JOURNAL OF AGRICULTURAL PRODUCTION
https://agriprojournal.com ISSN: 2757-6620

REVIEW ARTICLE

Use of Phytochemicals as Feed Supplements in Aquaculture: A Review on Their Effects on Growth, Immune Response, and Antioxidant Status of Finfish

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ARTICLE INFO

Article History:
Received: 25.05.2021
Accepted: 22.06.2021
Available Online: 29.06.2021

Keywords:
Aquaculture
Feed additive
Fish
Growth
Immunostimulation
Phytochemical

ABSTRACT

Aquaculture production is increasing day by day to meet the protein need of the global population. Various feed additives are used in aquaculture to enhance growth, stimulate immunity, prevent diseases, and strengthen the antioxidant status of fish. Phytochemicals attract attention among these feed additives. As phytochemicals are natural products, they are considered to be safe for fish, humans, and the environment. In this paper, we reviewed recent studies that utilize phytochemicals as feed additives in cultured fish species. In agreement with the available literature, we inferred that phytochemicals could be used in aquaculture. However, as some studies reported undesirable effects on growth, we believe that phytochemicals are more effective in immunostimulation and enhancing antioxidant status rather than growth-promoting. Possible reasons for growth retardation were emphasized. Although available evidence suggests that phytochemicals display beneficial effects, we discussed the possible use of phytochemical combinations to obtain even more desirable results. To conclude, we think that phytochemicals can exert synergistic effects, and this approach should be investigated in future studies.

Please cite this paper as follows:

Taştan, Y., & Salem, M. O. A. (2021). Use of phytochemicals as feed supplements in aquaculture: A review on their effects on growth, immune response, and antioxidant status of finfish. *Journal of Agricultural Production*, 2(1), 32-43. https://doi.org/10.29329/agripro.2021.344.5

Introduction

Aquaculture has become an important industry and the world's fastest-growing agricultural business sector and is an important commercial activity in many countries (Kumari & Sahoo, 2006; Villa-Cruz et al., 2009; Karga et al., 2020). Global aquaculture production has increased vastly in the last years for the protein requirement of humans (Özçelik et al., 2020; Salem et al., 2021). Aquaculture practices have become more intense to supply the demand because the wild fish stocks are getting scarce as days pass. With this intensification, problems and threats started increasing. These are high production costs, diseases, stress, environmental impact, animal welfare issues, and organic production demand (Sönmez, Bilen, Alak, et al., 2015; Sönmez, 2017; Arslan et al., 2018; Elbesthi et al., 2020). For example, fish are exposed to several infectious diseases, reducing the fish yield (Erguig et al., 2015; Syahidah et al., 2015). The use of antibiotics and chemotherapeutic agents for controlling diseases can reduce mortality and improve growth rates; however, they are often considered an expensive and unhealthy way to treat any disease (Ferguson et al., 2010). Moreover, the antibiotic and chemotherapeutic residues can remain in fish tissues, which may threaten the health of human consumers and cause pollution in the aquatic environment (Bulfon et al., 2017; Erguig et al., 2015; Syahidah et al., 2015). Another problem that arises in aquaculture is high production costs, mostly due to the feed expense. Feed is a limiting factor, particularly in carnivorous fish culture, because so far, the fish meal in the feed has not been successfully replaced with another substance. And since the fish meal also comes from the wild fish populations, the

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scarcity of the fish stocks also affects feed availability and therefore has a great impact on the sustainability of aquaculture. Studies in the last few decades have intensely focused on natural products to overcome these problems (Cavalcante et al., 2020; de Oliviera et al., 2020; Ganeva et al., 2020; Adeshina et al., 2021; Sangari et al., 2021). Among these natural products, phytochemicals attract attention due to their great health benefits. Phytochemicals are, in simple terms, bioactive compounds of plant origin (Lillehoj et al., 2018), which exhibit a wide array of beneficial effects such as antiviral, anticancer, growth-promoting, antibiotic, antioxidant, immune-stimulating, and anti-inflammatory effects (Lillehoj et al., 2018; Mani et al., 2020; Zheng et al., 2019; Choudhari et al., 2020, Terzi et al., 2021). In this paper, we reviewed recent studies that utilize phytochemicals in fish culture.

Health Benefits of Phytochemicals

Phytochemicals are non-nutritive compounds, and they often have a pharmacological effect (Leitzmann, 2016). Based on its definition, although phytochemicals may include various groups, Chakraborty et al. (2014) classified them as essential oils, steroids, terpenoids, phenolics, pigments, flavonoids, and alkaloids according to their chemical structures. For humans, Oomah (1999) reviewed certain phytochemicals' preventive or therapeutic health effects on cardiovascular diseases, diabetic neuropathy, gastrointestinal disorders, gynecological disorders, neurological disorders, inflammation, immunological disorders, vision, cancer, urinary tract infection. Previous studies on fish have also reported beneficial effects of phytochemicals, including but not limited to antimicrobial properties, immunostimulation, appetite stimulation, growth promotion, and antistress (Citarasu, 2010; Chakraborty & Hancz, 2011). Phytochemicals have great potential to be used in animal diets as the main active substance and/or source for the new drugs (Sutili et al., 2017).

Phytochemicals as Growth Promoters

The cost of aquaculture has led business owners to desire to harvest the maximum yield per unit area, while the scarcity of natural resources has driven scientists to do the same. Both situations add up to the same objective: faster growth of the fish with fewer costs. Hence, growth promotion is among the most important purposes of recent studies (Sönmez, Bilen, Albayrak, et al., 2015). Phytochemicals are successfully demonstrated to promote growth in various fish species. However, some studies obtained adverse effects on growth, probably due to the presence of anti-nutritional factors (Glencross et al., 2006; Chakraborty et al., 2014). Nonetheless, these anti-nutritional factors may be partially eliminated through processing techniques (Chakraborty et al., 2014). Recent studies investigating the effects of dietary phytochemical supplementation on growth in fish culture are presented in Table 1.

Table 1. Effects of dietary phytochemical supplementation on growth in fish

Phytochemical	Fish species	Dose* and duration	Notable results**	References
Quercetin	Blunt snout bream (*Megalobrama amblycephala*)	0.4 and 0.8%, 56 days	↑ FW ↑ WG	Jia, Yan, et al. (2019)
	Grass carp (*Ctenopharyngodon idella*)	0.4 g kg^{-1}, 60 days	↑ FW ↑ WG ↓ FCR	Xu et al. (2019)
	Nile tilapia (*Oreochromis niloticus*)	0.2, 0.4, 0.8, and 1.6 g kg^{-1}, 49 days	↑ FW ↑ WG ↓ FCR ↑ CF	Zhai and Liu (2013)
Genistein	Nile tilapia (*O. niloticus*)	3 g kg^{-1}, 56 days	↓ FW ↓ SGR	Chen et al. (2015)
Ferulic acid	GIFT (*O. niloticus*)	0.52 nmol kg^{-1}, 56 days	↑ FW ↑ WG ↓ FCR	Yu et al. (2017)
Organic acid blend (Formic acid, lactic acid, malic acid, tartaric acid, and citric acid)	Red hybrid tilapia (*Oreochromis sp.*)	0.5 and 1%, 140 days	↔ Growth	Koh et al. (2016)
Sesamin	Atlantic salmon (*Salmo salar*)	5.8 g kg^{-1}, 120 days	↓ FW ↓ SGR	Schiller Vestergren et al. (2012)
Resveratrol	Blunt snout bream (*M. amblycephala*)	1%, 56 days	↓ FW ↓ WGR	Jia, Yan, et al. (2019)
Curcumin	Common carp (*Cyprinus carpio*)	5, 10, and 15 g kg^{-1}, 56 days	↑ FW ↑ WG ↓ FCR	Giri et al. (2019)
	Grass carp (*C. idella*)	393.67 mg kg^{-1}, 60 days	↑ FW ↑ WG ↑ SGR ↓ FCR	Ming et al. (2020)
	Nile tilapia (*O. niloticus*)	5 mg kg^{-1}, 112 days	↔ Growth	Mahfouz (2015)

