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Abstract. Phytogenics are plant-derived natural compounds in the diets that aim to improve animal production. Several of these plant-derived substances have been tested in various aquaculture fish species particularly on their effects on growth and systemic immune response. Most of the previous studies demonstrated positive effects in improving growth, lowering the feed conversion ratio (FCR) and modulating the various immune response parameters in fish. While nutritional strategies are mostly designed towards the use of plant-based materials as feed ingredients or partial substitutions for the more expensive fish meal in the fish diets, recent initiatives have been targeting the use of these phytogenics as feed additives. The tissues and organs of the digestive system are the ones that have close contact with the phytogenic additives once these are ingested by the fish. Once, digested and absorbed, these substances are distributed throughout the body where they affect the physiological conditions of the fish, including its ability to provide resistance against various infectious diseases. The present work provides a short review on the effects during dietary administration with these phytogenics on gut health and disease resistance in fish. A synthesis of available information on these biological aspects in fish will provide a platform towards developing functional feeds in aquaculture.

1. Introduction

The shift of aquaculture operations towards intensification has placed tremendous pressure on the fish capture industry, which serves as the major source of fish and shrimp meal in the production of feeds for aquaculture species. There are several alternatives to the use of fish or shrimp meal as feed ingredients and one of them is the utilization of the plant resources. The use of plants as feed ingredients in the formulation of feeds for aquaculture offers the following advantages: these provide the needed nutrients requirements of the fish and do not have deleterious effects to the environment [1]. Studies on the use of plants as protein sources for aquaculture feeds have been conducted and yielded promising results [1, 2]. While most of these plant materials have been used as feed ingredients in the formulation of aquafeeds, plant wastes and by-products also show potential as main components of these aquafeeds [3].

Aside from being tapped as feed ingredients in the production of aquafeeds, plant materials are also good sources of bioactive compounds that are incorporated in the diets as feed additives. These plant-based additives resulted in improved health and growth performance of various aquacultured species [4]. The emerging popularity of using phytoadditives is brought about by the fact that the indiscriminate use of antibiotics either for the treatment of diseases or as feed additives in animal

production has raised concern particularly on the emergence of antibiotic resistance in some human pathogenic bacteria [5, 6], the release of residues that contaminate the environment [7] and the potential risk on the presence of antibiotic residues in foods of animal origin [6]. Phytogenics, on the other hand, are of natural origin, free from residues and are generally considered as safe when incorporated in the diets of animals that are used in food production [8].

This brief review focused on the beneficial effects of phytogenics as feed additives on gut health and disease resistance in fish. The direct effects on the health of the gastrointestinal system of the fish in terms of the immune responses and dynamics of the microbiota in the host are presented. The roles of these phytoadditives in providing protection to the fish during infection with various pathogens are also discussed. These two areas, gut health and disease resistance, are crucial in any aquaculture operations as these address issues on sustainability and production. Future research directions on the expansion of these important areas in aquaculture by exploring the mechanisms of actions of these phytoadditives and their potential application to the development of the feed industry in aquaculture are also highlighted in this paper.

2. Characteristics of phytogenics

Plants produce a wide array of secondary metabolites that function as defenses against a number of physiological and environmental stressors [9]. Some of these secondary metabolites are toxic, but there are certain groups that have beneficial effects to the farmed animals when used as feed additives [10] and consequently safe for human consumption. Moreover, these metabolites do not produce residues that could harm the environment [11, 12].

Phytogenics are plant-derived products that are incorporated to the feed with the aim of enhancing health status and improving growth of animals that are intended for food production. These are used as additives in the production of feeds for livestock, and recently these are being utilized in the manufacture of feeds for aquaculture [13]. Inspite of the popularity of using phytogenics in animal diets, the results from earlier studies have mostly been inconsistent and the mechanisms and modes of action are still inconclusive [14, 15, 16]. However, given the limitations in our understanding of the exact mechanisms of phytogenics in animals, these plant-based products are thought to possess the following beneficial properties: these products have antioxidant, anticarcinogenic, analgesic, antimicrobial, insecticidal and antiparasitic effects; can be used as growth promoters and appetite stimulators; and can trigger the secretion of bile and other digestive enzymes [17, 18,19].

