DOI : [http://doi.org/10.22438/jeb/415\(SI\)/MS_12](http://doi.org/10.22438/jeb/415(SI)/MS_12)

Phytotherapy in aquaculture: Integration of endogenous application with science

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Paper received: 17.09.2019

Revised received: 12.01.2020

Accepted: 14.08.2020

Abstract

Aquaculture is a growing industry that contributes about half of the global fish production. However, the production growth of this industry is restricted by many factors and challenges amongst which, infectious disease plays a major role. Some of the convenient and common practices to mitigate diseases in aquaculture are through the use of antibiotics and chemical disease-control agents. These practices, although well-meaning pose tremendous public and environmental health concerns. An alternative approach is via the use of medicinal plants, though this has been practised as an endogenous application to treat or prevent diseases. This biodegradable and environmental-friendly application is known as phytotherapy, or more often commonly called herbalism. Hence, this review article will emphasise on phytotherapy as an alternative treatment for disease in aquaculture and its role in aquaculture. Common diseases threatening aquaculture and the corresponding clinical signs are also discussed in this review. In addition, the mode of action, major classes and side effects of antibiotics are also highlighted. Finally, this review addresses current issues and prospects of phytotherapeutic application in aquaculture.

Keywords: AMR, Antibiotics, Aquaculture, Immunoprophylactics, Phytotherapy

How to cite : Chong, C.M., A.V.S. Ganaseh Murthy, C.Y. Choy and K.S. Lai: Phytotherapy in aquaculture: Integration of endogenous application with science. *J. Environ. Biol.*, **41**, 1204-1214 (2020).

Introduction

Aquaculture is a system which uses various methods and techniques to cultivate aquatic organisms, this involves the action of farming aquatic species ranging from freshwater to saltwater. According to the Food and Agriculture Organization of the United Nations (FAO, 2019), aquaculture is a booming industry representing 46% of the total global fish production (about 172.6 million tonnes) worth of USD 238 billion in 2017. The average annual increase in global fish consumption (3.2 percent) exceeded that of meat produced from all terrestrial animals combined (2.8 percent) between 1961 and 2016 (FAO, 2018). Furthermore, fish accounted for about 20% of animal protein consumed by humans globally (FAO, 2019). This massive global demand for fish was supplied mainly by aquaculture as captured fishery failed to expand since the late 1980s (FAO, 2018).

However, the production growth of this industry is restricted by several factors and challenges, amongst which infectious disease plays a major role. The outbreak of disease is often due to poor fish health management, such as poor water quality, nutrition and sanitation as well as high stocking intensity. Infectious disease has a negative impact on the industry which caused a loss of over USD 6 billion per annum in the global aquaculture industry according to FAO (Brummett *et al.*, 2014). This great financial loss has altered the supply and demand for food fish but has also devastated the livelihood of fish farmers, resulting in increased rate of unemployment and a decrease in their main income.

To overcome this constraint, appropriate treatments and techniques to control the diseases, which are scientifically proven to be effective, have to be applied. For years, many different culture techniques (Dauda *et al.*, 2018) and types of treatment such as administering antibiotics, vaccines, probiotics, prebiotics, dietary supplements and medicinal plants have been used to control many diseases in the aquaculture sector (Assefa and Abunna, 2018; Chong and Maha, 2014; Ebrahimi *et al.*, 2017; Masduki *et al.*, 2018; Romano *et al.*, 2016; Romano *et al.*, 2018). The use of medicinal plants to treat or prevent disease is known as phytotherapy and often commonly called herbalism (Falzon and Balabanova, 2017). This review article emphasises on phytotherapy as an alternative treatment for disease in aquaculture and its role in aquaculture.

Types of common fish diseases : A fish disease occurs through the interaction between the fish (host), pathogen and its environment which often results in the presentation of certain signs unique to the disease (Said *et al.*, 2018). The mechanics of these three variables (Fig. 1) have to be studied and understood well so that measures can be taken to prevent and restrict the disease. Disease causing pathogens that give rise to infections in fish can be classified into fungal, protozoan, bacterial and viral.

Fig. 1 : Interaction between host, pathogen and environment resulting in disease.