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Table 1 continued

Phytochemical	**Fish species**	**Dose* and duration**	**Notable results****	**References**
Curcumin	Nile tilapia (*O. niloticus*)	50, 100, 150, and 200 mg kg^{-1}, 84 days	↑ FW ↑ WG ↑ SGR ↓ FCR	Mahmoud et al. (2017)
	Rainbow trout (*Oncorhynchus mykiss*)	1, 2, and 4%, 56 days	↑ FW ↑ WG ↑ SGR ↓ FCR	Yonar et al. (2019)
Carvacrol	Rainbow trout (*O. mykiss*)	1, 3, and 5 g kg^{-1}, 60 days	↔ Growth	Yilmaz et al. (2015)
Alkaloids (Koumine, gelsemine, gelsenicine)	Blunt snout bream (*M. amblycephala*)	40 mg kg^{-1}, 84 days	↑ FW ↑ WG ↑ SGR ↓ FCR	Ye et al. (2019)
Sparteine	Rainbow trout (*O. mykiss*)	0.25, 0.5, 1, 2.5, and 5 g kg^{-1}, 62 days	↓ Growth	Serrano et al. (2011)
Tannic acid	European seabass (*Dicentrarchus labrax*)	10, 20, and 30 g kg^{-1}, 35 days	↓ Growth	Omnes et al. (2017)
Tannins	Beluga sturgeon (*Huso huso*)	0.05 and 0.1%, 42 days	↑ FW ↑ WG ↑ SGR ↓ FCR	Safari et al. (2020)
Condensed tannins	Japanese seabass (*Lateolabrax japonicus*)	100, 200, and 400 mg kg^{-1}, 56 days	↔ Growth	Peng et al. (2020)
Saponins	Common carp (*C. carpio*)	150 mg kg^{-1}, 56 days	↑ WG	Francis et al. (2002)
	Olive flounder (*Paralichthys olivaceus*)	6.4 g kg^{-1}, 56 days	↓ Growth	Chen et al. (2011)

***** Doses given in the table are those supplemented to the fish groups where the notable results were observed. Not every dose was given since otherwise, the presentation of the varying results would be complicated.
****** Results of some studies, in which some of the doses displayed different results, were given based on the general conclusions of that particular study. The reader is referred to the relevant article in the references list for exact results.
Symbols: ↑ indicates increase, ↓ indicates decrease, ↔ indicates no change.
Abbreviations: CF Condition factor, **FCR** Feed conversion ratio, **FW** Final weight, **GIFT** Genetically improved farmed tilapia, **SGR** Specific growth rate, **WG** Weight gain.

Phytochemicals as Immunostimulators

The immune system consists of various humoral and cellular components that protect the body from extraneous substances (Biller-Takahashi & Urbinati, 2014). Immunostimulation is a phenomenon in which the immune response of an organism is stimulated beforehand so that when an extraneous substance enters the body, it must face a more strengthen immune system. Studies have demonstrated that a wide variety of products other than phytochemicals successfully stimulate the immune response in finfish (Mohamed et al., 2018; Bilen et al., 2020; Makled et al., 2020). Phytochemicals are usually considered safe for fish, humans, and the environment (Chakraborty & Hancz, 2011). Therefore, immunostimulation with phytochemicals is particularly important due to its possibility to replace or minimize the use of antibiotics or chemicals that display undesirable effects. Table 2 shows the studies conducted on the immunity of cultured finfish with dietary administration of phytochemicals.

Table 2. Effects of dietary phytochemical supplementation on serum biochemistry and immunity in fish

Phytochemical	**Fish species**	**Dose* and duration**	**Notable results****	**References**
Quercetin	Blunt snout bream (*Megalobrama amblycephala*)	0.4 and 0.8% alone or combined with 0.5 or 1% resveratrol, 56 days	• Reversing high-fat diet-induced depression of immunity	Jia, Yan, et al. (2019)
	Olive flounder (*Paralichthys olivaceus*)	0.5% combined with 6.8% spirulina, 70 days	↑ LYS	Kim et al. (2013)
	Olive flounder (*P. olivaceus*)	0.25 and 0.5%, 60 days	↑ LYS • Improved immunity against external stress	Shin et al. (2010a)
	Rainbow trout (*Oncorhynchus mykiss*)	1%, 14 days	↑ LYS ↑ MPO ↑ Total protein ↑ Antiprotease activity ↑ Bactericidal activity	Awad et al. (2013)

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Table 2 continued

Phytochemical	Fish species	Dose* and duration	Notable results**	References
Daidzein	Turbot (*Scophthalmus maximus*)	40 and 400 mg kg^{-1}, 84 days	• Mitigating intestinal inflammation • Improving the tight junction barrier	Ou et al. (2019)
Caffeic acid	Nile tilapia (*Oreochromis niloticus*)	5 g kg^{-1}, 60 days	↑ Phagocytic index ↑ Potential killing activity ↑ Respiratory burst activity ↑ MPO ↑ IRGE • Resistance against *Aeromonas veronii*	Yilmaz (2019)
Ferulic acid	Nile tilapia (*O. niloticus*)	80 mg kg^{-1}, 60 days	↑ Phagocytic activity ↑ LYS ↑ IRGE	Dawood et al. (2020)
	Common carp (*Cyprinus carpio*)	100 mg kg^{-1}, 56 days	↑ Total IgM ↑ Respiratory burst activity ↑ LYS • Resistance against *Aeromonas hydrophila*	Ahmadifar et al. (2019)
Trans-cinnamic acid	Rainbow trout (*O. mykiss*)	250 and 500 mg kg^{-1}, 60 days	↑ Blood granulocyte percentage ↑ Total protein ↑ Globulin ↑ LYS ↑ Total Ig ↑ Phagocytic activity ↑ Respiratory burst activity ↑ Potential killing activity ↑ IRGE • Resistance against *Yersinia ruckeri*	Yılmaz and Ergün (2018)
Resveratrol	GIFT (*O. niloticus*)	0.5 g kg^{-1}, 45 days	• Enhanced immunity	Zheng et al. (2019)
	Turbot (*S. maximus*)	0.05%, 56 days	• Mitigating inflammatory response caused by soybean meal	Tan et al. (2019)
Curcumin	Common carp (*C. carpio*)	10, and 15 g kg^{-1}, 56 days	↑ LYS ↑ Total Ig ↑ Total protein ↑ ALP ↑ Protease activity ↑ Peroxidase activity • Resistance against *Aeromonas hydrophila* • Anti-inflammatory effect	Giri et al. (2019)
	Grass carp (*Ctenopharyngodon idella*)	393.67 mg kg^{-1}, 60 days	↑ LYS ↑ Acid phosphatase ↑ C3 and C4 ↓ ALT ↓ AST ↑ LYS, C3, and antimicrobial peptide gene expression levels • Anti-inflammatory effect	Ming et al. (2020)
	Nile tilapia (*O. niloticus*)	200 mg kg^{-1}, 60 days	↑ Total protein ↑ Globulin ↑ α globulin-1 ↑ α globulin-2 • Resistance against *Aeromonas hydrophila*	Abd El-Hakim et al. (2020)
	Nile tilapia (*O. niloticus*)	50, 100, 150, and 200 mg kg^{-1}, 84 days	↑ LYS ↑ IgG ↑ IgM • Antibacterial effect • Resistance against *Aeromonas hydrophila*	Mahmoud et al. (2017)

