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Beneficial effects of medicinal plants in fish diseases

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Abstract Fish are constantly in contact with pathogens inhabiting water. High population density as well as poor hydrodynamic conditions and feeding lead to an increased sensitivity towards infections. In order to prevent major economic losses due to diseases, various medications are used for treatment and prevention of infections. The use of antimicrobial drugs in aquacultures could lead to emergence of resistance in pathogenic microorganisms. Alternatives are being sought over the last few years to replace antibiotics, and medicinal plants are one of available options for this purpose. These plants are rich in secondary metabolites and phytochemical compounds, which have an effect against viral, bacterial, and parasitic diseases in fish. Their main advantage is their natural origin and most of these plants do not represent threat for human health, the fish, and the environment. The goal of this review is to present information on the treatment of viral, bacterial, and parasitic diseases in fish through medicinal plants, with focus on the mechanisms of action of the identified secondary metabolites, fractions, or plant extracts.

Keywords Fish diseases · Medicinal plants · Treatment

Introduction

Fish yields from the world ocean have reached the maximum production level (Bud et al. 2009), which makes aquaculture one of the fastest growing fields in the animal product industry, with an average annual growth of 6% during the period 1990–2010 (FAO 2012).

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Fish are susceptible to numerous diseases, which could lead to partial or complete loss of produce (Bondad-Reantaso et al. 2005). They are exposed to numerous pathogenic microorganisms inhabiting the water environment. The high density of breeding, poor hydrodynamic conditions, and feeding lead to physiological changes in the organisms, stress, and suppression of the immune system, thus increasing the fishes' sensitivity to infections. The lack of sanitary barriers facilitates the spread of pathogenic microorganisms, leading to high mortality levels (Naylor et al. 2000; Cabello 2006; Quesada et al. 2013).

In order to prevent large economic losses due to fish illnesses, various medications are used for prevention and treatment. These are often used as additives in fish feeds to promote growth, and sometimes, in the form of baths or injections (Rico et al. 2013). The use of antibacterial drugs could lead to emergence of resistance in microbial pathogens and accumulation of residues in fish tissues (Dorucu et al. 2009). Inoculation could prevent the occurrence of various fish diseases; yet, the development of vaccines against many of the intracellular pathogens is not yet very successful (Fazlolahzadeh et al. 2011). Alternatives have been sought over the last few years, which could replace antibiotics, and medicinal plants can be one such alternative. Even though medicinal plants have been used to treat illnesses in humans for millennia, studies on their effects against fish diseases are relatively few. Medicinal plants can be used not only as a means of treatment, but also as growth promoters, for the prevention of stress and infectious diseases (Ahilan et al. 2010). Therefore, this review aims at presenting information on the treatment of viral, bacterial, and parasitic illnesses in fish via medicinal plants, with focus on the mechanisms of action of identified secondary metabolites, fractions, or plant extracts.

Source of medicinal plants, preparation and active compounds

Medicinal plants have been used in human medicine as immune boosters for millennia. Furthermore, they are alternatives to antibiotics in aquaculture (Van Hai 2015). A large number of medicinal plants with antiviral, antibacterial, and antiparasitic properties are used in the treatment of fish diseases (Table 1).

Several parts of these medicinal plants are used to extract the active substances. Leaves are mostly used (Abutbul et al. 2004; Ekanem et al. 2004; Rattanachaikunsopon and Phumkhachorn 2009; Alexander et al. 2010; Kim et al. 2011; Harikrishnan et al. 2011b), as well as the rhizome (Talpur et al. 2013), fruits (Pan et al. 2013), roots (Zhang et al. 2014), seeds (Ekanem et al. 2004), bark (Ji et al. 2012; Zhou et al. 2017), and bulbs (Madsen et al. 2000; Fridman et al. 2014).

Medicinal plants are rich in various secondary metabolites and phytochemical compounds, such as tannins, alkaloids, and flavonoids, which affect various diseases in fish (Citarasu 2010; Pandey and Madhuri 2010; Ravikumar et al. 2010; Pandey et al. 2012). These active substances are mostly extracted with methanol (Ekanem et al. 2004; Wu et al. 2011; Hu et al. 2014; Bilen et al. 2016; Zhou et al. 2017), ethanol (Yao et al. 2010; Kim et al. 2011; Harikrishnan et al. 2011b; Harikrishnan et al. 2011c; Hu et al. 2014; Thanigaivel et al. 2015), ethyl acetate (Abutbul et al. 2004; Wu et al. 2011; Zhang et al. 2013; Hu et al. 2014; Zhang et al. 2014), chloroform (Wu et al. 2011; Hu et al. 2014), petroleum ether (Ekanem et al. 2004), and water (Rattanachaikunsopon and Phumkhachorn 2009; Alexander et al. 2010; Pan et al. 2013; Fridman et al. 2014; Hu et al. 2014; Thanigaivel et al. 2015), while garlic can be used raw and squeezed (Madsen et al. 2000). Some extracts are commercial products. Nantong

