg/L, respectively. An experimental *I. multifiliis* infection in goldfish (*Carassius auratus*) showed that a 5-hour bath treatment with 1.5 mg/L Magnolol significantly reduced the number of theronts released from tomonts in infected fish (Song et al., 2018). The phytochemical 10-gingerol isolated from extracts of *Zingiber officinale* has been reported to protect grass carp (*Ctenopharyngodon idella*) against *I. multifiliis* infection when administered as a bath treatment at a dose of 4 mg/L for 10 days (Fu et al., 2019). The compound 10-gingerol extracted from *Z. officinale* demonstrated 100% antiprotozoal activity against encysted tomonts, nonencysted tomonts, and theronts at concentrations of 16, 8, and 2 mg/L, respectively, in laboratory conditions (without the use of live experimental animals, in petri dishes). The application of tea tree oil (*Melaleuca alternifolia*) at a dose of 50 µL/L for 1 hour per day over 4 days has been recorded to be effective in the treatment of Ichthyophthiriasis in South American catfish (*Rhamdia quelen*) and significantly reduced hepatic oxidative stress (Baldissera et al., 2017).

Based on *in vitro* antiparasitic analyses, the phytochemicals Chelerythrine and Chloroxylonine obtained from the *Toddalia asiatica* plant showed 100% effectiveness at concentrations of 1.2 and 3.5 mg/L, respectively, after 4 hours. Additionally, when 1.8 mg/L Chelerythrine and 8.0 mg/L Chloroxylonine were applied as a bath for 72 hours to infected goldfish (*C. auratus*), they exhibited low parasite prevalence compared to the control group (Shan et al., 2014).

Ekanem et al. (2004) reported that an extract obtained from *Mucuna pruriens* leaves using crude methanol (200 mg/L bath/72 hours) and an extract obtained from the seeds of *Carica papaya* using petroleum ether (250 mg/L bath/96 h) helped significantly reduce parasite load and fish mortality in goldfish with Ichthyophthiriasis, and the extracts could be effectively used. The same researchers reported that *M. pruriens* and *C. papaya* extracts, when used at concentrations of 150 mg/L and 200 mg/L for 6 hours, killed the *I. multifiliis* pathogen 100%.

In the case of grass carp (*C. idella*) infected with *I. multifiliis*, the antiparasitic effect of the chemical Sanguinarine derived from the leaves of *Macleaya cordata* (0.9 mg/L 48-hour bath) proved to be 96.8% effective. Moreover, experimental parasite inhibition tests conducted without fish have reported that chloroform and ethanol extracts from *M. cordata* at a concentration of 70.0 mg/L for 4 hours demonstrated 100% effectiveness against Ichthyophthiriasis (Yao et al., 2010).

In *I. multifiliis* infected barbel chub (*Squaliobarbus curriculus*), the active components Dihydrosanguinarine and Dihydrochelerythrine isolated from *Macleaya microcarpa* leaves were effective in bath doses of 5.18 and 9.43 mg/L for 48 hours, respectively (Yao et al., 2011a).

In goldfish (*Carassius auratus*) infected with *I. multifiliis*, the use of a water-based extract derived from the *Capsicum frutescens* plant at dilutions of 1:32 and 1:64 (for a 4-hour bath) reduced parasite infection prevalence by 13.3% and 40% respectively (Ling et al., 2012). In another study, goldfish treated with methanol extracts obtained from *Magnolia officinalis* and *Sophora alopecuroides* showed a reduction in theronts by 24.7% and 44.7%, respectively, after a 1-hour bath treatment at concentrations of 40 and 320 mg/L (Yi et al., 2012).