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Table 2 continued

Phytochemical	Fish species	Dose* and duration	Notable results**	References
Curcumin	Rainbow trout (*O. mykiss*)	1, 2, and 4%, 56 days	↑ WBC ↑ Oxidative Radical Production ↑ Phagocytic activity ↑ Phagocytic index ↑ Total protein ↑ IgM ↑ Bactericidal activity ↑ LYS ↑ MPO • Resistance against *Aeromonas salmonicida* subsp. *achromogenes*	Yonar et al. (2019)
Alkaloids (Koumine, gelsemine, gelsenicine)	Blunt snout bream (*M. amblycephala*)	20 and 40 mg kg^{-1}, 84 days	↑ C3 and C4 ↑ IgM • Resistance against *Aeromonas hydrophila* ↑ IRGE ↓ TGF-β and IL10 expression levels	Ye et al. (2019)
Tannins	Beluga sturgeon (*Huso huso*)	0.05 and 0.1%, 42 days	↑ LYS ↑ Peroxidase activity ↔ ALT ↔ AST ↔ ALP	Safari et al. (2020)
Condensed tannins	Japanese seabass (*Lateolabrax japonicus*)	100, 200, and 400 mg kg^{-1}, 56 days	↔ ALP ↔ LYS ↔ IgM ↓ TNF-α ↓ IL-6 ↔ IL-8 ↔ Serum biochemistry • Protection against hypoxia	Peng et al. (2020)

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****** Results of some studies, in which some of the doses displayed different results, were given based on the general conclusions of that particular study. The reader is referred to the relevant article in the references list for exact results.
Symbols: ↑ indicates increase, ↓ indicates decrease, ↔ indicates no change.
Abbreviations: ALP Alkaline phosphatase, **ALT** Alanine aminotransferase, **AST** Aspartate aminotransferase, **C3** Complement 3, **C4** Complement 4, **GIFT** Genetically improved farmed tilapia, **Ig** Immunoglobulin, **IgG** Immunoglobulin G, **IgM** Immunoglobulin M, **IRGE** Immune-related gene expression, **LYS** Lysozyme, **MPO** Myeloperoxidase, **WBC** White blood cell.

Phytochemicals as Antistress Agents

The survival of an animal depends on its internal balance and its compatibility with the environment (Cengiz, 2001). When an animal's internal balance is stable and compatible with its environment, the very animal lives under normal conditions. Stress, on the other hand, is the response of an animal to an abnormal condition (Cengiz, 2001). Stress response in fish generates a variety of physiological changes in mechanisms such as metabolism, immunity, behavior, gene expression, protein synthesis, endocrine, et cetera (Tort, 2011). In aquaculture, stress can cause susceptibility to diseases, growth retardation, and interference of reproduction (Pickering, 1993). Furthermore, fish may get stressed easily in farm conditions due to handling, transportation, high stocking density, and poor water quality (Bilen et al., 2013; Almabrok et al., 2018). Phytochemicals are good feed additives for fish in farm conditions to cope with stress because some phytochemicals may exert a direct antioxidant effect beyond supporting the antioxidant system of the fish (Yu et al., 2017; Ahmadifar et al., 2019; Bhattacharjee et al., 2020). Recent studies investigating the antioxidant potential of dietary photochemical supplementation in finfish are presented in Table 3.

Table 3. Effects of dietary phytochemical supplementation on antioxidant status in fish

Phytochemical	Fish species	Dose* and duration	Stressor	Notable results**	References
Quercetin	Blunt snout bream (*Megalobrama amblycephala*)	0.4 and 0.8% alone or combined with 0.5 or 1% resveratrol, 56 days	High-fat diet	↑ SIRT1 ↑ Cu/Zn-SOD ↑ CAT ↑ GPx	Jia, Yan, et al. (2019)
	Channa punctata	0.14 g L^{-1}, 21 days	Deltamethrin	• Amelioration of oxidative stress and acetylcholinesterase inhibition • Recovery from nucleic acid impairment and alteration of blood parameters	Bhattacharjee et al. (2020) [A]
	Grass carp (*Ctenopharyngodon idella*)	0.4 and 0.6 g kg^{-1}, 60 days	-	↑ SOD	Xu et al. (2019)
	Olive flounder (*Paralichthys olivaceus*)	0.25 and 0.5%, 60 days	Hypo-osmotic conditions	↓ SOD ↓ CAT ↓ H_2O_2 ↓ Cortisol • Protection against stress	Shin et al. (2010a)
	Olive flounder (*P. olivaceus*)	0.25 and 0.5%, 60 days	Cadmium	↓ SOD ↓ CAT ↓ H_2O_2 ↓ MDA • Protection against Cd exposure	Shin et al. (2010b)
	Silver catfish (*Rhamdia quelen*)	1.5 g kg^{-1}, 21 days	OTC	↓ LPO ↑ SOD ↑ GST ↔ GPx ↔ GR	Pês et al. (2018)
Rutin	Silver catfish (*R. quelen*)	0.15 and 0.30%, 21 days	-	↓ Cortisol ↓ LPO • Increased antioxidant status in various tissues	Pês et al. (2016)
	Rainbow trout (*Oncorhynchus mykiss*)	500, 1000, and 2000 ppm, 28 days	OTC	• Preventing OTC induced hepatic damage and oxidative stress	Nazeri et al. (2017)
Daidzein	Turbot (*Scophthalmus maximus*)	5, 10, and 20 mg kg^{-1}, 84 days	-	↑ SOD ↑ GPx ↓ MDA	Hu et al. (2014)
Ferulic acid	GIFT (*Oreochromis niloticus*)	1.04 and 2.08 nmol kg^{-1}, 56 days	-	↑ SOD ↑ CAT ↑ GPx ↓ MDA	Yu et al. (2017)
	Nile tilapia (*O. niloticus*)	80 mg kg^{-1}, 60 days	Heat stress	↑ SOD ↑ CAT ↑ GPx ↓ MDA • Mitigating the effects of heat stress	Dawood et al. (2020)
	Common carp (*Cyprinus carpio*)	100 mg kg^{-1}, 56 days	-	↔ SOD ↑ CAT ↑ GPx	Ahmadifar et al. (2019)
Sesamin	Common carp (*C. carpio*)	0.5 and 1 g kg^{-1}, 90 days	Fluoride	• Alleviating renal damage and apoptosis ↓ ROS • Reduction of oxidative stress	Cao et al. (2015)
Resveratrol	Nile tilapia (*O. niloticus*)	0.1, 0.3, and 0.6 g kg^{-1}, 60 days	Oxidative stress-induced liver damage by H_2O_2 injection	• Amelioration of liver injury ↑ Antioxidant activity ↓ LPO	Jia, Li, et al. (2019)
Curcumin	*Anabas testudineus*	0.5 and 1%, 2 and 56 days	-	• 14 days ↓ MDA ↓ GSH • 56 days ↔ MDA ↑ GSH	Manju et al. (2012)
	Common carp (*C. carpio*)	10, and 15 g kg^{-1}, 56 days	-	↑ SOD ↑ CAT ↓ MDA	Giri et al. (2019)