Table 1 Source of medicinal plants

Medicinal plant	Family	Plant part used	Active compounds	Beneficial effect in fish diseases	References
Achyranthes aspera	*Amaranthaceae*	Seeds	NI	Antibacterial	Chakrabarti and Srivastava (2012)
Allium sativum	*Amaryllidaceae*	Bulbs	Allicin	Antiparasitic	Chitmanat et al. (2005); Fridman et al. (2014); El-Galil and Aboelhadid (2012); Madsen et al. (2000); Martins et al. (2002); Militz et al. (2013); Militz et al. (2014)
Andrographis paniculata	*Acanthaceae*	Leaves	Arabinogalactan proteins, andrographolides	Antibacterial	Rattanachaikunsopon and Phumkhachorn (2009)
Artemisia argyi	*Compositae*	Leaves	NI	Antiparasitic	Huang et al. (2013)
Asparagopsis taxiformis	*Bonnemaisoniaceae*	Seaweed	Halogenated alkanes, alkenes, alkynes, and acrylic acids	Antiparasitic	Hutson et al. (2012)
Astragalus membrana-ceus	*Fabaceae*	NI	Polysaccharides, monosaccharides, flavonoid, and alkaloid	Antibacterial	Yin et al. (2009)
Bupleurum chinense	*Umbelliferae*	Root	Saikosaponin, essential oil, and polysaccharides	Antiparasitic	Wu et al. (2011)
Caesalpinia sappan	*Leguminosae*	Rhizome	NI	Antiparasitic	Huang et al. (2013)
Camellia sinensis	*Theaceae*	Leaves and buds	Catechins	Antiparasitic	Suzuki et al. (2006)
Carica papaya	*Caricaceae*	Seeds	Tannins, papain, nicotine, cyanogenicglucosides, and quercetin	Antiparasitic	Ekanem et al. (2004)
Cinnamomum cassia	*Lauraceae*	Tree bark	Cinnamaldehyde, cinnamon oil, eugenol, salicylaldehyde, and trans-cinnamic acid	Antiparasitic	Ji et al. (2012)
Citrus medica	*Rutaceae*	Fruit	Limonene, geranial, and neral	Antiparasitic	Hu et al. (2014)
Clematis chinensis	*Ranunculaceae*	Roots	Saponins	Antiparasitic	Huang et al. (2013)
Curcuma longa	*Zingiberaceae*	NI	Polysaccharide	Antibacterial	Sahu et al. (2008)
	Poaceae	NI		Antibacterial	Kaleeswaran et al. (2011)

Table 1 (continued)

Medicinal plant	Family	Plant part used	Active compounds	Beneficial effect in fish diseases	References
Cynodon dactylon			Cynodin, hydrocyanic acid, triticin, and beta-carotene		
Dioscorea collettii	*Dioscoreaceae*	Rhizome	Saponins	Antiparasitic	Hu et al. (2014)
Dryopteris crassirhizoma	*Dryopteridaceae*	Rhizomes	Triterpenes	Antiparasitic	Lu et al. (2012)
Eriobotrya japonica	*Rosaceae*	Leaves	Triterpenes, sesquiterpenes, flavonoids, tannins, megastigmane glycosides, and phenolic compounds	Antibacterial	Kim et al. (2011)
Eupatorium fortunei	*Compositae*	Leaves	NI	Antiparasitic	Huang et al. (2013)
Euphorbia fischeriana	*Euphorbiaceae*	Root	Diterpenoids	Antiparasitic	Zhang et al. (2014)
Euphorbia hirta	*Euphorbiaceae*	Leaves	Leukocyanidol, quercitol, camphol, quercetin, dihydroellagitannins, and dimeric hydrolysable tannins–euphorbins	Antibacterial	Pratheepa and Sukumaran (2011)
Ficus carica	*Moraceae*	NI	Polysaccharides	Antibacterial	Wang et al. (2016)
Galla chinensis	*Anacardiaceae*	NI	Pentagalloylglucose	Antiparasitic	Zhang et al. (2013)
Ganoderma lucidum	*Ganodermataceae*	NI	Polysaccharides	Antibacterial	Yin et al. (2009)
Hericium erinaceum	*Hericiaceae*	Mycelium	Polysaccharides, lectins, proteins, lipids, hericenone, erinacol, erinacine, and terpenoids	Antiparasitic	Harikrishnan et al. (2011c)
Kochia scoparia	*Chenopodiaceae*	Fruits	Glycoside (momordin)	Antiparasitic	Lu et al. (2012)
Lactuca indica	*Compositae*	NI	NI	Antibacterial	Harikrishnan et al. (2011a)
Lindera aggregata	*Lauraceae*	Roots	Alkaloids, volatile oils, and sesquiterpene esters	Antiparasitic	Ji et al. (2012)
Lonicera japonica	*Caprifoliaceae*	NI	Chlorogenic acid	Antibacterial	Ardó et al. (2008)

Table 1 (continued)

Medicinal plant	Family	Plant part used	Active compounds	Beneficial effect in fish diseases	References
Lysima chiachristi-nae	*Primulaceae*	Leaves	Quercetin, quercetin glucuronides, and triterpenoid saponin	Antiparasitic	Huang et al. (2013)
Melia azedarach	*Meliaceae*	Bark	NI	Antiparasitic	Zhou et al. (2017)
Mucuna pruriens	*Fabaceae*	Leaves	L-dopa, phenols, tannins, saponins, nicotine, physostigmine, bufotenine, serotonin, N,N-dimethyltryptamine, and 5-methoxy-DMT	Antiparasitic	Ekanem et al. (2004)
Ocimum sanctum	*Lamiaceae*	Leaves	Ursolic acid, oleanolic acid, and salrigenin	Antibacterial	Das et al. (2015)
Olea europaea	*Oleaceae*	Leaves	Biophenols	Antiviral	Micol et al. (2005)
Padina gymnospora	*Dictyotaceae*	Seaweed	Squalene, lupeol acetate, betulin, and taraxasterol	Antibacterial	Thanigaivel et al. (2015)
Polygala tenuifolia	*Polygalaceae*	Roots	Onjisaponins A–G xanthones, alkaloids, polygalitol	Antiparasitic	Lu et al. (2012)
Polygonum multiflorum	*Polygonaceae*	Stem	Phenols	Antiparasitic	Hu et al. (2014)
Pseudolarix kaempferi	*Pinaceae*	Tree bark	Diterpenoids, pseudolaric acid A, pseudolaric acid B	Antiparasitic	Ji et al. (2012)
Punica granatum	*Punicaceae*	Leaves	Polyphenols	Antiviral	Harikrishnan et al. (2010)
Radix isatidis	*Brassicaceae*	NI	Polysaccharides	Antibacterial	Wang et al. (2016)
Rosmarinus officinalis	*Labiatae*	Leaves	Polyphenols	Antibacterial	Abutbul et al. (2004)
Schisandra chinensis	*Schisandraceae*	NI	Polysaccharides	Antibacterial	Wang et al. (2016)
Scutellaria baicalensis	*Lamiaceae*	Leaves	Polysaccharides, organic acids, alkaloids, glucosides, and volatile oil	Antibacterial	Harikrishnan et al. (2011b)
Siegesbecki glabrescens	*Compositae*	NI	Flavones	Antibacterial	Harikrishnan et al. (2012)

Table 1 (continued)