Phytogenics include a wide range of substances and can be classified according to botanical origin, processing, and composition [20]. Figure 1 shows the classification of phytogenics that are utilized as phytoadditives for feeds in aquaculture. Phytogenics can be categorized either as: botanicals, which include herbs and spices, or as plant extracts, which include essential oils and oleoresins [21, 22]. Herbs are non-woody flowering plants with medicinal properties; spices, are also herbs but have intense smell or taste and are commonly added to human food. Essential oils are aromatic oily liquids, which are derived from plant materials such as flowers, leaves, fruits, and roots; while, oleoresins are plant extracts which are extracted using non-aqueous solvents. With the identification of the active components of these phytogenic compounds (Table 1) and with progresses being made in the acquisition of relevant information to elucidate their modes of action in both terrestrial and aquatic animals, the use of phytogenics as an alternative to antibiotics in animal diets looks promising in the future [24, 25].

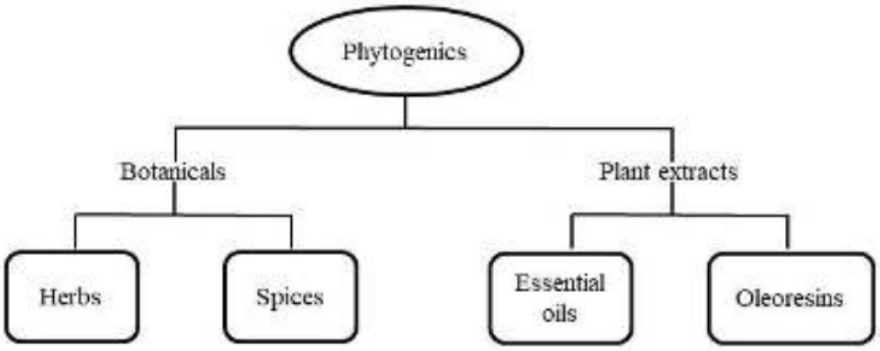

Figure 1. Sources of phytoadditives for feed in aquaculture. Modified from Jacela et al [20].

Table 1. Selected phytogenic feed additives and their active components that are being used in animal diets.

English name	Scientific name	Plant part	Active substance
Banana	*Musa* sp.	roots and peels	Anthocyanadins
Capsicum	*Capsicum annum longum*	fruit	Capsaicin
Cinnamon	*Cinnamomum* sp.	bark	Ammameldehyde
Clove	*Syzygium aromaticum*	cloves	Eugenol
Coffee	*Coffea arabica*	fruit shells	Caffeic acid
Garlic	*Allium tuberosum*	buld	Allicin
Ginger	*Zingiber officinale*	rhizome	Zingerole
Nutmeg	*Myristica flagrans*	seed	Sabinene
Onion	*Allium cepa*	bulb, leaves	Allyl propyl sulphide
Oregano	*Origanum* sp.	leaves	Carvacrol, thymol
Papaya	*Carica papaya*	leaves and peels	Papain
Pepper	*Piper nigrum*	fruit	Piperine
Rosemary	*Aniba rosaedora*	leaves	Cineole
Sage	*Salvia apiana*	leaves	Cineole
Thyme	*Thymus vulgaris*	whole plant	Thymol
Turmeric	*Curcuma longa*	rhizome	Curcumin

Modified from Asimi and Sahu [23] and Caipang et al [3]

3. Impacts on gut health

The gut functions as the site of absorption of nutrients as well as for the secretion of some immune-response substances and as a protective barrier against infectious agents [26, 27]. Aside from its role in digestion, the epithelial cells of the gut serve as "watch dogs" of the immune system [27] as they can trigger the host's innate and acquired immune responses by activating cytokine production [28, 29]. When the gut is exposed to pathogens, this causes disruption in the feeding activity, intestinal disorders, and suppression of the immune responses that will result in physiological imbalance in the

host [30]. Once the normal functioning of the host is altered, metabolism is affected, which could lead to impairment of growth and reduction in productivity.