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Table 3 continued

Phytochemical	Fish species	Dose* and duration	Stressor	Notable results**	References
Curcumin	Grass carp (*C. idella*)	393.67 mg kg^{-1}, 60 days	-	↑ GSH ↑ SOD ↑ CAT ↑ GPx ↑ GST ↑ GR ↓ ROS ↓ MDA	Ming et al. (2020)
	Nile tilapia (*O. niloticus*)	200 mg kg^{-1}, 60 days	Melamine	↑ GPx ↑ SOD ↓ MDA • Mitigating adverse effects of melamine	Abd El-Hakim et al. (2020)
	Nile tilapia (*O. niloticus*)	5 mg kg^{-1}, 112 days	Aflatoxin B1	• Amelioration of aflatoxin-induced down-regulation of antioxidant gene expression levels	Mahfouz (2015)
	Rainbow trout (*O. mykiss*)	1, 2, and 4%, 56 days	-	↑ SOD ↑ CAT ↑ GPx ↓ MDA	Yonar et al. (2019)
Tannins	Beluga sturgeon (*Huso huso*)	0.05 and 0.1%, 42 days	-	↑ SOD ↑ CAT	Safari et al. (2020)
Condensed tannins	Japanese seabass (*Lateolabrax japonicus*)	100, 200, and 400 mg kg^{-1}, 56 days	Hypoxic stress	↑ Total antioxidant capacity ↑ CAT ↑ GPx ↔ GST ↔ SOD ↓ MDA	Peng et al. (2020)

***** Doses given in the table are those supplemented to the fish groups where the notable results were observed. Not every dose was given since otherwise, the presentation of the varying results would be complicated.
****** Results of some studies, in which some of the doses displayed different results, were given based on the general conclusions of that particular study. The reader is referred to the relevant article in the references list for exact results.
[A] This study, unlike others, administered the phytochemical via bathing.
Symbols: ↑ indicates increase, ↓ indicates decrease, ↔ indicates no change.
Abbreviations: CAT Catalase, **Cu/Zn-SOD** Copper zinc superoxide dismutase, **GIFT** Genetically improved farmed tilapia, **GPx** Glutathione peroxidase, **GR** Glutathione reductase, **GSH** Glutathione, **GST** Glutathione s-transferase, **H_2O_2** Hydrogen peroxide, **LPO** Lipid peroxidation, **MDA** Malondialdehyde, **OTC** Oxytetracycline, **ROS** Reactive oxygen species, **SIRT1** Sirtuin-1, **SOD** Superoxide dismutase.

Overview on the Use of Phytochemicals in Aquaculture

In the present paper, we observed that phytochemicals have great potential to be used in aquaculture as feed additives. According to studies reviewed (Tables 1-3), we can infer that phytochemicals are more effective in immunostimulation and improvement of antioxidant status in fish than enhancing growth because some studies reported growth retardation after phytochemical supplementation. The reason behind this inference is that some phytochemicals may exhibit inhibitory effects on digestive enzyme activities (Chen et al., 2015) or adversely affect feed palatability (Serrano et al., 2011; Omnes et al., 2017). The phenomenon regarding palatability is particularly important for carnivorous fish as normally their diets do not contain herbal compounds; thus, certain phytochemicals may reduce ingestion (Lall & Tibbetts, 2009). Moreover, growth retardation may also be attributed to the dosage of the phytochemical supplement. As can be seen in Table 1, studies reporting decreased growth performance usually administered relatively high levels of phytochemicals. Furthermore, one should not neglect that the palatability is also under the influence of several other factors such as the chemical nature of the substances in the feed, water pH, water temperature, genetic factors, the threshold of the substance for a particular species, et cetera (Kasumyan & Døving, 2003). To avoid such undesirable outcomes, further studies should consider the possibilities mentioned above while selecting the phytochemical and the dose of administration.

In terms of immunostimulation and antioxidant status, none of the reviewed studies (Tables 2 and 3) reported adverse effects. It is clear from the presented tables that phytochemicals are potent antioxidant and immunostimulatory substances that can be used in aquaculture. However, we have observed that only a small fraction of the studies utilized more than one phytochemical, but we think that combinations of phytochemicals may exhibit synergistic effects that can possibly result in more beneficial results. For example, Eberhardt et al. (2000) reported that Vitamin C is responsible only for 0.4% of the total antioxidant activity of apples. Based on this, Liu (2003) proposed that the antioxidant potency of fruit and vegetables comes from the synergistic effects of phytochemicals rather than one particular compound. As recently reviewed by Zhang et al. (2019), synergistic effects of combined phytochemicals were studied in other animals or human cell lines. However, there is a lack of studies on fish.

Conclusion

To conclude, the use of phytochemicals as feed additives is currently a popular field in aquaculture, and it has been heavily investigated in recent years. There is an adequate quantity of evidence to conclude that dietary supplementation of phytochemicals improves growth, stimulates the immune response, and improves antioxidant status in finfish. However, we think that further studies should investigate the possible synergistic effects of combined phytochemicals. Moreover, more comprehensive research is needed to evaluate the industrial application of phytochemicals at a larger scale.

Conflict of Interest

The authors declare that they have no conflict of interest.

References

Abd El-Hakim, Y. M., El-Houseiny, W., Abd Elhakeem, E. M., Ebraheim, L. L., Moustafa, A. A., & Mohamed, A. A. R. (2020). Melamine and curcumin enriched diets modulate the haemato-immune response, growth performance, oxidative stress, disease resistance, and cytokine production in *Oreochromis niloticus*. *Aquatic Toxicology*, *220*, 105406. https://doi.org/10.1016/j.aquatox.2020.105406

Adeshina, I., Abdel-Tawwab, M., Tijjani, Z. A, Tiamiyu, L. O., & Jahanbakhshi, A. (2021). Dietary *Tridax procumbens* leaves extract stimulated growth, antioxidants, immunity, and resistance of Nile tilapia, *Oreochromis niloticus*, to monogenean parasitic infection. *Aquaculture*, *532*, 736047. https://doi.org/10.1016/j.aquaculture.2020.736047

Ahmadifar, E., Dawood M. A. O., Moghadam, M. S., Sheikhzadeh, N., Hoseinifar, S. H., & Musthafa, M. S. (2019). Modulation of immune parameters and antioxidant defense in zebrafish (*Danio rerio*) using dietary apple cider vinegar. *Aquaculture*, *513*, 734412. https://doi.org/10.1016/j.aquaculture.2019.734412