Medicinal plant	Family	Plant part used	Active compounds	Beneficial effect in fish diseases	References
Terminalia catappa	*Combretaceae*	Leaves	Punicalin	Antiparasitic	Chitmanat et al. (2005)
Tinospora cordifolia	*Menispermaceae*	Leaves	Alkaloids, diterpenoid lactones, glycosides, steroids, and sesquiterpenoids	Antibacterial	Alexander et al. (2010)
Tinospora cordifolia	*Menispermaceae*	Leaves	Cordioside, cordifolioside, and cordiol	Antibacterial	Sudhakaran et al. (2006)
Toona sinensis	*Meliaceae*	Leaves	Triterpenes and phenols	Antibacterial	Wu et al. (2010)
Urtica dioica	*Urticaceae*	NI	NI	Antibacterial	Bilen et al. (2016)
Withania somnifera	*Solanaceae*	Root	Alkaloids, steroidal lactones, saponins, and withanolides	Antibacterial	Sharma et al. (2010)
Zingiber officinale	*Zingiberaceae*	Rhizomes	Polyphenols, flavonoids, saponins	Antibacterial	Talpur et al. (2013)

NI - no information

Sihai Plant Extracts Co., Ltd., China supplies powdered *Astragalus* extract containing 90% of *Astragalus* polysaccharide and powdered *Lonicera* extract containing 25% of chlorogenic acid (Ardo et al., 2008), and *Ganoderma* extract containing 30% polysaccharides is a commercial product of Xuancheng Baicao Plants Industry and Trade Ltd., China (Yin et al., 2009). The efficacy of solvents used for extraction of active substances of medicinal plants is various. Organic solvents are more efficient in extracting secondary active metabolites with antimicrobial and immunostimulatory action than water (Van Hai 2015). Hu et al. (2014) reported that the anthelminthic activity of methanol and chloroform extracts of *Dioscorea collettii* was 100% against *Dactylogyrus intermedius* at concentrations of 120 and 80 mg/l following 48-h treatment while 120 mg/l aqueous extract was ineffective against helminths. Wu et al. (2011) established a high anthelminthic activity of chloroform and ethyl acetate extracts of *Bupleuri chinensis* against *Dactylogyrus intermedius*, whereas petroleum ether and aqueous extracts were less active. Opposite to these findings, Hu et al. (2014) demonstrated that aqueous extract of *Polygonum multiflorum* was 100% effective against *Dactylogyrus intermedius* at 100 mg/l following 48-h treatment but the effects of chloroform and petroleum ether extracts (100 mg/l) were less pronounced (81.8 and 77%, respectively). The results of Thanigaivel et al. (2015) also showed higher efficacy of aqueous vs ethanol extract of *Padina gymnospora* vs *Pseudomonas aeruginosa*. Survival rates of *Pseudomonas aeruginosa* infected fish were 70% after treatment with ethanol extract for 15 days and 80% after treatment with aqueous extract for the same period of time.

Administration and safety of medicinal plants in aquaculture

The methods of applying medicinal plants in aquaculture include supplementation to the feed, producing extract, and submerging the fish into it, as well as intraperitoneal injection (Treves-Brown 2000; Sekkin and Kum 2011). These three methods of prevention and treatment of various fish illnesses are reported to not entail any risks of polluting the environment, damage to the fish, people, or other animals because medicinal plants are natural products (Reverter et al. 2014). Unlike the use of various veterinary drugs, for which it is recommended to treat a small number of fish in order to check their tolerance (Sekkin and Kum 2011), this is not necessary when using medicinal plants. It is also not necessary to undergo a specific quarantine period before consumption of the herb-treated fish (Rico et al. 2013), because herbs are natural products and most of them are safe for consumers (Direkbusarakom 2011).

Oral application of medicinal plants is a preferred method. Their addition into the feed can treat bacterial diseases in fish (Reverter et al. 2014). Medicinal plants could also be added to the feed for prophylaxis purposes, and some of them stimulate growth as well (Rico et al. 2013). The treatment or prevention dose is determined per the used medicinal plant and the quantity of fish (Gabor et al. 2010), yet overdosing is nearly impossible. A potential drawback could be the fact that many of these medicinal plants are not sufficiently studied for various fish species and their absorption within the gastrointestinal tract can vary in the different species.

Bathing fish in various solutions of medicinal plants can also give good results (Wu et al. 2011; Thanigaivel et al. 2015). By preparing different plant extracts and immersing fish into these, bacterial and fungal diseases can be treated (Hu et al. 2014). The treatment or prophylactic dose has to be determined in accordance with the used medicinal plant and the quantity of fish (Reverter et al. 2014); yet, overdosing is nearly impossible, unlike when using

chemicals. The method's drawback is that fish have to be taken out of the water, treated, and returned, which leads to stress.

Intraperitoneal injection of medicinal plant extracts is a relatively rare practice for treating bacterial infections, but is the best way to provide the suitable dose (Alexander et al. 2010; Reverter et al. 2014). An injection quickly leads to high blood and tissue levels of the antibacterial substance (Sekkin and Kum 2011). Nevertheless, this method is very demanding and is only applicable for high-value specimens, not in large production operations. Its drawbacks include the stress from being taken out of the water and the injection itself. The fish must not be fed 24 h before the injection. Incorrect injection could lead to peritoneal adhesion, ovulation problems, and death (Sekkin and Kum 2011).

Medicinal plants could be applied either solely or co-administered with trace elements and probiotics for treatment of diseases in fish. Ardo et al. (2008) supplemented *Astragalus membranaceus* and *Lonicera japonica* independently or in combination, either with or without 0.05% boron to the feed of tilapia (*Oreochromis niloticus*) throughout 4 weeks and this led to increased phagocytic and respiratory burst activity of blood phagocytic cells. In experimental infection with *A. hydrophila*, the lowest death rate was demonstrated in the group of fish both fed with medicinal plants plus boron. Jian and Wu (2004) found out that the combination of *Astragalus* root and Chinese Angelica Root (5:1) supplemented at 1% to the feed of carps (*Cyprinus carpio*) over 20 days enhanced non-specific immunity. The same medicinal plants at a specific ratio increased the non-specific immunity and the resistance of large yellow croaker (*Pseudosciaena crocea*) against *Vibrio alginolyticus* (Jian and Wu 2003). Among tilapia (*Oreochromis niloticus*), experimentally infected with *A. hydrophila,* the highest survival rate was found out in groups supplemented with the combination of *Echinacea purpurea* (1 ppt) and *Allium sativum* (3%) for 3 months (Aly and Mohamed 2010). The combination of *Astragalus* and *Ganoderma* was found to increase the resistance of carps (*Cyprinus carpio*) to *A. hydrophila* infection (Yin et al. 2009). Harikrishnan et al. (2011b) applied a combination of *Scutellaria baicalensis* and the probiotic *Lactobacillus sakei* BK19 to boost the resistance of rock bream (*Oplegnathus fasciatus*) to *Edwardsiella tarda*.