The effects of the phytoadditives in the gut health of fish are discussed in the context of the immune responses and the dynamics of the microbial population in the gastrointestinal system of the aquacultured fish. In monogastric animals, phytogenics influenced gut health in these following ways: (a) increased antimicrobial activity, (b) reduced infections, (c) reduced nutrient utilization of microbes, (d) improved nutrient absorption, (e) reduced production of growth-depressing metabolites, (f) regulated gut microbiota, and (g) suppressed production of pro-inflammatory cytokines [31]. There is increasing evidence that some, if not all of these mechanisms are also exhibited in the gut of fish [32]. The addition of herbs, spices or their extracts in the diets of monogastric animals stimulated appetite and increased production of digestive enzymes [33]. Similar observations were also noted in fish [13, 23]. Nile tilapia, *Oreochromis niloticus* fed diets supplemented with a mixture of herbal extracts and emulsifying agents showed better feed conversion rate and protein efficiency than those fed without the herbal extracts [34]. Feeds containing extracts from pepper and cinnamon stimulated amylase production [35]. A commercial phytogenics product, Livol (IHF-1000), which is a herbal growth promoter that contains plant ingredients including *Bohaevia diffusa*, *Solanum nigrum*, *Terminaelia arjuna*, *Colosynth*, and black salt significantly improved digestion in cultivable fishes [36, 37, 38]. The inclusion of onion and walnut leaf residues in the diets of African catfish, *Clarias gariepinus* led to an increase in growth brought about by enhanced digestive activity and increased villi height, width cryptal depth that facilitated greater capacity for the absorption of nutrients [39]. Supplementation with carvacrol and thymol in the diets of rainbow trout, *Oncorhynchus mykiss* resulted in improved anti-oxidant activity [40], while diets added with essential oils from American basil, *Ocimum americanum* increased the stomach pH in red drum, *Sciaenops ocellatus* after feeding [41].

In terms of the effects of phytogenics in the gut microbiota of fish, there were studies that clearly demonstrate the changes in microbial composition, which eventually resulted in the stabilization of the populations of the beneficial microbes in the gut of the fish [32]. Although such studies are few, fish nutritionists are becoming more aware that the diet has a crucial role in altering microbial diversity in the gastrointestinal tract, which may have an effect in the metabolism of the host as shown in terrestrial animals [42]. It is expected that more research initiatives along this interesting field will be carried out in the future. Nevertheless, results from previous studies demonstrated that, for example, higher loads of beneficial bacteria, *Bacillus* spp., colonized and became more established in the gut of carp when their diets were supplemented with various Chinese herbs [43]. Similarly, higher loads of *Lactobacillus* spp. were observed in the gut of rainbow trout fed diets containing carvacrol [40]. Incorporation of a commercial essential oil feed additives, that were extracted from a mixture of garlic and labiate-plants, in a low fishmeal and fish oil diets of European sea bass, *Dicentrarchus labrax* exhibited a reduction of coliforms and Vibrionales bacteria in the gut of the fish [44], although no significant differences were observed in growth, feed conversion ratio and production from the control group. The exact mechanisms on how these various phytogenic feed additives contribute in the proliferation of beneficial bacteria in the gastrointestinal tract of the fish are not fully known; thus, further studies are needed to elucidate the relationship between the phytogenics and the gut environment. As experimental evidence on the phytogenics-gut interaction in fish continues to progress, this will contribute towards improving our understanding on why phytogenic feed additives favour the proliferation of beneficial microbes instead of the pathogenic ones in the gastrointestinal tract.