Table 1 summarises common pathogenic diseases in aquaculture.

Use of antibiotics and chemical disease-control agents:

Bacterial infections are the most common and play a major role in limiting aquaculture production. While vaccination remains a fascinating approach in prevention of bacterial disease, the functional immunology knowledge of many tropical fish species is still in its infancy. This constraint has hindered the development of effective vaccines in these species (Chong and Low, 2019). Hence, antibiotics are used to control these infections and are often given prophylactically. This leads to a growing risk of bacteria evolving into antibiotic resistant strains resulting in superbugs which will be extremely difficult to treat (Chong *et al.*, 2019; Moo *et al.*, 2019). In some cases, bacterial diseases can no longer be treated with antibiotics. A report by Karunasagar *et al.* (1994) showed mass mortality in *Penaeus monodon* larvae caused by *Vibrio harveyi* having strains resistant to cotrimoxazole, chloramphenicol, erythromycin and streptomycin. Note that cotrimoxazole and chloramphenicol have often been used as prophylactics (Defoirdt *et al.*, 2011; Karunasagar *et al.*, 1994). The major classes of antibiotics used in the aquaculture sector and their corresponding mode of action against pathogens is shown in Table 2.

Aside from increasing the risk of developing multi resistant strains of bacteria, excessive use of antibiotics results in the presence of residual antibiotics in commercialised fish and shellfish products (Cabello *et al.*, 2011; Mahizan *et al.*, 2019). This leads to undetected consumption of antibiotics in fish consumers which may cause antibiotic allergies and toxicities (Bassetti *et al.*, 2019). These allergies and toxicities may also develop in unprotected workers working in the aquaculture sector through contact with large amount of antibiotics on skin, intestinal and bronchial tracts. Hence, novel strategies that cause less harm and risks have to be used to target pathogens that lead to disease and infection in aquaculture.

Like any other animal, fishes are prone to different diseases such as parasitic infection, bacterial infections and viral infection. Several significant cases of fish disease that resulted in high mortality has been documented around the globe. Example

of a reported case occurred in 1995 and 1998-1999 when *Pilchard herpesvirus* caused a high epizootic mortality in Australia (Whittington *et al.*, 2008). Such situation further proved that fish living in the wild or reared in fish farms are susceptible to

Table 1 : Overview of common fish diseases caused by different classes of pathogenic microorganisms

Pathogens	Diseases	Signs and Symptoms
Protozoa	<i>Ichthyophthirius multifiliis</i>	Ichthyophthiriasis (White spot disease)
	<i>Costia necatrix</i>	Costiasis
	<i>Trichodina</i> spp.	Trichodiniasis
	<i>Heteropolaria colisarum</i>	Epistylis (Red sore disease)
Fungi	Myxosporidian parasites	Myxosporidian infestation
	<i>Saprolegnia parasitica</i>	Saprolegniasis (Cotton wool disease)
	<i>Branchiomyces sanguinis</i> (in carps) & <i>Branchiomyces demigrans</i> (in pike and tench)	Branchiomycosis (Gill rot)
	<i>Ichthyophonus hoferi</i>	Ichthyophonosis disease (Swinging disease)
Bacteria	<i>Aeromonas</i> , <i>Pseudomonas fluorescens</i> , or <i>Vibrio</i> bacteria	Fin and tail rot disease
	<i>Flexibacter columnaris</i>	Ulcer
	<i>Aeromonas</i> bacteria	Dropsy
	<i>Aeromonas liquefaciens</i>	Eye disease

To be cont...

Virus	<i>Rhabdovirus carpio</i>	Spring viremia	<ul style="list-style-type: none"> • Fish turns black and develops lesions on the skin and gills (LaPatra et al., 2016). • Bleeding from scales. • Accumulation of fluid in the body. • Inflammation of alimentary canal. • Presence of coelomic distension (dropsy), pale gills, hemorrhages in the gills, skin, and eye; and a protruding vent with a thick white to yellowish fecal cast (Petty et al., 2012).
	<i>Herpesvirus cyprini</i>	Fish pox	<ul style="list-style-type: none"> • Dermal lesions and blisters (Haenen et al., 2004). • Dark pigmentation on infected sites, growth retardation, distended abdomen, exophthalmia, haemorrhage on the operculum and abdomen (Lepa, and Siwicki, 2013).

numerous diseases. Other than infectious disease, fish may also be susceptible to potentially harmful pathogens due to weakening of immune system. Both environmental and stress causing factors are examples of external components which can have dramatic effects on the physiology of fish (Balasch, and Tort, 2019; Magnadottir, 2010; Yap et al., 2011a; Yap et al., 2011b). Hence, treatments are required and often necessary when it comes to curing the fish from various diseases.