A method of choice for application of medicinal plants in fish with bacterial diseases is their dietary supplementation at levels from 0.1 to 2% for 5 to 42 days. In some instances, affected fish are treated through immersion or intraperitoneal injection of aqueous extract of the medicinal plant (Table 2). Ectoparasitoses are treated by immersion for 1 h to 10 days, while other medicinal plants are added to the feed of diseased fish (Table 3). According to Fridman et al. (2014), the concentration of the medicinal plant correlated positively to the time needed for perishment of ectoparasites. Harikrishnan et al. (2010) and Novriadi and Haw (2015) performed intraperitoneal injection of extracts for 8 weeks and 72-h immersion to treat viral diseases in fish. The dose depended on the plant extracts, fish species, and the route of application. The effect of medicinal plants is dose-dependent and there is a risk of overdose (Van Hai 2015). Militz et al. (2013, 2014) provided proofs that garlic (*Allium sativum*) given as dietary supplement or applied by immersion to barramundi (*Lates calcarifer*) was effective against *Neobenedenia* sp. infection. Dietary supplementation of garlic for 30 days reduced infection rate up to 70% as compared to control group of fish. Garlic extract containing 0.76 and 1.52 μl/l alicin reduced substantially *Neobenedenia* infection rates to 25 and 11%, respectively.

According to Gabor et al. (2010), the main advantage of medicinal plants is that they are of natural origin and are not a threat to people's health, the fish, and the environment. Abutbul

Table 2 Antibacterial effect of medicinal plants

Medicinal plant	Mode of administration	Preparation	Dose	Fish	Antibacterial effect against	Reference
Lactuca indica	Feed additive	Powder	1 and 2% for 4 weeks	*Epinephelus bruneus*	*Streptococcus iniae*	Harikrishnan et al. (2011a)
Urtica dioica	Feed additive	Methanolic extract	0.1 and 0.5 g/kg feed for 30 days	*Oncorhynchus mykiss*	*Aeromonas hydrophila*	Bilen et al. (2016)
Zingiber officinale	Feed additive	Powder	5 and 10 g/kg feed for 15 days	*Lates calcarifer*	*Vibrio harveyi*	Talpur et al. (2013)
Padina gymnospora	Bath	Aqueous and ethanol extracts	100–500 mg/l for 15 days	*Oreochromis mossambicus*	*Pseudomonas aeruginosa*	Thanigaivel et al. (2015)
Astragalus membranaceus, Ganoderma lucidum	Feed additive	Extracts	0.5% for 5 weeks	*Cyprinus carpio*	*Aeromonas hydrophila*	Yin et al. (2009)
Astragalus membranaceus, *Lonicera japonica*	Feed additive	Powder	0.1% for 4 weeks	*Oreochromis niloticus*	*Aeromonas hydrophila*	Ardo et al. (2008)
Ficus carica, *Radix isatidis*, *Schisandra chinensis*	Feed additive	Polysaccharides	500 mg/kg feed for 21 days	*Carassius carassius*	*Aeromonas hydrophila*	Wang et al. (2016)
Eriobotrya japonica	Feed additive	Ethanol extract	1 and 2% for 4 weeks	*Epinephelus bruneus*	*Vibrio carchariae*	Kim et al. (2011)
Scutellaria baicalensis	Feed additive	Ethanol extract	1% for 6 weeks	*Oplegnathus fasciatus*	*Edwardsiella tarda*	Harikrishnan et al. (2011b)
Astragalus membranaceus, Scutellaria baicalensis, Forsythia spp.	Feed additive	Water extract	2% for 4 weeks	*Sciaenops ocellatus*	*Vibrio splendidus*	Pan et al. (2013)
Siegesbeckia glabrescens	Feed additive	Extract	1 and 2% for 4 weeks	*Epinephelus bruneus*	*Vibrio parahaemolyticus*	Harikrishnan et al. (2012)
Andrographis paniculata	Feed additive	Aqueous extract	4:36 and 5:35 ratios (*w*/*w*) for 2 weeks	*Oreochromis niloticus*	*Streptococcus agalactiae*	Rattanachaikunsopon and Phumkhachorn (2009)
Tinospora cordifolia	Intraperitoneally	Water-soluble fraction of leaves	6, 60, and 600 mg/kg, single or double dose	*Oreochromis mossambicus*	*Aeromonas hydrophila*	Alexander et al. (2010)
Rosmarinus officinalis	Feed additive	Dry leaves, dried ethyl acetate extract	3:17 and 1:24 ratios (*w*/*w*) for 5 days	*Oreochromis* spp.	*Streptococcus iniae*	Abutbul et al. (2004)
Euphorbia hirta	Feed additive	Aqueous extract	5, 10, 20, 25, and 50 g/kg feed for 50 days	*Cyprinus carpio*	*Pseudomonas fluorescens*	Pratheepa and Sukumaran (2011)
Ocimum sanctum	Feed additive	Water extract		*Labeo rohita*		Das et al. (2015)

Table 2 (continued)