4. Influence on disease resistance

There are a number of comprehensive reviews that report on the wide range of bioactivities exhibited by phytogenics in the prevention or treatment of infectious diseases in fish [*e.g.*, 13, 45, 46]. The efficacy of these phytogenics in providing protection against infections in fish is largely dependent on the plant part or raw materials, the extraction methods and the concentration of the phytoadditives that were used in the diets [45]. Various fish species had improved resistance following infection with *Aeromonas hydrophila* when given feeds supplemented with phytogenic additives obtained from

garlic and its peels [47, 48], cinnamon [49], mixed herbal products composed of *Azadirachta indica*, *Ocimum sanctum* and *Curcuma longa* [49] and many other plant products and their extracts [45, 46]. Some Vibrios are also considered serious bacterial pathogens of fish. Using a commercially available phytogenic product that is composed of extracts from garlic and labiate plants, European seabass, *D. labrax* fed diets with the phytoadditives were better protected against experimental infection with *Vibrio anguillarum* [50, 51] in comparison with the non-fed group. Plant components from garlic [52], neem, *A. indica* [53] and peppermint, *Mentha piperita* [54] conferred protection in Asian seabass, *Lates calcarifer* fingerlings following experimental challenge with *V. harveyi*, another bacterial pathogen belonging to the Vibrio family. These plant components were incorporated in the diets of the fish in varying amounts ranging 1-20 g of the additives per kilogram of feeds and fed to the fish for at least a month before pathogen challenge.

Aside from bacterial pathogens, phytogenic feed additives conferred protective ability to fish against viruses. Although studies are limited, results from these earlier works established significant antiviral activity in the host. For example, an *in vitro* study using oleuropein, a bioactive compound from the leaves of olive, *Olea europaea* demonstrated significant inhibition on the growth and multiplication of the viral hemorrhagic septicemia virus (VHSV), a salmonid novirhabdovirus [55]. At the *in vivo* level, dietary administration of the leaf extracts from *Punica granatum* reduced the mortality of olive flounder, *Paralichthys olivaceus* following experimental infection with the lymphocystis disease virus (LDV) [56]. The feeds were added with extracts at 50-100 g per kilogram of feeds and the protective ability was thought to be due to the enhancement of the innate immune responses of the fish during the duration of feeding with the phytoadditives-enriched diets. In all these studies, the upregulation of both the humoral and cellular immune responses in fish as a consequence of dietary administration with the phytobiotics apparently provided protection against bacterial and viral infections due to the immune-stimulating properties of these various plant products [57]. The contribution of the immune responses and mechanisms in the gastrointestinal system of the fish in the resistance against these pathogens has not been clearly elucidated with the exception of the recent study of [50], which highlighted the possible role of the gut-phytogenics interaction in the improved survival against bacterial infections. In their study, the phytogenics in the feeds were able to exert their action in the pre-ileorectal valve region of the gastrointestinal tract. The increased activities in this particular region of the gut are believed to be responsible in the reduced “in vivo” translocation rates of the pathogen, *V. anguillarum* in the gut; thus, the fish were better protected against the infection, leading to higher survival rates. Clearly the contribution of the gut-phytogenics interaction during infections in fish needs to be studied further in detail using other fish models and pathogens.

5. Conclusion and Future Perspectives

Phytogenic compounds are composed of a wide array of active ingredients, which can be explored as alternatives to the use antibiotics in fish production. Inspite of the growing popularity on the use of phytogenics as a preventive or therapeutic means to control infectious diseases, their widescale application is limited due to issues in consistency of the effects to the host and the lack of full understanding on the modes of action in the host. To address these shortcomings, further studies must focus on exploring the potential side effects of the phytoadditives to the host, possible long-term effects to the environment, effects on the physiology of the pathogen and the mechanisms of the gut-phytogenics interaction in disease resistance. Another important aspect that needs further study is to develop analytical methods that can identify and trace these phytogenic compounds in feeds and in the tissues of the farmed animal as well as their fate in the environment. These methods will ensure that the phytoadditives pose no danger to the fish, the consumers and to the environment. A thorough assessment that will address issues on toxicity and safety of these phytogenic substances that are being used to manufacture feeds for fish are required before these can be utilized extensively in the aquaculture industry.