Almabrok, A. A., Amhamed, I. D., Mohamed, G. A., Bilen, S., & Altief, T. A. S. (2018). Effect *of Tilia tomentosa* methanolic extract on growth performance, digestive enzyme activity, immune system and haematological indices of common carp (*Cyprinus carpio*). *Marine Science and Technology Bulletin*, *7*(1), 12-20. https://doi.org/10.33714/masteb.421047

Arslan, G., Sönmez, A. Y., & Yanık, T. (2018). Effects of grape *Vitis vinifera* seed oil supplementation on growth, survival, fatty acid profiles, antioxidant contents and blood parameters in rainbow trout *Oncorhynchus mykiss*. *Aquaculture Research*, *49*(6), 2256–2266. https://doi.org/10.1111/are.13686

Awad, E., Austin, D., & Lyndon, A. R. (2013). Effect of black cumin seed oil (*Nigella sativa*) and nettle extract (Quercetin) on enhancement of immunity in rainbow trout, *Oncorhynchus mykiss* (Walbaum). *Aquaculture*, *388–391*, 193–197. https://doi.org/10.1016/j.aquaculture.2013.01.008

Bhattacharjee, P., Borah, A., & Das, S. (2020). Quercetin-induced amelioration of deltamethrin stress in freshwater teleost, *Channa punctata*: Multiple biomarker analysis. *Comparative Biochemistry and Physiology Part C: Toxicology & Pharmacology*, *227*, 108626. https://doi.org/10.1016/j.cbpc.2019.108626

Bilen, S., Kızak, V., & Gezen, A. M. (2013). Floating fish farm unit (3FU). Is it an appropriate method for salmonid production?. *Marine Science and Technology Bulletin*, *2*(1), 9-13.

Bilen, S., Karga, M., Çelik Altunoğlu, Y., Ulu, F., & Biswas, G. (2020). Immune responses and growth performance of the aqueous methanolic extract of *Malva sylvestris* in *Oncorhynchus mykiss*. *Marine Science and Technology Bulletin*, *9*(2), 159-167. https://doi.org/10.33714/masteb.746951

Biller-Takahashi, J. D., & Urbinati, E. C. (2014). Fish immunology. The modification and manipulation of the innate immune system: Brazilian studies. *Anais da Academia Brasileira de Ciências*, *86*(3), 1484-1506. https://doi.org/10.1590/0001-3765201420130159

Bulfon, C., Bongiorno, T., Messina, M., Volpatti, D., Tibaldi, E., & Tulli, F. (2017). Effects of *Panax ginseng* extract in practical diets for rainbow trout (*Oncorhynchus mykiss*) on growth performance, immune response and resistance to *Yersinia ruckeri*. *Aquaculture Research*, *48*(5), 2369-2379. https://doi.org/10.1111/are.13072

Cao, J., Chen, J., Xie, L., Wang, J., Feng, C., & Song, J. (2015). Protective properties of sesamin against fluoride-induced oxidative stress and apoptosis in kidney of carp (*Cyprinus carpio*) via JNK signaling pathway. *Aquatic Toxicology*, *167*, 180–190. https://doi.org/10.1016/j.aquatox.2015.08.004.

Cavalcante, R. B., Telli, G. S., Tachibana, L., de Carla Dias, D., Oshiro, E., Natori, M. M., da Silva, W. F., & Ranzani-Paiva, M. J. (2020). Probiotics, prebiotics and synbiotics for nile tilapia: Growth performance and protection against *Aeromonas hydrophila* infection. *Aquaculture Reports*, *17*, 100343. https://doi.org/10.1016/j.aqrep.2020.100343

Cengiz, F. (2001). Hayvanlarda zorlanım (stres) oluşturan etkenler. *Journal of Research in Veterinary Medicine*, *20*, 147-153.

Chakraborty, S. B., & Hancz, C. (2011). Application of phytochemicals as immunostimulant, antipathogenic and antistress agents in finfish culture. *Reviews in Aquaculture*, *3*(3), 103–119. https://doi.org/10.1111/j.1753-5131.2011.01048.x

Chakraborty, S. B., Horn, P., & Hancz, C. (2014). Application of phytochemicals as growth-promoters and endocrine modulators in fish culture. *Reviews in Aquaculture*, *6*(1), 1-19. https://doi.org/10.1111/raq.12021

Chen, W., Ai, Q., Mai, K., Xu, W., Liufu, Z., Zhang, W., & Cai, Y. (2011). Effects of dietary soybean saponins on feed intake, growth performance, digestibility and intestinal structure in juvenile japanese flounder (*Paralichthys olivaceus*). *Aquaculture*, *318*(1-2), 95-100. https://doi.org/10.1016/j.aquaculture.2011.04.050

Chen, D., Wang, W., & Ru, S. (2015). Effect of dietary genistein on growth performance, digestive enzyme activity, and body composition of nile tilapia *Oreochromis niloticus*. *Chinese Journal of Oceanology and Limnology*, *33*(1), 77-83. https://doi.org/10.1007/s00343-015-4037-6

Choudhari, A. S., Mandave, P. C., Deshpande, M., Ranjekar, P., & Prakash, O. (2020). Phytochemicals in cancer treatment: From preclinical studies to clinical practice. *Frontiers in Pharmacology*, *10*, 1614. https://doi.org/10.3389/fphar.2019.01614

Citarasu, T. (2010). Herbal biomedicines: A new opportunity for aquaculture industry. *Aquaculture International*, *18*, 403–414. https://doi.org/10.1007/s10499-009-9253-7

Dawood, M. A., Metwally, A. E. S., El-Sharawy, M. E., Ghozlan, A. M., Abdel-Latif, H. M., Van Doan, H., & Ali, M. A. (2020). The influences of ferulic acid on the growth performance, haemato-immunological responses, and immune-related genes of Nile tilapia (*Oreochromis niloticus*) exposed to heat stress. *Aquaculture*, *525*, 735320. https://doi.org/10.1016/j.aquaculture.2020.735320

de Oliveira, S. T. L., Soares, R. A. N., de Negreiros Sousa, S. M., Fernandes, A. W. C., Gouveia, G. V., & da Costa, M. M. (2020) Natural products as functional food ingredients for nile tilapia challenged with *Aeromonas hydrophila*. *Aquaculture International*, *28*, 913-926. https://doi.org/10.1007/s10499-019-00503-1

Eberhardt, M. V., Lee, C. Y., & Liu, R. H. (2000). Antioxidant activity of fresh apples. *Nature*, *405*, 903–904. https://doi.org/10.1038/35016151

Elbesthi, R. T. A., Yürüten Özdemir, K., Taştan, Y., Bilen, S., & Sönmez, A. Y. (2020). Effects of ribwort plantain (*Plantago lanceolata*) extract on blood parameters, immune response, antioxidant enzyme activities, and growth performance in rainbow trout (*Oncorhynchus mykiss*). *Fish Physiology and Biochemistry*, *46*, 1295-1307. https://doi.org/10.1007/s10695-020-00790-z

Erguig, M., Yahyaoui, A., Fekhaoui, M., & Dakki, M. (2015). The use of garlic in aquaculture. *European Journal of Biotechnology and Bioscience*, *8*(3), 28-33.