Medicinal plant	Mode of administration	Preparation	Dose	Fish	Antibacterial effect against	Reference
			0.05, 0.1, 0.2, 0.5, and 1% for 42 days		*Aeromonas hydrophila*	
Tinospora cordifolia	Intraperitoneally	Ethanol and petroleum ether extracts	0.8, 8, or 80 mg/kg b.w. for 3 weeks	*Oreochromis mossambicus*	*Aeromonas hydrophila*	Sudhakaran et al. (2006)
Cynodon dactylon	Feed additive	Ethanolic extract	0.05, 0.5, and 5% for 60 days	*Catla catla*	*Aeromonas hydrophila*	Kaleeswaran et al. (2011)
Curcuma longa	Feed additive	Powder	0.1, 0.5, 1, and 5 g/kg of feed for 60 days	*Labeo rohita*	*Aeromonas hydrophila*	Sahu et al. (2008)
Withania somnifera	Feed additive	Powder	1.2 and 3 g/kg for 42 days	*Labeo rohita*	*Aeromonas hydrophila*	Sharma et al. (2010)
Achyranthes aspera	Feed additive	Seeds	0.1, 0.25, and 0.5% for 70 days	*Labeo rohita*	*Aeromonas hydrophila*	Chakrabarti and Srivastava (2012)
Toona sinensis	Intraperitoneally	Hot-water extract	4 or 8 μg/g	*Oreochromis mossambicus*	*Aeromonas hydrophila*	Wu et al. (2010)

Table 3 Antiparasitic effect of medicinal plants

Medicinal plant	Mode of administration	Preparation	Dose	Fish	Antiparasitic effect against	Reference
Allium sativum	Bath	Aqueous extract	7.5 and 12.5 ml/l for 1 h	*Poecilia reticulata*	*Gyrodactylus turnbulli*	Fridman et al. (2014)
Euphorbia fischeriana	Bath	Ethyl acetate extract	14 mg/l for 48 h	*Carassius auratus*	*Dactylogyrus vastator*	Zhang et al. (2014)
Allium sativum	Bath	Garlic oil	3 ppt for 1 h	*Oreochromis niloticus*	*Trichodina, Gyrodactylus*	El-Galil and Aboelhadid (2012)
Galla chinensis	Bath	Ethyl acetate extract	20 mg/l for 10 days	*Ictalurus punctatus*	*Ichthyophthirius multifiliis*	Zhang et al. (2013)
Mucuna pruriens *Carica papaya*	Bath	Methanolic extract of leaves Petroleum ether extract of seeds	200 mg/l for 72 h 200 mg/l for 96 h	*Carassius auratus*	*Ichthyophthirius multifiliis*	Ekanem et al. (2004)
Allium sativum, Terminalia catappa	Bath	Crude extracts	800 mg/l for 48 h	*Oreochromis niloticus*	*Trichodina*	Chitmanat et al. (2005)
Macleaya cordata	Bath	Dried ethanol extract	0.9 mg/l for 48 h	*Ctenopharyngodon idella*	*Ichthyophthirius multifiliis*	Yao et al. (2010)
Allium sativum	Bath	Raw and squeezed	200 ppm for 24 h	*Anguilla anguilla*	*Trichodina*	Madsen et al. (2000)
Camellia sinensis	Bath	Extract	0.3–0.9% for 1–5 min	*Oncorhynchus keta, Oncorhynchus masou*	*Ichthyobodo necator*	Suzuki et al. (2006)
Melia azedarach	Bath	Methanol extract	381 mg/l for 48 h	*Carassius auratus*	*Gyrodactylus kobayashii*	Zhou et al. (2017)
Hericium erinaceum	Feed additive	Ethanol extract	0.1 and 1% for 4 weeks	*Paralichthys olivaceus*	*Philasterides dicentrarchi*	Harikrishnan et al. (2011c)
Bupleurum chinense	Bath	Methanol, chloroform and ethyl acetate extracts	6.9, 8.4, and 11.2 mg/l for 48 h	*Carassius auratus*	*Dactylogyrus intermedius*	Wu et al. (2011)
Polygonum multiflorum	Bath	Water, methanol and ethyl acetate extracts	100, 12.5, and 25 mg/l for 48 h	*Carassius auratus*	*Dactylogyrus intermedius*	Hu et al. (2014)
Dioscorea collettii	Bath	Ethyl acetate, chloroform and methanol extracts	80, 80, and 120 mg/l for 48 h	*Carassius auratus*	*Dactylogyrus intermedius*	Hu et al. (2014)
Citrus medica	Bath	Chloroform and ethyl acetate extracts	100 and 125 mg/l for 48 h	*Carassius auratus*	*Dactylogyrus intermedius*	Hu et al. (2014)

Table 3 (continued)

Medicinal plant	Mode of administration	Preparation	Dose	Fish	Antiparasitic effect against	Reference
Allium sativum	Feed additive	Powder	1 and 2 mg/kg feed for 15 days	*Piaractus mesopotamicu*	*Anacanthorus penilabiatus*	Martins et al. (2002)
Cinnamomum cassia	Bath	Water and methanol extracts	200 mg/l for 48 h	*Carassius auratus*	*Dactylogyrus intermedius*	Ji et al. (2012)
Lindera aggregata	Bath	Methanol extract	40 mg/l for 48 h	*Carassius auratus*	*Dactylogyrus intermedius*	Ji et al. (2012)
Pseudolarix kaempferi	Bath	Methanol and ethyl acetate extracts	100 mg/l for 48 h	*Carassius auratus*	*Dactylogyrus intermedius*	Ji et al. (2012)
Allium sativum	Feed additive	Water extract	50 or 150 ml/kg feed for 30 days	*Lates calcarifer*	*Neobenedenia* sp.	Militz et al. (2013)
Allium sativum	Bath	Water extract	1, 2, and 10 ml/l for 1 h	*Lates calcarifer*	*Neobenedenia* sp.	Militz et al. (2014)
Dryopteris crassirhizoma	Bath	Methanolic extract	22.97 mg/l after 48 h of exposure	*Carassius auratus*	*Dactylogyrus intermedius*	Lu et al. (2012)
Kochia scoparia	Bath	Methanolic extract	31.28 mg/l after 48 h of exposure	*Carassius auratus*	*Dactylogyrus intermedius*	Lu et al. (2012)
Polygala tenuifolia	Bath	Methanolic extract	154.79 mg/l after 48 h of exposure	*Carassius auratus*	*Dactylogyrus intermedius*	Lu et al. (2012)
Asparagopsis taxiformis	Bath	Water extract	1 ml of extract to 100 mL of seawater after 24 h of exposure	*Lates calcarifer*	*Neobenedenia sp.*	Hutson et al. (2012)
Caesalpinia sappan	Bath	Chloroform extract	125 mg/l after 48 h of exposure	*Carassius auratus*	*Dactylogyrus intermedius*	Huang et al. (2013)
Lysima chiachristinae	Bath	Ethyl acetate extract	150 mg/l after 48 h of exposure	*Carassius auratus*	*Dactylogyrus intermedius*	Huang et al. (2013)
Clematis chinensis	Bath	Ethyl acetate extract	225 mg/l after 48 h of exposure	*Carassius auratus*	*Dactylogyrus intermedius*	Huang et al. (2013)
Artemisia argyi	Bath	Ethyl acetate extract	300 mg/l after 48 h of exposure	*Carassius auratus*	*Dactylogyrus intermedius*	Huang et al. (2013)
Eupatorium fortunei	Bath	Chloroform extract	500 mg/l after 48 h of exposure	*Carassius auratus*	*Dactylogyrus intermedius*	Huang et al. (2013)