In channel catfish (*Ictalurus punctatus*) infected with *I. multifiliis*, treatment with Pentagalloylglucose derived from the *Galla chinensis* plant (20 mg/L/10 days/bath) has been reported to increase fish survival rates up to 93.3%. Antiparasitic assesments in cell culture have shown that Pentagalloylglucose eliminated all theronts (at concentrations of 2.5-20 mg/L over 5.6-233.9 minutes) and reduced tomont

Table 1. A summary of effective herbal therapeutic agents in finfish and shellfish protozoan parasites infection applied in finfish and shellfish aquaculture

In vivo* and *In vitro	**Parasite**	**Agent, dosage, time, and administration**	**Effect***	**Reference**
Goldfish (*C. auratus*)	*I. multifiliis*	Magnolol 1.5 mg/L/5 h, bath	Theronts number ↓ Theronts mortality ↑↑↑	Song et al. (2018)
In vitro		0.6 mg/L/4 h 0.8 mg/L/6 h 1.0 mg/L/6 h	Protomont ↓ Tomont ↓	
Grass carp (*C. idella*)	*I. multifiliis*	10-gingerol 4 mg/L /10 d., bath	+, Fish survival rate↑ Encysted tomonts mortality↑↑↑	Fu et al. (2019)
In vitro		16 mg/L 8 mg/L 2 mg/L	Nonencysted tomonts mortality ↑↑↑ Theronts mortality ↑↑↑	
Silver catfish (*R. quelen*)	*I. multifiliis*	*Melaleuca alternifolia* essential oil. Tea tree oil 50 µL/L/1h/d/4 d, bath	Hepatic oxidative stress↓	Baldissea et al. (2017)
In vitro		*Mucuna pruriens* 150 mg/L/6 h *Carica papaya* 200 mg/L/ 6 h	↑↑	
Goldfish (*C. auratus*)	*I. multifiliis*	Antiparasitics from *Toddalia asiatica* Chelerythrine1.8 mg/L, bath Chloroxylonine 8.0 mg/L/72 h	Parasite prevalence ↓ Parasite Prevalence ↓	Shan et al. (2014)
In vitro		Chelerythrine 1.2 mg/L/4 h Chloroxylonine 3.5 mg/L/4 h	↑↑ ↑↑	
Goldfish (*C. auratus*)	*I. multifiliis*	Crude methanolic extract *Mucuna pruriens,* 200 mg/L/72 h, bath Petroleum-ether extract of *Carica papaya*, 250 mg/L/96 h, bath	↑↑, Fish mortality↓ ↑↑, Fish mortality ↓↓	Ekanem et al. (2004)
In vitro		*Mucuna pruriens* 150 mg/L/6 h *Carica papaya* 200 mg/L/ 6 h	↑↑	
Grass carp (*C. idella*)	*I. multifiliis*	Sanguinarine (*Macleaya cordata*) 0.9 mg/L/48 h, bath	↑↑	Yao et al. (2010)
In vitro		Chloroform ethanol extract *M. cordata* of 70.0 mg/L/4 h	↑↑	
Barbel chub (*S. curriculus*)	*I. multifiliis*	Dihydrosanguinarine (*Macleaya macrocarpa*) 5.18 mg/L Dihydrochelerythrine 9.43 mg/L/48 h	+	Yao et al. (2011a)
In vitro		Two compounds (crystals) were separated from Fraction B compound 1 7.0 mg/L/4 h Compound 2 10.0 mg/L/4 h	↑↑ ↑↑	
Goldfish (*C. auratus*)	*I. multifiliis*	Aqueous extract *Capsicum frutescens* 1:32- 1:64/4 h, bath	Parasite prevalence ↓	Ling et al. (2012)
Goldfish (*C. auratus*)	*I. multifiliis*	Methanol extracts *Magnolia officinalis* 40 mg/L and *Sophora alopecuroides* 320 mg/L/1 h, bath	Tomont survival ↓	Yi et al. (2012)
Channel catfish (*I. punctatus*)	*I. multifiliis*	Pentagalloylglucose from *Galla chinensis* 20 mg/L/10 d, bath	Fish survival ↑	Zhang et al. (2013)
In vitro		2.5-20 mg/L/5.6-233.9 min 40 mg/L	Theronts mortality ↑↑↑ Tomonts reproduction ↓↓	
In vitro	*I. multifiliis*	Sage *(S. officinalis)* 0.50 mL/L, *lavender* (*L. officinalis)* at 0.25-0.50 mL/L, *and* oregano *(O. onites)* at 0.1, 0.25, 0.50mL/L/60 min, Onion (*A. cepa*), menthe (*M. spicata*), and garlic (*A. sativum*) essential oils at 0.1, 0.25, 0.50mL/L/60 min	Anti-trophonts ↑↑	Özil (2023)
Grass carp (*C.idella*)	*I. multifiliis*	Commercial curcumin from *Curcuma longa* plant at 4 mg/L/10 d., bath	Anti-trophonts ↑↑ Fish	Liu et al. (2017)
In vitro		Curcumin 1 mg/L/38.7 min, 8 mg/L/47.3 min and at 4 mg/L/16 h	Theronts mortality ↑↑↑,	
Grass carp (*C. Idella*)	*I. multifiliis*	*Cynanchum atratum* and *Sophora flavescens* combination as 6 mg/L/10 d, bath	Infection intensity ↓↓, Fish	Fu et al. (2021)
In vitro		Ethanol extract of *Psoralea corylifolia* 4 mg/L/37 min, *Cynanchum atratum* 8 mg/L/197 min	Theronts mortality ↑↑↑,	