Taken together, this review on the use of phytogenics as additives in the development of aquafeeds provided an overview on the effects of these substances on gut health in terms of immune responses and microbial composition and disease resistance in fish. These studies demonstrated the benefits in the host fish following dietary inclusion of phytogenics. There are still areas that need to be

addressed, but with the amount of data that are being generated from these research studies, we are getting a better picture of the how these phytogenics exert their effects on the fish. As more initiatives are being directed towards elucidating the mechanisms behind the positive effects of these compounds to the host, these will allow us to fully utilize these phytogenic substances in producing functional feeds for an efficient and sustainable fish production.

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References
[1] Gatlin III DM, Barrows FT, Brown P, Dabrowski K, Gibson Gaylord T, Hardy RW, Herman E, Hu G, Krogdal A, Nelson R, Overturf K, Rust M, Sealey W, Skonberg D, Souza EJ, Stone D, Wilson R, Wurtele E. 2007. Expanding the utilization of sustainable plant products in aquafeeds: a review. Aquaculture Research 38: 551-579.
[2] Daniel N. 2018. A review on replacing fish meal in aqua feeds using plant protein sources. International Journal of Fisheries and Aquatic Studies 6: 164-179.
[3] Caipang CMA, Mabuhay-Omar J, Gonzales-Plasus MM. 2019. Plant and fruit waste products as phytogenic feed additives in aquaculture. AACL Bioflux 12: 261-268.
[4] Coutteau P, van Halteren A, Ceulemans S. 2011. Botanical extracts improve productivity of shrimp, Pangasius. Global Aquaculture Advocate May/June 2011, pp. 90-92.
[5] Manero A, Vilanova X, Cerda-Cuellar M, Blanch AR. 2006. Vancomycin- and erythromycin-resistant enterococci in a pig farm and its environment. Environmental Microbiology 8: 667–674.
[6] Jouany J-P, Morgavi DP. 2007. Use of 'natural' products as alternatives to antibiotic feed additives in ruminant production. Animal 1: 1443-1466.
[7] Yang S, Carlson K. 2004. Routine monitoring of antibiotics in water and wastewater with a radioimmunoassay technique. Water Research 38: 3155–3166.
[8] Li HN, Zhao PY, Yan L, Hossain MM, Kang J, Kim IH. 2016. Dietary phytoncide supplementation improved growth performance and meat quality of finishing pigs. Asian Australas J Anim Sci 9: 1314–1321.
[9] Sethiya NK. 2016. Review on natural growth promoters available for improving gut health of poultry: an Alternative to antibiotic growth promoters. Asian J Poultry Sci 10: 1-29.
[10] Huyghebaert G, Ducatelle R, Van Immerseel F. 2011. An update on alternatives to antimicrobial growth promoters for broilers. Vet J 187: 182–188.
[11] Liu H-W, Tong J-M, Zhou D-W. 2011. Utilization of Chinese herbal feed additives in animal production. Agricult Sci China 10: 1262-1272.
[12] Pavela R. 2015. Essential oils for the development of eco-friendly mosquito larvicides: a review. Industrial Crops Prod 76: 174–187.
[13] Citarasu T. 2010. Herbal biomedicines: a new opportunity for aquaculture industry. Aquaculture International 18: 403–414.
[14] Si W, Gong J, Chanas C, Cui S, Yu H, Caballero C, Friendship RM. 2006. *In vitro* assessment of antimicrobial activity of carvacrol, thymol and cinnamaldehyde towards *Salmonella* serotype *Typhimurium* DT104: effects of pig diets and emulsification in hydrocolloids. Journal of Applied Microbioogy 101: 1282–1291.
[15] Michiels J, Missotten J, Dierick N, Fremaut D, Maene P, de Smet S. 2008. In vitro degradation and in vivo passage kinetics of carvacrol, thymol, eugenol and trans-cinnamaldehyde along the gastrointestinal tract of piglets. J Sci Food Agric 88: 2371–2381.
[16] Liu Y, Song M, Che TM, Bravo D, Maddox CW, Pettigrew JE. 2014. Effects of capsicum oleoresin, garlic botanical, and turmeric oleoresin on gene expression profile of ileal mucosa in weaned pigs. J Anim Sci 92: 3426–3440.