Ferguson, R. M. W., Merrifield, D. L., Harper, G. M., Rawling, M. D., Mustafa, S., Picchietti, S., Balcazar, J. L., & Davies, S. J. (2010). The effect of *Pediococcus acidilactici* on the gut microbiota and immune status of on-growing red tilapia (*Oreochromis niloticus*). *Journal of Applied Microbiology*, *109*(3), 851-862. https://doi.org/10.1111/j.1365-2672.2010.04713.x

Francis, G., Makkar, H. P., & Becker, K. (2002). Dietary supplementation with a *quillaja saponin* mixture improves growth performance and metabolic efficiency in common carp (*Cyprinus carpio* L.). *Aquaculture*, *203*(3-4), 311-320. https://doi.org/10.1016/S0044-8486(01)00628-7

Ganeva, V. O., Korytář, T., Pecková, H., McGurk, C., Mullins, J., Yanes-Roca, C., Gela, D., Lepič, P., Policar, T., & Holzer, A. S. (2020). Natural feed additives modulate immunity and mitigate infection with *Sphaerospora molnari* (Myxozoa: Cnidaria) in common carp: A pilot study. *Pathogens*, *9*(12), 1013. https://doi.org/10.3390/pathogens9121013

Giri, S. S., Sukumaran, V., & Park, S. C. (2019). Effects of bioactive substance from turmeric on growth, skin mucosal immunity and antioxidant factors in common carp, *Cyprinus carpio*. *Fish & Shellfish Immunology*, *92*, 612-620. https://doi.org/10.1016/j.fsi.2019.06.053

Glencross, B., Evans, D., Rutherford, N., Hawkins, W., McCafferty, P., Dods, K., Jones, B., Harris, D., Morton, L., & Sweetingham, M. (2006). The influence of the dietary inclusion of the alkaloid gramine, on rainbow trout (*Oncorhynchus mykiss*) growth, feed utilisation and gastrointestinal histology. *Aquaculture*, *253*(1-4), 512-522. https://doi.org/10.1016/j.aquaculture.2005.07.009

Hu, H., Liu, J., Li, Y., Zhang, Y., Mai, K., Ai, Q., Shao, M., & Yang, P. (2014). Effects of dietary daidzein on growth performance, activities of digestive enzymes, anti-oxidative ability and intestinal morphology in juvenile turbot (*Scophthalmus maximus* L.). *Journal of Fisheries of China*, *38*(9), 1503-1513.

Jia, E., Yan, Y., Zhou, M., Li, X., Jiang, G., Liu, W., & Zhang, D. (2019). Combined effects of dietary quercetin and resveratrol on growth performance, antioxidant capability and innate immunity of blunt snout bream (*Megalobrama amblycephala*). *Animal Feed Science and Technology*, *256*, 114268. https://doi.org/10.1016/j.anifeedsci.2019.114268

Jia, R., Li, Y., Cao, L., Du, J., Zheng, T., Qian, H., Gu, Z., Jeney, G., Xu, P., & Yin, G. (2019). Antioxidative, anti-inflammatory and hepatoprotective effects of resveratrol on oxidative stress-induced liver damage in tilapia (*Oreochromis niloticus*). *Comparative Biochemistry and Physiology Part C: Toxicology & Pharmacology*, *215*, 56-66. https://doi.org/10.1016/j.cbpc.2018.10.002

Karga, M., Kenanoğlu, O. N., & Bilen, S. (2020). Investigation of antibacterial activity of two different medicinal plants extracts against fish pathogens. *Journal of Agricultural Production*, *1*(1), 5-7. https://doi.org/10.29329/agripro.2020.341.2

Kasumyan, A. O., & Døving, K. B. (2003). Taste preferences in fishes. *Fish and Fisheries*, *4*(4), 289–347. https://doi.org/10.1046/j.1467-2979.2003.00121.x

Kim, S. S., Rahimnejad, S., Kim, K. W., Lee, B. J., & Lee, K. J. (2013). Effects of dietary supplementation of spirulina and quercetin on growth, innate immune responses, disease resistance against *Edwardsiella tarda*, and dietary antioxidant capacity in the juvenile olive flounder *Paralichthys olivaceus*. *Fisheries and Aquatic Sciences*, *16*(1), 7-14. https://doi.org/10.5657/FAS.2013.0007

Koh, C. B., Romano, N., Zahrah, A. S., & Ng, W. K. (2016). Effects of a dietary organic acids blend and oxytetracycline on the growth, nutrient utilization and total cultivable gut microbiota of the red hybrid tilapia, *Oreochromis sp.*, and resistance to *Streptococcus agalactiae*. *Aquaculture Research*, 47(2), 357-369. https://doi.org/10.1111/are.12492

Kumari, J., & Sahoo, K. P. (2006). Dietary levamisole modulates the immune response and disease resistance of asian catfish *Clarias batrachus* (Linnaeus).

Aquaculture Research, *37*, 500-509. https://doi.org/10.1111/j.1365-2109.2006.01456.x

Lall, S. P., & Tibbetts, S. M. (2009). Nutrition, feeding, and behavior of fish. *Veterinary Clinics of North America: Exotic Animal Practice*, *12*(2), 361–372. https://doi.org/10.1016/j.cvex.2009.01.005

Leitzmann, C. (2016). characteristics and health benefits of phytochemicals. *Complementary Medicine Research*, *23*(2), 69–74. https://doi.org/10.1159/000444063

Lillehoj, H., Liu, Y., Calsamiglia, S., Fernandez-Miyakawa, M. E., Chi, F., Cravens, R. L., Oh, S., & Gay, C. G. (2018). Phytochemicals as antibiotic alternatives to promote growth and enhance host health. *Veterinary Research*, *49*(1), 1-18. https://doi.org/10.1186/s13567-018-0562-6

Liu, R. H. (2003). Health benefits of fruit and vegetables are from additive and synergistic combinations of phytochemicals. *The American Journal of Clinical Nutrition*, *78*(3), 517–520. https://doi.org/10.1093/ajcn/78.3.517s

Mahfouz, M. E. (2015). Ameliorative effect of curcumin on aflatoxin B1-induced changes in liver gene expression of *Oreochromis niloticus*. *Molecular Biology*, *49*(2), 275-286. https://doi.org/10.1134/S0026893315020089

Mahmoud, H. K., Al-Sagheer, A. A., Reda, F. M., Mahgoub, S. A., & Ayyat, M. S. (2017). Dietary curcumin supplement influence on growth, immunity, antioxidant status, and resistance to *Aeromonas hydrophila* in *Oreochromis niloticus*. *Aquaculture*, *475*, 16-23. https://doi.org/10.1016/j.aquaculture.2017.03.043

Makled, S. O., Hamdan, A. M., & El-Sayed, A. F. M. (2020). Growth promotion and immune stimulation in nile tilapia, *Oreochromis niloticus*, fingerlings following dietary administration of a novel marine probiotic, *Psychrobacter maritimus* S. *Probiotics and Antimicrobial Proteins*, *12*(2), 365-374. https://doi.org/10.1007/s12602-019-09575-0

Mani, J. S., Johnson, J. B., Steel, J. C., Broszczak, D. A., Neilsen, P. M., Walsh, K. B., & Naiker, M. (2020). Natural product-derived phytochemicals as potential agents against coronaviruses: A review. *Virus Research*, *284*, 197989. https://doi.org/10.1016/j.virusres.2020.197989