*↑↑↑: 100%, ↑↑: antiprotozoal efficacy >75%, ↓↓: completely eliminated +: express as an effective without specific rate, ↑: increased, ↓: decreased. µL: micro liter, ML: milliliter, L: Liter, mg: milligram, g: gram, kg: kilogram, min: minute, h: hour, d: day, w: week.

Table 1. (Continued)

In vivo and In vitro	Parasite	Agent, dosage, time, and administration	Effect*	Reference
Goldfish (*C. auratus*)	*I. multifiliis*	Dietary *Artemisia annua* 20 g/kg/45 d	Trophonts ↓, fish survival ↑	Wu et al. (2017)
Goldfish (*C. auratus*)	*I. multifiliis*	Dietary Magnolol (*Magnolia officinalis*) 90 mg/kg/d/3 d	Fish survival ↑	Zhang et al. (2022)
Tambaqui (C. *macropomum*)	*I. multifiliis*	Essential oil of *Lippia alba* at 150 mg/L/30 min, bath	Antiprotozoal efficacy ↑	Soares et al. (2016)
Pacu (*P. mesopotamicus*)	*I. multifiliis*	*Melaleuca alternifolia* essential oil 50 µL/L/2 h/d/5 d, bath	↑↑↑, Fish survival rate ↑	Valladão et al. (2016)
In vitro		*Melaleuca alternifolia, Lavandula angustifolia,* and *Mentha piperita* essential oils 455 µL/L/1 h or 227µL/L/4 h	Trophont mortality ↑↑↑	
Molly (*P. latipinna*)	*I. multifiliis*	Garlic (*A. sativum*) 0.1 g/L and *Matricaria chamomilla* extract 0.4 g/L />5 d., bath	Antiprotozoal efficacy ↑↑↑	Gholipour-Kanani et al. (2012)
Silver catfish (*R. quelen*)	*I. multifiliis*	*Hyptis mutabilis* leaf essential oil 20 mg/L/96 h, bath	Fish survival ↑↑↑	Da Cunha et al. (2017)
Tambaqui (*C. macropomum*)	*I. multifiliis*	*Varronia curassavica* essential oil VCUR-202 accession 0.5 and 2.0 mg/L/1 h bath	Trophonts on infected fish ↓	de Castro Nizio et al. (2018)
In vitro		Essential oil of the VCUR-202 accession 10 mg/L/1 h, 50 mg/L/1 h	Trophonts mortality ↑↑↑	
Pompano (*Trachinotus ovatus*)	*C. irritans*	Dietary Honokiol 400 mg/kg/7 d	Trophonts ↓, Fish survival ↑	Zhong et al. (2019)
Tambaqui (*C. macropomum*)	*Piscinoodinium pillulare*	*Mentha piperita* (peppermint) essential oil 20 mg/L/3 d/24-h intervals,10 min bath	Parasite load reduction ↑	Ferreira et al. (2019)
Salmon (*Oncorhynchus. keta*) and (*O. masou*)	*Ichthyobodo necator*	Green tea extract (*Camellia sinensis*) Epigallocatechin gallate 0.9%/5 min, bath	↑↑	Suzuki et al. (2006)
Tilapia (*O. niloticus*)	*Trichodina* sp.	Extracts of *A. sativum* and *Terminalia catappa* 800 mg/L/2 d, bath	↓↓	Chitmanat et al., (2005)
Tilapia (*O. niloticus*)	*Trichodina* sp.	*Camellia sinensis* extract 0.9%/5 min, bath	↓	Noor El-Deen, (2010)
Parabramis pekinensis	*Trichodina* sp.	*Chelidonium majus*, chelidonine 1.0 mg/L, chelerythrine 0.8 mg/L, and sanguinarine 0.7 mg/L/48 h, bath	↑↑	Yao et al., (2011b)
