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Review

Lamiaceae as Feed Additives in Fish Aquaculture

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Abstract: The growing demand for high-quality food has induced a rapid expansion of the aquaculture sector. On the other hand, this sector has to overcome numerous challenges and problems triggered by the adoption of intensive farming systems, such as stress and high susceptibility to diseases. The improper use of chemicals and antibiotics has led to the development of antibiotic resistance in fish, with consequent health risks for consumers. Natural additives are increasingly used in aquaculture and, among these, medicinal plants are constantly under investigation as safe and environmentally friendly alternatives to chemicals. Great attention has been paid to *Lamiaceae* plants as feed additives capable of enhancing the growth performance, immune system, and antioxidant status of farmed fish. The aim of this review is to provide an updated picture of the employment of the *Lamiaceae* species (oregano, rosemary, sage, thyme, and mint) to enhance farmed fish health. The benefits of oregano, rosemary, sage, thyme, and mint feed supplementation on growth performance, immune system, antioxidant status, hemato-biochemical parameters, and resistance to stress, parasites, and bacteria have been described, highlighting weaknesses and drawbacks and proposing possible implementations.

Keywords: *Lamiaceae*; fish; health; growth performance; antioxidant; immunity; nutrition

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1. Introduction

In recent decades, the aquaculture sector has shown rapid expansion in order to meet the food needs of the growing human population [1]. Aquaculture products represent an important source of high-quality animal proteins, as well as essential macro- and micronutrients. The growing demand for fish, both salty and freshwater, has prompted the aquaculture industry to adopt intensive and even ultra-intensive farming systems to increase productivity. However, intensive practices are responsible for numerous problems, such as poor water quality, overcrowding, high temperature, and poor nutrition, that contribute to lowering the growth performances of fish health and immune competence, with consequently increased stress and high susceptibility to diseases. Although aquaculture plays an important role today, it is a sector that must overcome numerous challenges that hinder its expansion, such as the spreading of infectious diseases, fish health problems, and consequent economic damage [2]. In recent years, disinfectants, chemotherapeutics and synthetic antibiotics have been used in order to prevent or mitigate the economic losses caused by diseases in farmed fish [3,4]. Unfortunately, as there are no antibiotics developed specifically for fish [4], veterinary or human antibiotics have been used, contributing to the onset of antibiotic-resistance [5]. Furthermore, the recurrent and uncontrolled use of antibiotics in farmed fish leads to the accumulation of residues of these substances in fish products, with consequent health risks for consumers [6].

Recently, researchers have paid great attention to identifying safe and environmentally friendly alternatives to antibiotics [7–9]. The use of natural additives capable of replacing pharmaceutical substances in intensive farming appears to have many potential benefits, including immunostimulation, the inhibition of pathogens in the intestinal tract, and the improvement of the absorption and utilization of nutrients [10,11]. Numerous studies have evaluated the effects of several natural feed additives, including probiotics [12], prebiotics [13], synbiotics [14], functional amino acids [15], minerals [16], and additives of origin vegetable or phytochemicals [8,17–20].

Medicinal plants, which include herbs, spices, and their extracts, have been increasingly used in aquaculture due to their low cost and simple use. In farmed fish, medicinal plants promote a vast array of effects, including the improvement of growth [21], immunity [22], antimicrobial and anti-stress activities [23], as well as resistance against pathogens [24]. In general, the efficacy of medicinal plants and their derivatives (extracts, and essential oils) is closely related to the abundance of bioactive substances such as alkaloids, quinones, lectins, steroids, phenolic compounds, tannins, terpenoids, saponins and flavonoids [25]. Among the medicinal plants used as a feed supplement for fish, growing scientific interest is directed to aromatic plants, both as extracts and essential oils [26]. Many of these aromatic plants belong to the *Lauraceae*, *Umbelliferae*, *Myrtaceae* and *Lamiaceae* families. In particular, the plant species of the *Lamiaceae* family are among the most studied and are frequently used as feed additives in aquaculture [27]. The aim of this review is to furnish a general outlook of the main *Lamiaceae* species (oregano, rosemary, sage, thyme, and mint) on the health and pathogen resistance in farmed fish, with the aim of providing a picture as complete as possible of *Lamiaceae* employment in aquaculture, highlighting the weaknesses and drawbacks of their implementation and proposing possible alternatives.