Before introducing of phytotherapy to the aquaculture industry, malachite green was one of the most commonly used methods for treating fish diseases. With the increased usage over the years, it was found that malachite green has toxicological effects on the “treated” fish (Ma et al., 2020). Further studies showed that the toxicity and severity of side effects are correlated with increased exposure time and the concentration given (Srivastava et al., 2004). Despite the fact that malachite green could be the most effective treatment, it has been banned in several countries due to the negative effect on fish health. Other than malachite green, peracetic acid (PAA) was also used as a treatment for *Ichthyophthirius multifiliis* (Sudová et al., 2010). However, peracetic acid had several limitations and disadvantages. The effectiveness of peracetic acid decreased over time due to peroxide degradation (Lindholm-Lehto et al., 2019; Srivastava et al., 2004). In addition, the by-products of degradation, acetic acid and acetate, encouraged the formation of biofilm which in turn became a protection for opportunistic pathogens (Liu, 2016). Most of the time, the adverse impacts of using synthetic medications outweigh the advantages of saving fish. Treatments are usually costly, especially when there is a need for continual treatment with chemicals over a long period of time. It is, therefore, important to explore other choices and techniques that can be used as an alternative to synthetic medications for preventing of fish disease. One such promising methods is phytotherapy.

Role of phytotherapy in aquaculture : Phytotherapy is a medical practice which focus more on traditional approaches rather than modern medication. It highly involves the knowledge

and usage of medical herbalism. The application of phytotherapy is rather new to the aquaculture industry but it is slowly being recognised as an alternative to the use of synthetic drugs for treatment (Eirna-Liza et al., 2018). Unlike synthetic chemicals, phytotherapy is a relatively simple and safe method for both affected fish and environment. This is because the treatments or substances used are derived from plants. Most active compounds are extracted from natural sources and they are eco-friendly, farmer-friendly and have little side-effects on fish health. Many researchers have been carried out studies and come to the conclusion that phytotherapy is effective in treating fish disease (Doan et al., 2020; Marco, 2018; Pathirana et al., 2019; Valladão et al., 2015). One common way of treating parasitic fish disease is directly bathing the fish in a medium containing herbs or active compounds extracted from plants. Higher concentration of herbs, within the range of effective concentration, lower than that of lethal concentration (LC_{50}), were often reported to yield good efficacy in acute bath treatment of herbs. Acute treatment should be performed within 1-8 hr. Prolonged phytotherapeutic treatment of high concentration may impair fish physiology and behaviour (Doan et al., 2020). Indefinite bath treatment of herbs of lower concentration are also applied to treat the parasitic infections. El-Galil and Aboelhadid (2012) demonstrated that indefinite bath application of 300 mg l⁻¹ (about 200 times less than the reported LC_{50} of crushed garlic cloves) demonstrated 68% mitigation of gyrodactylosis in hatchery earthen ponds of tilapia. The other common route of administration is combining plant parts such as leaves, flowers, fruits or using the plant wholly together with fish feeds. This is to ensure that the active ingredients can be fed directly to the aquatic organisms in order to achieve the maximum potential effects. Table 3 shows some of the phytotherapy examples on fish disease.

Apart from treating fish disease, natural products derived from medicinal herbs can be used as a substitution for synthetic growth promoters. Antibiotic growth promoters are commonly used in fish feed to enhance the biological activities. However, extensive and excessive use of growth promoters will do more harm than good. One of the risks associated with the use of synthetic growth promoters is that it can inhibit biogas production

Table 2 : Different classes of antibiotics used in aquaculture, example of resistant bacteria.