Tilapia (*O. niloticus*)	*Trichodina* sp.	Garlic powder 300 mg/L, and garlic oil 3 g/L/1 h, bath	Parasitized fish ↓	Abd El-Galil and Aboelhadid, (2012)
Goldfish (*C. auratus*)	*Trichodina* and *Tripartiella*	Dietary *Swietenia mahagoni* extract 8 g/kg/5 d and *Cinnamomum tamala* 4-8 g/kg/15 d	+	Saha et al. (2020)
Tilapia (*O. niloticus*)	*Trichodina* sp.	Dietary garlic and Sheh el-baathran 1 g/kg/15 d	Parasite number and Fish	Aboud (2010)
White shrimp (*L. vannamei*)	*Gregarines* sporozoites	Dietary garlic paste (allicin) 40-50 g/kg	+, Number of sporozoites in intestine↓.	Madhuri et al. (2021)
Olive flounder (*Paralichthys olivaceus*)	*Uronema marinum*	*Punica granatum*, *Chrysanthemum cinerariaefolium*, *Zanthoxylum schinifolium* 5 mg/kg/6 d, extract injection	Mortality of fish ↓, Phagocytic activity ↑	Harikrishnan et al. (2010)
Olive flounder (*P. olivaceus*)	*Philasterides dicentrarchi*	Dietary *Hericium erinaceum* 0.1-1.0%/4 w	Immune response ↑, Mortality of fish ↓	Harikrishnan et al. (2011a)
Grouper (*Epinephelus bruneus*)	*Philasterides dicentrarchi*	Dietary *Kalopanax pictus* extract 1.0-2.0% for 30 d	Phagocytic/complement activity ↑, Mortality of fish ↓	Harikrishnan et al. (2011b)
Olive flounder (*P. olivaceus*)	*Miamiensis avidus*	Dietary *Suaeda maritima* 1.0%/4 w	Serum lysozyme, scuticocidal, respiratory burst activity ↑, Mortality of fish ↓	Harikrishnan et al. (2012)
Angelfish (*Pterophyllum. scalare*)	*S. vortens Hexamita*)	Dietary 0.5% Metronidazol (MTZ) and 0.5% Ajoene oil/5 d	Fecal trophozoite count. ↓	Williams et al. (2016)
In vitro		Synergetic effects tested MTZ and Ajoene oil	MTZ, min inhibition concentration (MIC) ↓	
In vitro	*Hexamita*	*Lavandula angustifolia* and hybrid lavandula essential oils 0.5-1%/30 min	Parasite mortality ↑	Moon et al. (2006)

*↑↑↑: 100%, ↑↑: antiprotozoal efficacy >75%, ↓↓: completely eliminated +: express as an effective without specific rate, ↑: increased, ↓: decreased. µL: micro liter, ML: milliliter, L: Liter, mg: milligram, g: gram, kg: kilogram, min: minute, h: hour, d: day, w: week.

reproduction at a concentration of 40 mg/L (Zhang et al., 2013). Özil (2023) reported that laboratory-based (*in vitro*) activity tests demonstrated 100% anti-trophont (*I. multifiliis*) efficacy after 60 minutes of application for essential oils derived from common sage, *Salvia officinalis* (0.50 mL/L), lavender, *Lavandula officinalis* (0.25 and 0.50 mL/L), and oregano, *Origanum onites* (0.1, 0.25, and 0.50 mL/L). Additionally, essential oils from onion (*Allium cepa*), mint (*Mentha spicata*), and garlic (*Allium sativum*) displayed anti-trophont activity ranging from 75-94%, 84-94%, and 72-92% at dosages of 0.1, 0.25, and 0.50 mL/L respectively.