[17] Brenes A, Roura E. 2010. Essential oils in poultry nutrition: Main effects and modes of action. Anim Feed Sci Tech 158: 1–14.
[18] Liu Y, Song M, Che TM, Almeida JAS, Lee JJ, Bravo D, Maddox CW, Pettigrew JE. 2013. Dietary plant extracts alleviate diarrhea and alter immune responses of weaned pigs experimentally infected with a pathogenic *Escherichia coli*. J Anim Sci 91: 5294–5306.
[19] Sutili FJ, Gatlin III DM, Heinzmann BM, Baldisserotto B. 2018. Plant essential oils as fish diet additives: benefits on fish health and stability in feed. Rev Aquacult 10: 716-726.
[20] Jacela JY, DeRouchey J M, Tokach MD, Goodband RD, Nelssen JL, Renter DG, Dritz SS. 2010. Feed additives for swine: fact sheets - prebiotics and probiotics, and phytogenics. Journal of Swine Health and Production 18:132-136.
[21] Windisch W, Schedle K, Plitzer C, Kroismayr A. 2008. Use of phytogenic products as feed additives for swine and poultry. Journal of Animal Science 86:140-148.
[22] Puvaca N, Stanacev V, Glamocic D, Levicc J, Peric L, Stanacev V, Milic D. 2013. Beneficial effects of phytoadditives in broiler nutrition. World's Poult Sci J 69: 27–34.
[23] Asimi OA, Sahu NP. 2013. Herbs/spices as feed additive in aquaculture. Scient J Pure Appl Sci 2: 284-292.
[24] Randrianarivelo R, Danthu P, Benoit C, Ruez P, Raherimandimby M, Starter S. 2010. Novel alternative to antibiotics in shrimp hatchery: Effects of the essential oil of *Cinnamosma fragrans* on survival and bacterial concentration of *Penaeus monodon* larvae. J Appl Microbiol 109: 642–650.
[25] Li SY, Ru YJ, Liu M, Xu B, PeÅLron A, Shi XG. 2012. The effect of essential oils on performance, immunity and gut microbial population in weaner pigs. Livest Sci 145: 119–123.
[26] Lallès JP, Boudry G, Favier C, le Floch N, Luron I, Montagne L, Oswald IP, Pié S, Piel C, Sève B. 2004. Gut function and dysfunction in young pigs. Physiol Anim Res 53: 301–306.
[27] Yang C, Chowdhury MA, Huo Y, Gong J. 2015. Phytogenic compounds as alternatives to in-feed antibiotics: potentials and challenges in application. Pathogens 4: 137–156.
[28] Eckmann L, Kagnoff MF, Fierer J. 1995. Intestinal epithelial cells as watchdogs for the natural immune system. Trends Microbiol 3: 118–120.
[29] Pitman RS, Blumberg RS. 2000. First line of defense: the role of the intestinal epithelium as an active component of the mucosal immune system. J Gastroenterol 35: 805–814.
[30] McDevitt RM, Brooker JD, Acamovic T, Sparks NHC. 2006. Necrotic enteritis: A continuing challenge for the poultry industry. World's Poult Sci J 62: 221-247.
[31] Humphrey BD, Klasing KC. 2003. Modulation of nutrient metabolism and homeostasis by the immune system. Proceedings of the European Symposium on Poultry Nutrition, August 10-14, 2003, Lillehammer, Norway.
[32] Caipang CMA. 2020. Phytogenics in aquaculture: a short review of their effects on gut health and microflora in fish. The Philippine Journal of Fisheries 27(2): 11-22.
[33] Wenk C. 2006. Are herbs, botanicals and other related substances adequate replacements for antimicrobial growth promoters? In: Antimicrobial Growth Promoters, Barug D., Jong J. de., Kies A.K., Verste M.W.A. (eds). Wageningen Academic Publishers, The Netherlands, pp. 329–340.
[34] Ceulemans S, Robles R, Coutteau P. 2009. Innovative Feed Additives Improve Feed Utilization In Nile Tilapia, Global Aquaculture Advocate. November/December 2009.
[35] Steiner T, Syed B. 2015. Phytogenic feed additives in animal nutrition. In Medicinal and Aromatic Plants of the World Scientific Production, Commercial and Utilization Aspects; Máthé, Á., Ed.; Springer: Dordrecht, Germany. pp 403-423.
[36] Maheshappa K. 1993. Effect of different doses of livol on growth and body composition of rohu, Labeo rohita (Ham.) M.F.Sc Thesis, University of Agricultural Science, Bangalore, p 59.
[37] Shadakshari GS. 1993. Effect of bioboost forte, Livol and Amchemin AQ on growth and body composition of common carp, *Cyprinus carpio* (Linn.). M.F.Sc. Thesis, University of Agriculture Sciences, Bangalore, p 155.
[38] Jayaprakas V, Euphrasia J. 1996. Growth performance of Labeo rohita (Ham.) to Livol (IHF-1000), a herbal product. Proc Indian Natl Sci Acad B 63: 1–10.