Class of antibiotics	Mode of action of antibiotics	Example	Resistant bacteria	Isolated from
Aminoglycosides	Inhibits bacterial protein synthesis by binding to the 30S ribosomal subunit (Romero <i>et al.</i> , 2012).	Streptomycin	<i>Edwardsiella ictulari</i>	Diseased striped catfish (<i>Pangasianodon hypophthalmus</i>), Vietnam (Dung <i>et al.</i> , 2008).
		Kanamycin	<i>Vibrio parahaemolyticus</i>	Shrimp farming in Jiangsu, China (He <i>et al.</i> , 2019).
Amphenicols	Inhibits bacterial protein synthesis by binding to the 50S ribosomal subunit (Swaney <i>et al.</i> , 1998).	Chloramphenicol	<i>Aeromonas</i> spp.	Integrated fish farms in Osun State, Nigeria (Samuel <i>et al.</i> , 2019).
		Florfenicol	<i>Enterobacter</i> spp. and <i>Pseudomonas</i> spp.	Freshwater salmon farms, Chile (Fernández-Larcón <i>et al.</i> , 2010).
Beta-lactams	Inhibits bacterial cell wall synthesis by blocking enzymes involved for the synthesis of the peptidoglycan layer (Romero <i>et al.</i> , 2012).	Amoxicillin	Not specified	50% of the surveyed tilapia and catfish farms in southwestern Vietnam used amoxicillin (Ström <i>et al.</i> , 2019).
			<i>Vibrio</i> spp., <i>Aeromonas</i> spp. and <i>Edwardsiella tarda</i>	Different aquaculture settings, Australia (Akinbowale <i>et al.</i> , 2006).
		Ampicillin	<i>Vibrio harveyi</i>	Shrimp farms and coastal waters, Indonesia (Defoirdt <i>et al.</i> , 2011).
		Penicillin	<i>Aeromonas hydrophila</i>	Fish farms in Jiangsu, China (Zhu <i>et al.</i> , 2020).
Fluoroquinolones	Inhibits DNA synthesis by causing double-strand DNA breaks during DNA replication (Romero <i>et al.</i> , 2012).	Enrofloxacin	<i>Tenacibaculum maritimum</i>	Diseased turbot (<i>Scophthalmus maximus</i>) and sole (<i>Solea senegalensis</i>), Spain and Portugal (Avendaño-Herrera <i>et al.</i> , 2008).
Macrolides	Inhibits protein synthesis by binding to the 30S subunit of the ribosome (Romero <i>et al.</i> , 2012).	Azithromycin	<i>Aeromonas hydrophila</i>	Fish farms in Jiangsu, China (Zhu <i>et al.</i> , 2020).
Nitrofurans	Interfere protein synthesis, aerobic ATP metabolism, nucleotide synthesis, and cell wall synthesis by disrupting reactive intermediates that are formed during reduction process by bacterial flavoproteins (Kashanian <i>et al.</i> , 2008).	Erythromycin	<i>Salmonella</i> spp.	Marketed fish, China (Defoirdt <i>et al.</i> , 2011).
		Furazolidone	<i>Vibrio anguillarum</i>	Diseased sea bass and seabream, Greece (Yiagnisis <i>et al.</i> , 2007).
Quinolones	Inhibits DNA synthesis by disrupting the activity of DNA gyrase which is involved in the folding and uncoiling of bacterial DNA and the process of packing nucleotides (Samuelsen 2006).	Nitrofurantoin	<i>Vibrio harveyi</i>	Diseased penaeid shrimp, Taiwan (Liu <i>et al.</i> , 1997).
		Levofloxacin	<i>Escherichia coli</i>	Fish faecal samples obtained from Rajasthan, India (Saharan <i>et al.</i> , 2019).
Sulphonamides	Inhibits the folic acid synthesis metabolic pathway which leads to DNA synthesis inhibition (Romero <i>et al.</i> , 2012).	Oxolinic acid	<i>Aeromonas</i> spp., <i>Pseudomonas</i> spp. and <i>Vibrio</i> spp.	Pond water, pond sediment and tiger shrimp (<i>Penaeus monodon</i>), Philippines (Defoirdt <i>et al.</i> , 2011).
		Sulfamethoxazole (In combination with trimethoprim)	<i>Laribacter hongkongensis</i>	Marketed grass carp (<i>Ctenopharyngodon idella</i>) in Shenzhen, China
		Sulphadiazine	<i>Aeromonas</i> spp.	Diseased catla (<i>Catla catla</i>), mrigel (<i>Cirrhinus mrigala</i>) and punti (<i>Puntius</i> spp.), India (Das <i>et al.</i> , 2009).
Tetracyclines	Inhibits protein synthesis by binding to the 30S subunit of the ribosome (Romero <i>et al.</i> , 2012).	Oxytetracycline	<i>Aeromonas salmonicida</i>	Atlantic salmon (<i>Salmo salar</i>) culture facilities, Canada (Defoirdt <i>et al.</i> , 2011).
		Tetracycline	<i>Aeromonas hydrophila</i>	Water from mullet and tilapia farms, Egypt (Ishida <i>et al.</i> , 2010).