In grass carp (*C. idella*) infected with the protozoan parasite (*I. multifiliis*), it was reported that curcumin, derived from the plant *Curcuma longa*, when applied at a dosage of 4 mg/L per bath for 10 days, inhibited all parasitic trophonts and showed a 100% fish survival rate. In vitro trials also revealed that curcumin at doses of 1 mg/L for 38.7 minutes, 8 mg/L for 47.3 minutes, and 4 mg/L for 16 hours completely killed theronts and all encysted tomonts (Liu et al., 2017).

A study by Fu et al. (2021) examined the synergistic and additive effects of medicinal plant combinations in combating *I. multifiliis* infections. They found high efficacy in grass carp infected with twenty-one combinations, particularly with plants *Cynanchum atratum* and *Sophora flavescens* at a dose of 6 mg/L for 10 days per bath treatment, recording zero infection intensity and 100% fish survival rate. In vitro results also found that the ethanol extract of the *Psoralea corylifolia* plant at a dose of 4 mg/L for 36.7 minutes and the extract of the *Cynanchum atratum* plant at a dose of 8 mg/L for 196.7 minutes completely killed theronts and non-encysted tomonts.

A study examining the pharmacokinetics of magnolol, a phytochemical from the *Magnolia officinalis* plant, in goldfish (*C. auratus*) determined that the oral route was the best method of administration. An effective dose of magnolol was established at 90 mg/kg of fish per day for 3 days, which showed promising results in terms of increasing survival rates and reducing infection levels in goldfish (Zhang et al., 2022). It was reported that when the powder of the *Artemisia annua* plant was applied at a concentration of 20 g/kg of feed for 45 days, it provided strong protection against the *I. multifiliis* disease in goldfish, reduced the infection rate, and increased the fish survival rate by 30% compared to control (Wu et al., 2017).

Trichodinosis is a disease caused by ciliate protozoans, commonly occurring in fish farms and intensive systems when fish are exposed to stress and high stocking densities. The *Trichodina* species of protozoan is characterized by causing skin and gill damage, decreased growth, increased susceptibility to secondary infections, and death in severe cases (Noga, 2010). It has been reported that *in vitro* trials of raw extracts from garlic (*A. sativum*) and Indian almond (*T. catappa*) at a dosage of 800 mg/L for 2 days per bath killed 100% of *Trichodina* protozoans (Chitmanat et al., 2005).

The application of green tea (*Camellia sinensis*) extract at 0.9% for 5 minutes per bath has been declared to reduce *Trichodina* infestations by 95% in tilapia (*Oreochromis niloticus*) hatcheries (Noor El-Deen, 2010). The use of three different bioactive alkaloids produced from the plant *Chelidonium majus* (chelidonine 1.0 mg/L for 48 hours per bath, chelerythrine 0.8 mg/L for 48 hours per bath, and sanguinarine 0.7 mg/L for 48 hours per bath) has been declared to prevent 100% of *Trichodina* infections in *Parabramis pekinensis* fish (Yao et al., 2011b).

It was recorded that crushed garlic (*A. sativum*) at 300 mg/L and garlic oil at 3 g/L reduced infections by 23% and 13%, respectively, in Trichodina-infected tilapia fry compared to the control group (Abd El-Galil & Aboelhadid, 2012). A study in goldfish (*C. auratus*) recommended incorporating mahogany (*Swietenia mahagoni*) powder at a diet dosage of 8 g/kg/day for 5 days and Indian bay leaf (*Cinnamomum tamala*) powder at dosages of 4-8 g/kg/day for 15 days to completely eliminate trichodinid ciliates (Saha et al., 2020). Garlic (*A. sativum*) and Sheh el-baathran (*Artemisia judaica* as a traditional Egyptian medicinal plant), in their ground dry forms, added to formulated diets of tilapia (*O. niloticus*) at a rate of 1 g/kg for 15 days, completely ended *Trichodina* ciliate infection and reduced the mortality rate of tilapia fish (Aboud, 2010).