[39] Bello OS, Emikpe BO, Olaifa FE. 2012. The body weight changes and gut morphometry of Clarias gariepinus juveniles on feeds supplemented with walnut (*Tetracarpium conophorum*) leaf and onion (*Allium cepa*) bulb residues. Int J Morphology 30: 253-257.
[40] Giannenas I, Triantafillou E, Stavrakakis S, Margaroni M, Mavridis S, Steiner T, Karagouni E. 2012. Assessment of dietary supplementation with carvacrol or thymol containing feed additives on performance, intestinal microbiota and antioxidant status of rainbow trout (*Oncorhynchus mykiss*). Aquaculture 350–353: 26–32.
[41] Sutili FJ, Velasquez A, Pinheiro CG, Heinzmann BM, Baldisserotto B, Gatlin DM III. 2016. Evaluation of Ocimum americanum essential oil as an additive in red drum (*Sciaenops ocellatus*) diets. Fish Shellfish Immunol 56: 155–161.
[42] Ley RE, Lozupone CA, Hamady M, Knight R, Gordon JI. 2008. Worlds within worlds: evolution of the vertebrate gut microbiota. Nature Rev Microbiol 6: 776–788.
[43] Liu HB, Zhang Y, Yang YH, Lu TY, Ye JD. 2004. Effects of five Chinese herb medicines as additive in feed on the growth and intestinal microflora in common carp (*Cyprinus carpio*). J. Dalian Fisheries Univ 19: 16-20.
[44] Rimoldi S, Torrecillas S, Montero D, Gini E, Makol A, Valdenegro VV, et al. 2020. Assessment of dietary supplementation with galactomannan oligosaccharides and phytogenics on gut microbiota of European sea bass (*Dicentrarchus labrax*) fed low fishmeal and fish oil based diet. PLoS ONE 15: e0231494.
[45] Reverter M, Bontemps N, Lecchini D, Banaigs B, Sasal P. 2014. Use of plant extracts in fish aquaculture as an alternative to chemotherapy: current status and future perspectives. Aquaculture 433: 50–61.
[46] Hoseinifar S.H., Sun Y.-Z., Zhou Z., Van Doan H., Davies S.J., Harikrishnan R. (2020). Boosting immune function and disease bio-control through environment-friendly and sustainable approaches in finfish aquaculture: herbal therapy scenarios. Reviews in Fisheries Science and Aquaculture. https://doi.org/10.1080/23308249.2020.1731420.
[47] Thanikachalam K, Kasi M, Rathinam X. 2010. Effect of garlic peel on growth, hematological parameters and disease resistance against *Aeromonas hydrophila* in African catfish *Clarias gariepinus* (Bloch) fingerlings. Asian Pacific Journal of Tropical Medicine 3: 614-618.
[48] Nya EJ, Austin B. 2009. Use of dietary ginger, Zingiber officinale Roscoe, as an immunostimulant to control *Aeromonas hydrophila* infections in rainbow trout, *Oncorhynchus mykiss* (Walbaum). J Fish Dis 32: 971–977.