Table 3 : Some of phytotherapy examples on fish disease

Pathogen	Host	Plant used	Type/Active compound	Method of administration
<i>Aeromonas hydrophila</i> (Eirna-Liza et al., 2018)	<i>Clarias gariepinus</i>	<i>Allium sativum</i>	Allicin	Orally
<i>Dactylogyrus intermedius</i> (Valladão et al., 2015; Wang et al., 2008)	<i>Carassius auratus</i>	<i>Fructus cnidii</i>	Osthol and isopimpinellin	Water / bath treatment
<i>Gyrodactylus turnbulli</i> (Schelkle et al., 2013; Valladão et al., 2015)	<i>Poecilia reticulata</i>	<i>Allium sativum</i>	Freeze-dried	Water / bath treatment
<i>Ichthyophthirius multifiliis</i> (Valladão et al., 2015)	<i>Ictalurus punctatus</i>	<i>Galla chinensis</i>	Pentagalloylglucose	Water / bath treatment
<i>Myxobolus</i> spp. (Valladão et al., 2015)	<i>Diplodus puntazzo</i>	<i>Origanum minutiflorum</i>	Essential oil	Oral
<i>Neobenedenia</i> spp. (Militz et al., 2014)	<i>Lates calcarifer</i>	<i>Allium sativum</i>	Allicin	Water / bath treatment

Table 4 : Shows examples of beneficial effects of phytotherapy on fish

Fish	Plant used	Effects
<i>Carassius auratus</i> (Chakraborty et al., 2014)	<i>Phyllanthus niruri</i>	Reduced blood glucose level
<i>Clarias gariepinus</i> (Abbassa, 2010)	<i>Artemisia cina</i>	Increased growth parameter and immune response
<i>Oreochromis aureus</i> (Turan et al., 2007)	<i>Trifolium pratense</i>	Improved growth rate and feed utilization
<i>Oreochromis niloticus</i> (Goda, 2008).	Dietary Ginseng Herb Supplementation (<i>Ginsana® G115</i>)	Enhanced growth performance, diet utilization efficiency and haematological indices
<i>Oreochromis niloticus</i> (Francis et al., 2001)	<i>Quillaja saponins</i>	Increased growth and reduced metabolic rate

(Hao et al., 2014). This is because antibiotics excreted into the environment partially inhibit methanogenesis which decreases the metabolic rate of bacteria to produce biogas (Hao et al., 2014). Thus, people are now more aware of the side effects and consequences of using antibiotics. This is because antibiotics increase the emergence of antibiotic-resistant pathogen and antibiotic residues indirectly discharge through excretion are harmful to the environmental microbial community (Chong et al., 2019). Hence, shifting to a more organic approach is seen to be more promising approach. In order to achieve the same objective, herbal drugs that promote growth are being considered. Herbal drugs are often safer and cheaper compared to synthetic growth promoters. Most importantly, they can achieve similar outcomes in terms of growth performance in aquatic organisms. In other words, farmed fish species can grow healthier and bigger in size by consuming herb-infused feeds. It has been prove that application of phytotherapy in aquaculture has not only resulted in increased growth parameters but also in healthier biological responses. One such study involved feeding *Oreochromis niloticus* with dietary ginseng herb supplementation (*Ginsana® G115*) (Goda, 2008). The results showed evidence of enhanced growth performance, diet utilization efficiency and hematological indices (Goda, 2008). Table 4 highlights examples of beneficial effects of phytotherapy on fish.