Parasites belonging to the *Hexamita* genus are a group of flagellated protozoa that live freely in both freshwater and saltwater environments. Most protozoal *Spironucleus* species reside in the intestines and gall bladders of fish (Moon et al., 2006). It has been indicated that the essential oils from *Lavandula angustifolia* and hybrid lavender as lavandin (*L.* x *intermedia*) used at concentrations of 1% and 0.5% respectively for 30 minutes, show complete effectiveness against *Hexamita inflata* infections.

Furthermore, Ajoene oil derived from A. sativum has been recorded to inhibit *Sprionucleus vortens* (syn: *Hexamita*) trophozoites found in the feces of freshwater angel fish (*Pterophyllum scalare*). The minimum inhibitory concentration (MIC) of Ajoene oil in laboratory tests (*in vitro*) is reported to be 40 µg/mL. Additionally, it has been emphasized that Ajoene oil acts in synergy with metronidazole (4 µg/mL MTZ), reducing the MIC level by 16 times. Researchers have shown the potential of Ajoene oil as an alternative therapeutic agent in the treatment of hexamitosis, a significant infection in angel fish (Williams et al., 2016).

The *Piscinoodinium* genus of protozoan (dinoflagellate) parasites is a freshwater equivalent to the pathogenic *Amyloodinium* genus in marine fish. Particularly, disease cases caused by *Piscinoodinium limneticum* in ornamental species have frequently been reported from North America, and problems caused by *P. pillulare* from Europe (Noga, 2010). It has been reported that Tambaqui fish (*Colossoma macropomum*), a commercially valuable edible fish species infected with *P. pillulare*, could be treated with *Mentha piperita* (peppermint) essential oil at a concentration of 40 mg/L for 3 days, with 10-minute baths at 24-hour intervals, showing anti-

Piscinoodinium efficacy of 79.91% in body mucus and 54.56% in gills (Ferreira et al., 2019).

In recent years, herbal therapeutic compounds have been used on ectoparasitic protozoans infecting teleost fish (e.g., *Ichthyophthirius* and *Trichodina*). It is known that protozoan ectoparasites more frequently cause diseases in the gills and skins of freshwater fish compared to marine fish (Rohde, 2005; Woo, 2006).

Recently, some studies have encountered the use of plant-derived compounds to control and prevent marine ciliate species such as *Cryptocaryon irritans* (Zhong et al., 2019) and *Scuticociliates* sp. (Harikrishnan et al., 2010, 2011b, 2012). Plant-based compounds have started to show promise in treating infections caused by protozoan pathogens in fish through these scientific studies, opening a discussion on artificial chemical and drug applications in modern aquaculture and even starting to offer a safer and more sustainable alternative solution (Li et al., 2022; Reverter et al., 2014; Valladão et al., 2015; Wunderlich et al., 2017). Extracts derived from medicinal plants have been used to treat *Enterocytozoon hepatopenaei* (EHP), a protozoan parasite causing severe pathological damage and economic losses in shrimp farming (Rajendran et al., 2016). In one of the few studies regarding the use of medicinal plants in the treatment of shrimp protozoan diseases (as mentioned in Table 1), supplementation with allicin in the feeds of shrimp against Gregarines sporozoites was tested, however, it was stated that the sporozoites were not completely eradicated from the white shrimp (*Lithopenaeus vannamei*) digestive tract (Maduri et al., 2021). Despite the presence of severe infectious diseases in mollusc culture, especially *Mytilicola intestinalis*, *M. orientalis*, *Urastoma cyprinae*, and *Parvatrema duboisi* from the Mediterranean mussel (*Mytilus galloprovincialis*) (Yılmaz et al., 2020) and diseases caused by *Marteilia refringens* and *Bonamia* sp. (Alcivar-Warren et al., 2023), and *Perkinsus marinus* (Andrews, 1996) in oyster culture, there are still no plant-based compound applications aimed at their treatment.