Manju, M., Akbarsha, M. A., & Oommen, O. V. (2012). In vivo protective effect of dietary curcumin in fish *Anabas testudineus* (Bloch). *Fish Physiology and Biochemistry*, *38*(2), 309-318. https://doi.org/10.1007/s10695-011-9508-x

Ming, J., Ye, J., Zhang, Y., Xu, Q., Yang, X., Shao, X., Qiang, Y., & Xu, P. (2020). Optimal dietary curcumin improved growth performance, and modulated innate immunity, antioxidant capacity and related genes expression of NF-κB and Nrf2 signaling pathways in grass carp (*Ctenopharyngodon idella*) after infection with *Aeromonas hydrophila*. *Fish & Shellfish Immunology*, *97*, 540-553. https://doi.org/10.1016/j.fsi.2019.12.074

Mohamed, G. A., Amhamed, I. D., Almabrok, A. A., Barka, A. B. A., Bilen, S., & Elbeshti, R. T. (2018). Effect of celery (*Apium graveolens*) extract on the growth, haematology, immune response and digestive enzyme activity of common carp (*Cyprinus carpio*). *Marine Science and Technology Bulletin*, 7(2), 51-59. https://doi.org/10.33714/masteb.457721

Nazeri, S., Farhangi, M., & Modarres, S. (2017). The effect of different dietary inclusion levels of rutin (a flavonoid) on some liver enzyme activities and oxidative stress indices in rainbow trout, *Oncorhynchus mykiss* (Walbaum) exposed to oxytetracycline. *Aquaculture Research*, *48*(8), 4356-4362. https://doi.org/10.1111/are.13257

Omnes, M. H., Le Goasduff, J., Le Delliou, H., Le Bayon, N., Quazuguel, P., & Robin, J. H. (2017). Effects of dietary tannin on growth, feed utilization and digestibility, and carcass composition in juvenile european seabass (*Dicentrarchus labrax* L.). *Aquaculture Reports*, *6*, 21-27. https://doi.org/10.1016/j.aqrep.2017.01.004

Oomah, B. (1999). Health benefits of phytochemicals from selected canadian crops. *Trends in Food Science & Technology*, *10*(6-7), 193–198. https://doi.org/10.1016/s0924-2244(99)00055-2

Ou, W., Hu, H., Yang, P., Dai, J., Ai, Q., Zhang, W., Zhang, Y., & Mai, K. (2019). Dietary daidzein improved intestinal health of juvenile turbot in terms of intestinal mucosal barrier function and intestinal microbiota. *Fish & Shellfish Immunology*, *94*, 132-141. https://doi.org/10.1016/j.fsi.2019.08.059

Özçelik, H., Taştan, Y., Terzi, E., & Sönmez, A. Y. (2020). Use of onion (*Allium cepa*) and garlic (*Allium sativum*) wastes for the prevention of fungal disease (*Saprolegnia parasitica*) on eggs of rainbow trout (*Oncorhynchus mykiss*). *Journal of Fish Diseases*, *43*(10), 1325-1330. https://doi.org/10.1111/jfd.13229

Peng, K., Wang, G., Wang, Y., Chen, B., Sun, Y., Mo, W., Li, G., & Huang, Y. (2020). Condensed tannins enhanced antioxidant capacity and hypoxic stress survivability but not growth performance and fatty acid profile of juvenile japanese seabass (*Lateolabrax japonicus*). *Animal Feed Science and Technology*, *269*, 114671. https://doi.org/10.1016/j.anifeedsci.2020.114671

Pês, T. S., Saccol, E. M. H., Ourique, G. M., Londero, É. P., Gressler, L. T., Finamor, I. A., Rotili, D. A., Golombieski, J. I., Glanzner, W. G., Llesuy, S. F., Gonçalves, P. B. D., Neto, J. R., Baldisserotto, B., & Pavanato, M. A. (2016). Effect of diets enriched with rutin on blood parameters, oxidative biomarkers and pituitary hormone expression in silver catfish (*Rhamdia quelen*). *Fish Physiology and Biochemistry*, *42*(1), 321-333. https://doi.org/10.1007/s10695-015-0140-z

Pês, T. S., Saccol, E. M., Londero, É. P., Bressan, C. A., Ourique, G. M., Rizzetti, T. M., Prestes, O. D., Zanella, R., Baldisserotto, B., & Pavanato, M. A. (2018). Protective effect of quercetin against oxidative stress induced by oxytetracycline in muscle of silver catfish. *Aquaculture*, *484*, 120-125. https://doi.org/10.1016/j.aquaculture.2017.10.043

Pickering, A. D. (1993). Growth and stress in fish production. In G. A. E. Gall & H. Chen (Eds.), *Genetics in Aquaculture* (pp. 51-63). Elsevier. https://doi.org/10.1016/b978-0-444-81527-9.50010-5

Safari, R., Hoseinifar, S. H., Imanpour, M. R., Mazandarani, M., Sanchouli, H., & Paolucci, M. (2020). Effects of dietary polyphenols on mucosal and humoral immune responses, antioxidant defense and growth gene expression in beluga sturgeon (*Huso huso*). *Aquaculture*, *528*, 735494. https://doi.org/10.1016/j.aquaculture.2020.735494

Salem, M. O. A., Salem, T. A., Yürüten Özdemir, K., Sönmez, A. Y., Bilen, S., & Güney, K. (2021). Antioxidant enzyme activities and immune responses in rainbow trout (*Onchorhynchus mykiss*) juveniles fed diets supplemented with dandelion (*Taraxacum officinalis*) and lichen (*Usnea barbata*) extracts. *Fish Physiology and Biochemistry*. https://doi.org/10.1007/s10695-021-00962-5

Sangari, M., Sotoudeh, E., Bagheri, D., Morammazi, S., & Mozanzadeh, M. T. (2021). Growth, body composition, and hematology of yellowfin seabream (*Acanthopagrus latus*) given feeds supplemented with organic acid salts (sodium acetate and sodium propionate). *Aquaculture International*, *29*, 261-273. https://doi.org/10.1007/s10499-020-00625-x

Schiller Vestergren, A., Wagner, L., Pickova, J., Rosenlund, G., Kamal-Eldin, A., & Trattner, S. (2012). Sesamin modulates gene expression without corresponding effects on fatty acids in Atlantic salmon (*Salmo salar* L.). *Lipids*, *47*(9), 897-911. https://doi.org/10.1007/s11745-012-3697-7

Serrano, E., Storebakken, T., Borquez, A., Penn, M., Shearer, K. D., Dantagnan, P., & Mydland, L. T. (2011). Histology and growth performance in rainbow trout (*Oncorhynchus mykiss*) in response to increasing dietary concentration of sparteine, a common alkaloid in lupins. *Aquaculture Nutrition*, *18*(3), 313-320. https://doi.org/10.1111/j.1365-2095.2011.00899.x

Shin, H. S., Yoo, J. H., Min, T. S., Lee, K. Y., & Choi, C. Y. (2010a). The effects of quercetin on physiological characteristics and oxidative stress resistance in olive flounder, *Paralichthys olivaceus*. *Asian-Australasian Journal of Animal Sciences*, *23*(5), 588-597. https://doi.org/10.5713/ajas.2010.90624