Plants produce a variety of bioactive compounds to tolerate their habitats, unfavourable weather conditions and pathogenic infections (Varijakzhan et al., 2020). These bioactive compounds are often referred to as secondary metabolites (SMs)

alkaloids, essential oils, phenolics, saponins, terpene and carbohydrates synthesised by plants. Although carbohydrates are primary metabolites, they are often incorporated into secondary metabolites by glycosylation (Varijakzhan et al., 2020). Secondary metabolites are able to modulate protein-protein interactions, such as recognition, binding, catalytic activity and turnover (Hoseinifar et al., 2020). These have given rise to an array of immunoprotective effects for the treatment of non-origin host, which includes: immunostimulants, antibacterial, antiviral, antifungal and anti-stress activities. Various studies have shown the importance of having strong immune system in commercial fish species so that mortalities can be reduced to the lowest during an outbreak of fish disease. These agents have potential to enhance the immune system of host in order to prevent disease infection or for treatment purposes. Nowadays, phytotherapeutic agents are synthesised in combination with natural ingredients, especially with naturally occurring compounds that are found in plants. Immunostimulants are mainly given to fish to enhance the defence mechanism so that fish can become more resistant to disease. Antibacterial agents are used for controlling infectious disease caused by microbes like *Aeromonas hydrophila*, *Vibrio parahaemolyticus* and *Vibrio damsela*. Antiviral agents are used against fish viruses like *White spot syndrome virus (WSSV)*, *salmonid rhabdovirus* and *viral haemorrhagic septicaemia virus* (Citarasu, 2010). Antifungal agents are used for treating diseases related to fungal pathogens like *Aeromonas hydrophila*, *Aspergillus flavus* and *Fusarium oxysporum* (Citarasu, 2010). Cultured fish are often affected by ambient abiotic and biotic

Table 5 : Shows examples of phytotherapeutic agents in aquaculture

Phytotherapeutic	Plant used	Type of organism	Pathogen/stressor	Effects
Immunostimulants	<i>Glycyrrhiza glabra</i> (Edahiro et al., 1991)	<i>Seriola quinqueradiata</i>	<i>Streptococcus</i> spp.	Increased protection against streptococcal infection with increment of 20% survival rate compared to the control group. Complement activity was significantly higher in the treatment group.
Antibacterial agent	<i>Helianthus tuberosus</i> (Ali et al., 2017)	<i>Lates calcarifer</i>	<i>Aeromonas hydrophila</i>	Increased white blood cell counts, as well as lysozyme activity, phagocytosis, and respiratory burst activity of leukocytes
	<i>Terminalia catappa</i> (Purivirojkul et al., 2012)	<i>Betta splendens</i>	<i>Aeromonas hydrophila</i>	Beneficial for improving survival rates and resistance against <i>Aeromonas hydrophila</i>
	<i>Terminalia catappa</i> (Chitmanat et al., 2012)	<i>Oreochromis niloticus</i>	<i>Aeromonas hydrophila</i>	The <i>Terminalia</i> extract added to the rearing water helps to control bacterial infection in fish eggs or larval fish in hatchery which are prone to bacterial infection.
Antiviral agent	<i>Cynodon dactylon</i> (Balasubramanian et al., 2012)	<i>Penaeus monodon</i>	White spot syndrome virus (WSSV)	Highly effective in preventing WSSV infection with no mortality
	<i>Lonicera japonica</i> (Liu et al., 2020)	<i>Epinephelus fuscoguttatus</i> & <i>E. lanceolatus</i>	Groupers iridovirus	<i>L. japonica</i> exhibited the antiviral activity against grouper iridovirus infection in a dose-dependent, with above 90% of inhibition was observed in some of the isolated compounds.
Antifungal agent	<i>Rheum palmatum</i> (Yao et al., 2017)	<i>Ctenopharyngodon idella</i>	<i>Saprolegnia</i> spp.	One week treatment of rhein, a compound isolated from <i>R. palmatum</i> , at 20 mg l ⁻¹ prevented 93.3% of infections by <i>Saprolegnia</i> in <i>Ctenopharyngodon idella</i> , with recovery rate of 67.7% observed in the infected fish.
	<i>Terminalia catappa</i> (Chitmanat et al., 2012)	<i>Oreochromis niloticus</i>	Not specified	Reduced fungal infection in tilapia eggs
Anti-stress agent	<i>Moringa oleifera</i> (Kaleo et al., 2019)	<i>Macrobrachium rosenbergii</i>	Ammonia stress	0.5% oral supplementation of <i>M. oleifera</i> leaf extract mitigated physiological changes of prawns caused by 72 hours of ammonia stress test.
	<i>Toona sinensis</i> (Hsieh et al., 2008)	<i>Litopenaeus vannamei</i>	<i>Vibrio alginolyticus</i>	Improved the biochemical, immunological and hematological parameters during stress conditions