Considering the potential for molluscs to be grown in hatchery conditions and closed-circuit system cultivation conditions under full control, as well as commonly being farmed in open sea, it is believed that phytochemicals derived from medicinal plants could find use against parasites in molluscs as phytotherapeutic agents. Given that invertebrates such as mussels, oysters, shrimp, crayfish, and lobsters, unlike vertebrates, usually do not have acquired immunity and must rely on innate immune systems to protect against infections, it is considered that plant extracts could benefit in generating appropriate immune responses for healthy growth in aquaculture. At this point, more research is needed to explore the potential of using natural remedies to combat parasites in shellfish aquaculture.

Research gaps, conclusions, and future perspectives

The integration of plant compounds into aquaculture operations signifies a burgeoning trend driven by a collective acknowledgment of their sustainability and environmental advantages. Beyond their conventional role as anti-parasitic agents in aquaculture, these compounds boast numerous benefits, including stimulating growth, enhancing immunity, and possessing potent antibacterial properties. Moreover, their versatility in serving as anaesthetic agents during fish handling and transportation underscores their value in promoting humane practices within aquaculture operations (Bulfon et al., 2015; Dawood et al., 2021; Vijayaram et al., 2023).

While recent research has shed light on the effectiveness of plant-derived compounds in combating protozoan parasites in finned fish farming, investigations into their efficacy in shellfish farms are notably deficient and necessitate immediate attention. Despite ample data showcasing the potential benefits of medicinal plants in enhancing fish farming, the limited availability of commercial products impedes their widespread adoption in the industry. Encouraging the development of large-scale herbal solutions for both finned fish and shellfish emerges as a critical step in bridging this gap. Additionally, the abundance of medicinal plants across various regions presents an untapped resource to optimize fish production, yet farmers often lack awareness of their potential contributions. To address these challenges, collaborative efforts must be coordinated among researchers, laboratories, aquaculture associations, cooperatives, and government agencies. By promoting synergy and facilitating information exchange, stakeholders can raise awareness among local farmers about the efficacy of native herbal plants in aquaculture environments. Such concerted efforts not only promote sustainable practices but also empower farmers to maximize production while minimizing negative environmental impacts, thus charting a course towards a more resilient and responsible aquaculture industry.

Furthermore, the pursuit of sustainability in aquaculture necessitates prioritizing responsible agricultural practices that uphold ethical standards. This includes minimizing the use of artificial chemicals and supporting the well-being of aquatic organisms. Aquaculture operations can ensure the humane treatment of fish and shellfish by prioritizing animal welfare and minimizing stress during handling and transportation. Moreover, responsible aquaculture extends beyond immediate operational practices to include broader considerations such as biodiversity conservation and habitat protection. Aquaculture efforts can coexist harmoniously with surrounding ecosystems by adopting habitat-friendly farming techniques and implementing measures to reduce the risk of pollution and habitat degradation.

Ethical considerations also encompass the welfare of workers in the aquaculture industry. Ensuring fair labour practices and providing adequate training and support to workers contribute to developing a culture of responsibility and accountability in the industry. Ultimately, maintaining environmentally friendly approaches and responsible aquaculture practices underscores a commitment to environmental stewardship and ethical behaviour. By adopting sustainable alternatives, promoting animal welfare, and keeping ethical considerations at the forefront, the aquaculture industry can strive towards a future that is both environmentally conscious and socially responsible.

AUTHOR CONTRIBUTION

All authors contributed to the study idea and design. The writing and editing of the article were done by the names listed above, and all authors have read and approved the article.

CONFLICT OF INTEREST STATEMENT

The authors declare that they have no conflicts of interest.

ETHICAL APPROVAL

No specific ethical approval was required for this study.

DATA AVAILABILITY

Data supporting the results are available in the review manuscript.

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