et al. (2004) evidenced that *Rosmarinus officinalis* containing feed was safe for tilapia. In the view of Thanigaivel et al. (2015), the aqueous extract of *Padina gymnospora* at a concentration of 500 mg/l and ethanol extract of *Padina gymnospora* at 250 mg/l were not toxic for tilapia. Rattanachaikunsopon and Phumkhachorn (2009) did not observe any lethal outcome in tilapia fed feed supplemented with *Andrographis paniculata*. Chum salmon fry and masu salmon fry immersion in 0.03% green tea extract for 30 or 60 min did not result in death (Suzuki et al. 2006). The survival of guppy (*Poecilia reticulata*) after immersion in 12.5 mg/l garlic aqueous extract for up to 1 h was 100% (Fridman et al. 2014). Zhang et al. (2013) did not report any dead channel catfish (*Ictalurus punctatus*) following treatment with 80 mg/l pentagalloylglucose extracted from *Galla chinensis*. *Carassius auratus* tolerated methanol extract of *Mucuna pruriens* at concentrations of 600 and 800 mg/l for 96 h and petroleum ether extract of *Carica papaya* at concentrations of 600, 800, and 1000 mg/l (Ekanem et al. 2004). Nevertheless, some medicinal plants were found to be toxic for fish. The LC_{50} of the methanolic extract of *Macleaya cordata* for *Carassius auratus* was 81.4 mg/l (Zhou et al. 2017). The toxicity of ethyl acetate and petroleum ether extracts was low at concentrations 1000 and 2000 mg/l. Abd El-Galil and Aboelhadid (2012) affirmed that LC_{50} of garlic oil for tilapia was 61.86 ppt. Zhang et al. (2014) demonstrated that the LC_{50} of ethyl acetate extract from *Euphorbia fischeriana* was 13.65 mg/l. for *Carassius auratus.* The LC_{50} of garlic (*Allium sativum*) extract for tilapia was 2259.44 mg/l while the LC_{50} of Indian almond (*Terminalia catappa*) was 46,665.94 mg/l (Chitmanat et al. 2005). The LC_{50} values of chloroform, ethyl acetate, and methanolic extracts of *Bupleuri chinensis* for *Carassius auratus* as affirmed by Wu et al. (2011) were 50.3, 31.4, and 35.2 mg/lm, respectively. Ji et al. (2012) have established the toxicity (48 h-LC_{50}) of *Cinnamomum cassia* (water extract—56.9 mg/l and methanolic extract—31.3 mg/l), *Lindera aggregata* (methanolic extract—165.7 mg/l), and *Pseudolarix kaempferi* (methanolic extract—88.7 mg/l and ethyl acetate extract—168.2 mg/l) for goldfish (*Carassius auratus*). According to Lu et al. (2012), the 48 h-LD_{50} values of methanolic extracts from *Dryopteris crassirhizoma*, *Kochia scoparia*, and *Polygala tenuifolia* for *Carassius auratus* were 94.09, 71.04, and 774.31 mg/l, respectively.

Mode of action of medicinal plants in fish diseases

It was reported that some mode of action of medicinal plants includes stimulation of the cellular and humoral immune response, monitored through elevation in immune parameters (Awad and Awaad 2017). These authors found that various levels of immune stimulation were shown by medicinal plants at different concentrations through injection or immersion or oral administration (Awad and Awaad 2017). It was also reported that *Staphylococcus aureus* is one of those bacterial pathogens that could cause skin infections, endocarditis, septicemia, meningitis, toxic shock syndrome, gastroenteritis, and staphylococcal food poisoning (Li et al. 2014). Chlorogenic acid (a secondary plant metabolite) exhibited antimicrobial activity against *S. aureus* and the mode of action of chlorogenic acid against *S. aureus* was studied by Li et al. (2014). They reported that when *S. aureus* was treated with chlorogenic acid, an observation with electron microscopy techniques revealed that the cell membrane of *S. aureus* was damaged by chlorogenic acid. It was concluded that chlorogenic acid inhibited the proliferation of *S. aureus* and destroyed the permeability of the cell membrane. The antimicrobial active principles containing in plant extracts to treat fish diseases could be acting similarly to Li et al. (2014) findings, but this needs to be confirmed in a dedicated study. The

herbs can also act as immunostimulants, conferring the non-specific defense mechanisms of fish and elevating the specific immune response (Pandey et al. 2012). Because plant extracts contain myriad of secondary metabolites belonging to several classes of natural products, specific studies should be carried out to exactly determine the mechanisms of action of plant extracts.