Shin, H. S., Yoo, J. H., Min, T. S., Lee, J., & Choi, C. Y. (2010b). Effect of quercetin on the activity and mRNA expression of antioxidant enzymes and physiological responses in olive flounder (*Paralichthys olivaceus*) exposed to cadmium. *Asian-Australasian Journal of Animal Sciences*, *23*(6), 742-749. https://doi.org/10.5713/ajas.2010.10006

Sönmez, A. Y. (2017). Evaluating two different additive levels of fully autolyzed yeast, *Saccharomyces cerevisiae*, on rainbow trout (*Oncorhynchus mykiss*) growth performance, liver histology and fatty acid composition. *Turkish Journal of Fisheries and Aquatic Sciences*, *17*(2), 379-385. https://doi.org/10.4194/1303-2712-v17_2_17

Sönmez, A. Y., Bilen, S., Alak, G., Hisar, O., Yanık, T., & Biswas, G. (2015). Growth performance and antioxidant enzyme activities in rainbow trout (*Oncorhynchus mykiss*) juveniles fed diets supplemented with sage, mint and thyme oils. *Fish Physiology and Biochemistry*, *41*(1), 165-175. https://doi.org/10.1007/s10695-014-0014-9

Sönmez, A. Y., Bilen, S., Albayrak, M., Yılmaz, S., Biswas, G., Hisar, O., & Yanık, T. (2015). Effects of dietary supplementation of herbal oils containing 1, 8-cineole, carvacrol or pulegone on growth performance, survival, fatty acid composition, and liver and kidney histology of rainbow trout (*Oncorhynchus mykiss*) fingerlings. *Turkish Journal of Fisheries and Aquatic Sciences*, *15*, 813-819. https://doi.org/10.4194/1303-2712-v15_4_04

Sutili, F. J., Gatlin, D. M., Heinzmann, B. M., & Baldisserotto, B. (2017). Plant essential oils as fish diet additives: benefits on fish health and stability in feed. *Reviews in Aquaculture*, *10*(3), 716–726. https://doi.org/10.1111/raq.12197

Syahidah, A., Saad, C., Daud, H., & Abdelhadi, Y. (2015). Status and potential of herbal applications in aquaculture: A review. *Iranian Journal of Fisheries Sciences*, *14*(1), 27-44. https://doi.org/10.22092/IJFS.2018.114421

Tan, C., Zhou, H., Wang, X., Mai, K., & He, G. (2019). Resveratrol attenuates oxidative stress and inflammatory response in turbot fed with soybean meal based diet. *Fish & Shellfish Immunology*, *91*, 130-135. https://doi.org/10.1016/j.fsi.2019.05.030

Terzi, E., Kucukkosker, B., Bilen, S., Kenanoglu, O. N., Corum, O., Özbek, M., & Parug, S. S. (2021). A novel herbal immunostimulant for rainbow trout (*Oncorhynchus mykiss*) against *Yersinia ruckeri*. *Fish & Shellfish Immunology*, *110*, 55-66. https://doi.org/10.1016/j.fsi.2020.12.019

Tort, L. (2011). Stress and immune modulation in fish. *Developmental & Comparative Immunology*, *35*(12), 1366-1375. https://doi.org/10.1016/j.dci.2011.07.002

Villa-Cruz, V., Davila, J., Viana, M., & Vazquez-Duhalt, R. (2009). Effect of broccoli (*Brassica oleracea*) and its phytochemical sulforaphane in balanced diets on the detoxification enzymes levels of tilapia (*Oreochromis niloticus*) exposed to a carcinogenic and mutagenic pollutant. *Chemosphere*, *74*(9), 1145-1151. https://doi.org/10.1016/j.chemosphere.2008.11.082

Xu, Z., Li, X., Yang, H., Liang, G., Gao, B., & Leng, X. (2019). Dietary quercetin improved the growth, antioxidation, and flesh quality of grass carp (*Ctenopharyngodon idella*). *Journal of the World Aquaculture Society*, *50*(6), 1182-1195. https://doi.org/10.1111/jwas.12663

Ye, Q., Feng, Y., Wang, Z., Zhou, A., Xie, S., Zhang, Y., Xiang, Q., Song, E., & Zou, J. (2019). Effects of dietary *Gelsemium elegans* alkaloids on growth performance, immune responses and disease resistance of *Megalobrama amblycephala*. *Fish & Shellfish Immunology*, *91*, 29-39. https://doi.org/10.1016/j.fsi.2019.05.026

Yilmaz, E., Ergün, S., & Yilmaz, S. (2015). Influence of carvacrol on the growth performance, hematological, non-specific immune and serum biochemistry parameters in rainbow trout (*Oncorhynchus mykiss*). *Food and Nutrition Sciences*, *6*(5), 523-531. https://doi.org/10.4236/fns.2015.65054

Yilmaz, S. (2019). Effects of dietary caffeic acid supplement on antioxidant, immunological and liver gene expression responses, and resistance of Nile tilapia, *Oreochromis niloticus* to *Aeromonas veronii*. Fish & Shellfish Immunology, *86*, 384-392. https://doi.org/10.1016/j.fsi.2018.11.068

Yılmaz, S., & Ergün, S. (2018). Trans-cinnamic acid application for rainbow trout (*Oncorhynchus mykiss*): I. Effects on haematological, serum biochemical, non-specific immune and head kidney gene expression responses. *Fish & Shellfish Immunology*, *78*, 140-157. https://doi.org/10.1016/j.fsi.2018.04.034

Yonar, M. E., Yonar, S. M., İspir, Ü., & Ural, M. Ş. (2019). Effects of curcumin on haematological values, immunity, antioxidant status and resistance of rainbow trout (*Oncorhynchus mykiss*) against *Aeromonas salmonicida subsp*. achromogenes. *Fish & Shellfish Immunology*, *89*, 83-90. https://doi.org/10.1016/j.fsi.2019.03.038

Yu, L., Wu, F., Liu, W., Tian, J., Lu, X., & Wen, H. (2017). Semisynthetic ferulic acid derivative: an efficient feed additive for Genetically Improved Farmed Tilapia (*Oreochromis niloticus*). *Aquaculture Research*, *48*(9), 5017-5028. https://doi.org/10.1111/are.13319

Zhai, S. W., & Liu, S. L. (2013). Effects of dietary Quercetin on growth performance, serum lipids level and body composition of tilapia (*Oreochromis niloticus*). *Italian Journal of Animal Science*, *12*(4), e85. https://doi.org/10.4081/ijas.2013.e85

Zhang, L., Virgous, C., & Si, H. (2019). Synergistic anti-inflammatory effects and mechanisms of combined phytochemicals. *The Journal of Nutritional Biochemistry*, *69*, 19-30. https://doi.org/10.1016/j.jnutbio.2019.03.009

Zheng, Y., Hu, G., Wu, W., Zhao, Z., Meng, S., Fan, L., Song, C., Qiu, L., & Chen, J. (2019). Transcriptome analysis of juvenile genetically improved farmed tilapia (*Oreochromis niloticus*) livers by dietary resveratrol supplementation. *Comparative Biochemistry and Physiology Part C: Toxicology & Pharmacology*, *223*, 1-8. https://doi.org/10.1016/j.cbpc.2019.04.011