[49] Harikrishnan R, Balasundaramb C, Heo MS. 2010. Herbal supplementation diets on hematology and innate immunity in goldfish against *Aeromonas hydrophila*, Fish & Shellfish Immunology 28: 354-361.
[50] Torrecillas S, Terova G, Makol A, Serradell A, Valdenegro V, Gini E, et al. 2019. Dietary phytogenics and galactomannan oligosaccharides in low fish meal and fish oil-based diets for European sea bass (*Dicentrarchus labrax*) juveniles: Effects on gut health and implications on *in vivo* gut bacterial translocation. PlosOne 14: e0222063.
[51] Serradell A, Torrecillas S, Makol A, Valdenegro V, Fernández-Montero A, Acosta F, Izquierdo MS, Montero D. 2020. Prebiotics and phytogenics functional additives in low fish meal and fish oil based diets for European sea bass (*Dicentrarchus labrax*): effects on stress and immune responses. Fish & Shellfish Immunology 100: 219-229.
[52] Talpur AD, Ikhwanuddin M. 2012. Dietary effects of garlic (*Allium sativum*) on haemato-immunological parameters, survival, growth, and disease resistance against *Vibrio harveyi* infection in Asian sea bass, *Lates calcarifer* (Bloch). Aquaculture 364–365: 6–12.
[53] Talpur AD, Ikhwanuddin M, Ambok Bolong A-M. 2013. Nutritional effects of ginger (*Zingiber officinale* Roscoe) on immune response of Asian sea bass, *Lates calcarifer* (Bloch) and disease resistance against *Vibrio harveyi*. Aquaculture 400–401: 46–52.
[54] Talpur AD. 2014. *Mentha piperita* (Peppermint) as feed additive enhanced growth performance, survival, immune response and disease resistance of Asian seabass, *Lates calcarifer* (Bloch) against *Vibrio harveyi* infection. Aquaculture 420:71–78.

[55] Micol V, Caturla N, Perez-Fons L, Mas V, Perez L, Estepa A. 2005. The olive leaf extract exhibits antiviral activity against viral haemorrhagic septicaemia rhabdovirus (VHSV). Antiviral Research 66(2/3): 129–136.
[56] Harikrishnan R, Heo J, Balasundaram C, Kim MC, Kim JS, Han YJ, Heo MS. 2010. Effect of *Punica granatum* solvent extracts on immune system and disease resistance in *Paralichthys olivaceus* against lymphocystis disease virus (LDV). Fish & Shellfish Immunology 29: 668–673.
[57] Caipang CMA, Lazado CC. 2015. Nutritional impacts on fish mucosa: immunostimulants, pre- and probiotics In: Mucosal health in aquaculture (Ed: Peatman BHB). Academic Press, San Diego, pp. 211–272.

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