Immune boosting effect

Plant extracts possess different properties such as antistress, growth promotion, appetite stimulation, and immunostimulation and prevent diseases in fish aquaculture. These activities are produced in part by alkaloids, terpenoids, tannins, saponins, glycosides, flavonoids, phenolics, steroids, and essential oils present in the plants (Reverter et al. 2014). It is well known that these bioactive compounds enhance both specific and nonspecific immune responses in fish (Harikrishnan et al. 2012). In the view of Van Hai (2015), the innate immune system consists of macrophages, monocytes, granulocytes, and lysozyme, and phagocytic cells are the most important components. Lysozyme is important in innate immune response because it damages bacterial cell wall and activates the complement and phagocytosis of bacteria, parasites, and virus (Harikrishnan et al. 2011b). Thus, the usage of plants as immunostimulants was found to enhance the innate immune system and prevent fish diseases (Harikrishnan et al. 2012). The ability of white blood cells to kill bacterial pathogens is among the most important mechanisms of defense. Reactive oxygen and nitrogen species are toxic for bacteria causing illnesses in fish. Reactive oxygen species produced by neutrophils and macrophages could kill bacteria and thus, constitute a primary element of non-specific defense in fish (Alexander et al. 2010). *Astragalus membranaceus* and *Lonicera japonica* enhanced substantially phagocytic and respiratory burst activities in tilapia (*Oreochromis niloticus*) (Ardo et al. 2008). Dietary supplementation of *Zingiber officinale* improved the non-specific immunity of Asian sea bass (*Lates calcarifer*) as affirmed by Talpur et al. (2013), whereas Bilen et al. (2016) proved the immunostimulatory effect of *Urtica dioica* through enhanced phagocytic and lysozyme activities in rainbow trouts (*Oncorhynchus mykiss*). The combination of *Astragalus* and *Ganoderma* stimulated respiratory burst activity, phagocytosis, and lysozyme in carps (*Cyprinus carpio*) (Yin et al. 2009). The immunostimulatory effect of *Tinospora cordifolia* was manifested through increased lysozyme, antiprotease and complement activities, and reactive oxygen and nitrogen species production in *Oreochromis mossambicus* (Alexander et al. 2010). In the view of Harikrishnan et al. (2011b), the co-administration of *Scutellaria baicalensis* and *Lactobacillus sakei* BK19 increased complement and antiprotease activities as well as reactive oxygen and nitrogen species production in rock bream (*Oplegnathus fasciatus*). The addition of 1 and 2% *Eriobotrya japonica* to the feed of kelp grouper (*Epinephelus bruneus*) (Kim et al. 2011) enhanced the immune response of fish. *Ficus carica*, *Radix isatidis*, and *Schisandra chinensis* were able to improve the immune response in crucian carps when used as immunostimulants (Wang et al. 2016). The dietary supplementation of kelp grouper (*Epinephelus bruneus*) with 1 and 2% *S. glabrescens* increased considerably complement activity as well as reactive oxygen and nitrogen species and myeloperoxidase production (Harikrishnan et al. 2012). The phagocytic and lysozyme activities were found to be improved following addition of 1 and 2% *Lactuca indica* to

the feed of kelp grouper (*Epinephelus bruneus*) (Harikrishnan et al. 2011a). Harikrishnan et al. (2011b) provided proofs that the co-administration of *Scutellaria baicalensis* and *Lactobacillus sakei* BK19 increased the activities of lysozyme, complement and antiprotease, and reactive oxygen and nitrogen species production in rock bream (*Oplegnathus fasciatus*). As reported by Pan et al. (2013), *A. membranaceus*, *S. baicalensis*, and Fructus Forsythiae acted as immunostimulants on red drum (*Sciaenops ocellatus*). Tilapia injected with aqueous extract of *Toona sinensis* exhibited significantly increased respiratory burst, phagocytic and lysozyme activity (Wu et al. 2010). Supplementation with 0.5% *Achyranthes aspera* increased lysozyme and nitric oxide concentrations in Rohu (*Labeo rohita*) (Chakrabarti and Srivastava 2012). According to Sharma et al. (2010), the addition of *Withania somnifera* to the feed of *Labeo rohita* resulted in higher phagocytic activity, total immunoglobulin level, and lysozyme activity. Sahu et al. (2008) affirmed that lysozyme activity, superoxide anion production, and serum bactericidal activity increased after 60-day dietary supplementation of *Labeo rohita* with *Curcuma longa*. *Cynodon dactylon* had an immunostimulatory effect on Indian major carp (*Catla catla*) as seen from increased lysozyme activity, antiprotease activity and haemolytic complement and reactive oxygen and nitrogen species and myeloperoxidase activity (Kaleeswaran et al. 2011). The ethanolic extract of *Tinospora cordifolia* increased significantly the activity of neutrophils (Sudhakaran et al. 2006). Das et al. (2015) affirmed that the dietary supplementation of *Ocimum sanctum* increased lysozyme activity, total immunoglobulin, serum total protein, globulin, total RBC counts, total WBC counts, and hemoglobin content of *Labeo rohita*. Pratheepa and Sukumaran (2011) found out increase in phagocytic activity in *Cyprinus carpio* proportionally to the dietary level of *Euphorbia hirta*.

Antiviral activity

According to Sivasankar et al. (2015), the most important viruses that cause high mortality rates in fish aquaculture are infectious hematopoietic necrosis virus, infectious pancreatic necrosis virus, hirame rhabdovirus, yellowtail ascites virus, striped jack nervous necrosis virus, and iridovirus. There are only few reports on antiviral activity of plants against viruses affecting fish aquaculture. Micol et al. (2005) reported that olive tree leaf (*Olea europaea*) inhibited in vitro viral haemorrhagic septicaemia rhabdovirus. In another in vitro research, Direkbusarakom et al. (1996) established antiviral activity of 18 herbs (*Cassia alata*, *Calophyllum inophyllum*, *Clinacanthus* spp., *Clinacanthus nutans*, *Glinus oppositifolis*, *Hura crepitan*, *Momordica cha rantina*, *Ocimum sanctum* (red), *Ocimum sanctum* (white), *Orchocarpus siamensis*, *Phyllanthus acidus*, *Phyllanthus amarus*, *Phyllanthus debelis*, *Phyllanthus reticulatus*, *Phyllanthus urinaria*, *Psidium guajava*, *Tinospora cordifolia*, and *Tinospora crispa*) against infectious hematopoietic necrosis virus, infectious pancreatic necrosis virus, and *Oncorhynchus masou* virus. Nevertheless, Harikrishnan et al. (2010) conducted in vivo research regarding the beneficial effect of plants in viral fish disease. They injected intraperitoneally leaf extracts of *Punica granatum* at 50 and 100 mg/kg body weight in olive flounder (*Paralichthys olivaceus)* naturally infected with lymphocystis disease virus for 8 weeks resulting in enhancement of innate immune responses and disease resistance. Novriadi and Haw (2015) stated that immersion in 20 mg/l of herbal solution (AquaHerb©) for 72 h provides resistance of tiger grouper (*Epinephelus fuscoguttatus)* against iridovirus

infection. According to Syahidah et al. (2015), the antiviral effect of plants is due to inhibition of virus transcription and reduction of its replication in the host cells, thus, enhancing the innate immune response of the host.