stressors. These stressors can affect metabolic state and eventually compromise the health status. Anti-stress agents are mainly used to reduce the overall stress levels of fish (Hoseinifar et al., 2020).

On account of great variations among the reported studies, in term of phytotherapeutic sources, treatment protocol, host and target pathogens, comparison between these data in the literature is complicated (Valladão et al. 2015). Table 5 provides some examples of bioactivity of phytotherapeutic agents in aquaculture.

Limitation and prospects : Various parts of medicinal plants have been used as an age-old practice to treat diseases; however, they were in the form of unrefined extracts. Modern drugs are developed from these extracts after substantial investigation of their bioactive mechanisms of action (which is often unknown), therapeutic and toxic effects, and also proper standardisation in clinical trials. Investigation on the biological activity and medicinal application of plants in combating diseases affecting the aquaculture industry is meagre. On the other hand, most studies conducted on their effectiveness are based on *in-*

vitro testing or under laboratory conditions. Further, practical studies are required to enable replacement of current treatments. Hence, more serious investigations are required to harness the therapeutic properties and herbal formulations for drug development of medicinal plants to combat disease problems in aquaculture. Studies carried out on phytotherapy of human and other animal diseases should also be taken advantage of by the aquaculture sector to extract suitable principles that can be applied in combating the diseases of fisheries world.

Another challenge that the industry has to tackle is the increasing commercial demand for wild-sourced plant drugs globally is occurring at the expense of rapid deforestation and degradation of species-rich forest ecosystems (Bodeker, 2003). A portion of medicinal plants suffer from resource destruction and are threatened or endangered. Those who are involved in herbal medicine production, trade and utilisation must adhere to the conservation of biological diversity so that sustainable use of its components and the benefits arising from the utilization of these precious resources can be acquired by all (Janke, 2018). Government organisations should emphasise on encouraging private companies to systematically cultivate medicinal herbs by providing positive support and incentives.

Another subject to consider is the ethical aspect of conducting research on animals. There is a risk involved of harming animals in aquaculture to further study the benefits of phytotherapy in the industry. This risk or the impact of risk can be reduced in several ways: for instance, a good study design will help to utilise minimum number of animals required for data collection. However, a sufficient number must be used to attain precise analysis and results, thus, preventing unnecessary repetition of experiments and the consequent need to use more animals (Ghasemi and Dehpour, 2009). Next, the researchers should work towards minimising pain and distress in the animals tested. Anaesthetics and analgesics should be administered whenever necessary during the experiments. Multiple surgeries on same animal must receive special approval from an animal care committee (Ghasemi and Dehpour, 2009).

Finally, with the success of previous research showing significant results with the experimentation of herbal drugs in aquaculture, it has raised the interest of exploring the possibilities of replacing modern synthetic chemicals with traditional naturally compounds. This will lead more researchers to conduct experiments and evaluate the potential and maximise the benefits of natural products.

Acknowledgments

This work was supported by the Fundamental Research Grant Scheme (FRGS; project code: FRGS/1/2015/SG03/UPM/02/4) Long Term Research Grant Scheme (LRGS; project code: LRGS/1/2019/UPM/1) and the SATREPS COSMOS-MOHE project, offered by the Ministry of Higher Education Malaysia.

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