Antibacterial activity

The antibacterial properties of medicinal plants are the most investigated with application in aquacultures (Reverter et al. 2014), and it is well known that these plants have antibacterial activity against Gram-positive and Gram-negative bacteria (Van Hai 2015). Most of these are administered against *Aeromonas hydrophila*, *Vibrio parahaemolyticus*, *Vibrio harveyi*, *Vibrio carchariae*, *Vibrio splendidus*, *Streptococcus iniae*, *Edwardsiella tarda*, *Pseudomonas aeruginosa*, and *Streptococcus agalactiae* (Table 2). *Urtica dioica* (Bilen et al. 2016), *Astragalus membranaceus, Ganoderma lucidum* (Yin et al. 2009), *Lonicera japonica* (Ardo et al. 2008), *Ficus carica*, *Radix isatidis*, *Schisandra chinensis* (Wang et al. 2016), *Tinospora cordifolia* (Alexander et al. 2010), *Toona sinensis* (Wu et al. 2010), *Achyranthes aspera* (Chakrabarti and Srivastava 2012), *Withania somnifera* (Sharma et al. 2010), *Curcuma longa* (Sahu et al. 2008), *Cynodon dactylon* (Kaleeswaran et al. 2011), *Tinospora cordifolia* (Sudhakaran et al. 2006), and *Ocimum sanctum* (Das et al., 2015) have been successfully used for treatment of aeromoniasis in fish. *Lactuca indica* and *Rosmarinus officinalis* are alternative antibacterial means for control of *Streptococcus iniae* infection in kelp grouper (*Epinephelus bruneus*) and tilapia (*Oreochromis* spp.) (Abutbul et al. 2004; Harikrishnan et al. 2011a), while *Andrographis paniculata* was efficient against *Streptococcus agalactiae* infection in *Oreochromis niloticus* (Rattanachaikunsopon and Phumkhachorn 2009). Feed supplemented with *Zingiber officinale* (Talpur et al. 2013), *Eriobotrya japonica* (Kim et al. 2011), *Astragalus membranaceus*, *Scutellaria baicalensis*, *Forsythia* spp. (Pan et al. 2013), and *Siegesbeckia glabrescens* (Harikrishnan et al. 2012) was applied for treatment of *Vibrio* illness in fish. *Padina gymnospora* could be used for treatment of *Pseudomonas aeruginosa*-induced infection in *Oreochromis mossambicus* (Thanigaivel et al. 2015), while *Scutellaria baicalensis* protected rock bream (*Oplegnathus fasciatus*) against *Edwardsiella tarda* (Harikrishnan et al. 2011b). The *Euphorbia hirta* extract increased antibody production in *Cyprinus carpio* following infection with *Pseudomonas fluorescens* (Pratheepa and Sukumaran 2011).

Antiparasitic activity

The antiparasitic effect of plants is mainly investigated against ectoparasites such as *Ichthyophthirius multifiliis*, *Dactylogyrus vastator*, *Dactylogyrus intermedius*, *Gyrodactylus turnbulli*, *Gyrodactylus kobayashii*, *Ichthyobodo necator*, *Philasterides dicentrarchi*, *Anacanthorus penilabiatus*, and *Trichodina* spp. (Table 3). The preferable method of administration is by immersion. According to Reverter et al. (2014), this is due to the lack of prevention methods in open aquaculture systems against ectoparasites, leaving immersion techniques as the only option for detached fish ectoparasites. Martins et al. (2002) suggested that serum and mucus of fish contain factors responsible for resistance to ectoparasites but the exact mechanism is still unknown. The garlic (*Allium sativum*) was a promising alternative

against *Gyrodactylus turnbulli* (Fridman et al. 2014), *Trichodina*, *Gyrodactylus* (Madsen et al. 2000; Chitmanat et al. 2005; El-Galil and Aboelhadid 2012), *Anacanthorus penilabiatus* (Martins et al. 2002), and *Neobenedenia* sp. (Militz et al. 2013; Militz et al. 2014). A good therapeutic efficacy and preventive effect against *Ichthyophthirius multifiliis* were exhibited by *Galla chinensis* (Zhang et al. 2013), *Mucuna pruriens*, *Carica papaya* (Ekanem et al. 2004), and *Macleaya cordata* (Yao et al. 2010). *Euphorbia fischeriana* (Zhang et al. 2014), *Bupleurum chinense* (Wu et al. 2011), *Polygonum multiflorum*, *Dioscorea collettii*, *Citrus medica* (Hu et al. 2014), *Cinnamomum cassia*, *Lindera aggregata*, *Pseudolarix kaempferi* (Ji et al. 2012), *Dryopteris crassirhizoma*, *Kochia scoparia*, *Polygala tenuifolia* (Lu et al. 2012), *Caesalpinia sappan*, *Lysima chiachristinae*, *Cuscuta chinensis*, *Artemisia argyi*, and *Eupatorium fortunei* (Huang et al. 2013) provided protection against infection with *Dactylogyrus* in fish. Antiparasitic activity was established for *Camellia sinensis* with respect to *Ichthyobodo necator* (Suzuki et al. 2006), of *Melia azedarach* against *Gyrodactylus kobayashii* (Zhou et al. 2017), *Hericium erinaceum* against *Philasterides dicentrarchi* (Harikrishnan et al. 2011c). *Asparagopsis taxiformis* delayed embryonic development and inhibited egg hatching of *Neobenedenia* sp. (Hutson et al. 2012).

Conclusion

Considering the increasing antibiotic resistance of pathogens isolated from sick fish, it appears that medicinal plants are promising new means of treating viral, bacterial, and parasitic diseases in fishes. Even though the number of studies into the application of medicinal plants in aquacultures is increasing, more researches are needed to determine the exact mode of preparation, application, the dosage, treatment duration, and the effects of various medicinal plants on the different species of fish. Prior to application of medicinal plants for therapeutic purposes, toxicity tests are mandatory due to the proved harmful effect of some of them on treated fish.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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