2. *Lamiaceae* Family

Lamiaceae are distributed all over the world, although the best environmental conditions for their growth were found in the Mediterranean basin [28]. The *Lamiaceae* family includes 245 genera and approximately 8000 species [29]. Since ancient times, the dried herb, leaves, and essential oils of *Lamiaceae* plants have been used in humans to treat various respiratory diseases, rheumatoid arthritis, gastrointestinal disorders, and urinary tract infections [29]. Plants of the *Lamiaceae* family represent a natural, economical, sustainable, and safe source of feed integrators capable of enhancing the growth performance, immune system, and antioxidant status of farmed fish [30–32]. Such beneficial effects are attributable to the bioactive molecules present in *Lamiaceae* plants, such as terpenes, terpenoids, alkaloids, and flavonoids [2]. For example, the immunomodulatory properties of the *Lamiaceae* plants are mediated by the predominant terpenes, carvacrol, and thymol, which are capable of modulating inflammatory processes through the activation of ion channels, such as TRP (Transient Receptor Potential) channels, and consequently activate the NFkB pathway [26]. Moreover, carvacrol and thymol show strong antioxidant activity due to their ability to neutralize the oxygen free radicals (ROS) in tissues and cells [26].

Lamiaceae, as feed additives, can be administered in different forms, as a whole plant or parts (leaves or seeds), as active compounds extracted from the plant, and individually or as a combination of extracted compounds [2]. It should be emphasized that the efficacy of *Lamiaceae* plants as feed additives depends on several crucial factors such as dose, duration, time schedule of administration, and fish species [2]. In particular, the most important factor is represented by the dose which, if suitable, can induce beneficial effects, while if too low or too high, may induce either no response or even be toxic [11]. As reported in a meta-analysis study on fish diets enriched with plants, the dosages used in aquaculture vary according to the plant species used. The higher dosages are used with powdered plants (0.1–420 mg/100 g of fish × day), followed by ethanolic and aqueous extracts (0.2–160 mg/100 g of fish × day; 0.03–200 mg/100 g of fish × day, respectively), while the lower doses are used with essential oils (0.005–30 mg/100 g of fish × day) [21]. Thus, to improve the growth performances and health of a specific fish species, the challenge for researchers is to identify the optimal conditions in terms of the part of the plant to be used, doses, duration, and time schedule.

3. Oregano

Among the *Lamiaceae* family, the oregano (*Origanum vulgare* L.) is the most worldwide spread species, distributed throughout Eurasia and North Africa, and particularly abundant in the Mediterranean area [33]. The richness of the chemical composition and aromatic compounds of oregano have led to its use, since ancient times, in the pharmaceutical and cosmetic fields, as well as in the food industry as a flavoring substance [34]. The efficacy of oregano in the treatment of a wide range of human diseases has been reported in both in vitro and in vivo studies [35,36]. Furthermore, several studies have reported the growth and health-promoting role of oregano in farmed animals, primarily in terrestrial monogastric animals (poultry and pigs) [37,38] and fish (Table 1).

The biological activities attributed to oregano are related to its bioactive components, which include a wide variety of secondary metabolites, most of which are monoterpenes (carvacrol and thymol) and polyphenols (rosmarinic acid, luteolin and derivatives, chlorogenic acid, quercetin and derivatives, caffeic acid, hyperoside, rutin, *p*-coumaric, ferulic, carnosic, ursoli acids) [29,39].

Table 1. Studies of oregano products added to the feed of aquaculture species.

Feeding			Fish			Effects	Ref.
Form	**Inclusion Doses (% in Feed)**	**Period (Days)**	**Species**	**Vital Stage**	**Stress/Toxicant/ Pathogen Challenge**		
O. vulgare essential oil	0.05, 0.1, 0.15, 0.2, 0.25	90	*Astyanax altiparanae*			↑ WG, SGR, PER	[40]
Origanum spp. essential oil	0.5, 1, 1.5, 2	56	*Cyprinus carpio*	Juvenile	*Aeromonas Hydrophila*	↑ LYS activity, phagocytic activity, and phagocytic index ↑ SOD and CAT activities ↑ IL-1β and IL-10	[41]
Origanum spp. essential oil	0.5, 1, 1.5, 2	60	*Cyprinus carpio*	Fingerling		↑ WG and SGR	[42]
O. vulgare essential oil	0.05, 0.15, 0.45	56	*Cyprinus carpio*	Juvenile	*Aeromonas Hydrophila*	↑ LYS and complement activities ↑ SOD, CAT and GPx activities ↓ TNFα and TGFβ	[43]
O. majorana hydroalcoholic extract	0.01, 0.02, 0.04	56	*Cyprinus carpio*	Juvenile	*Aeromonas Hydrophila*	↑ FW, WG and SGR ↑ RBC, WBC, Hct and Hb ↑ LYS and complement activities ↑ Total Ig levels ↑ SOD and CAT activities	[44]
O. vulgare ethanolic extract	0.5, 1, 2	56	*Danio rerio*	Adult	*Aeromonas Hydrophila*	↑ WG and SGR ↑ LYS and complement activities ↑ Total Ig levels ↑ SOD and CAT activities	[45]
O. vulgare essential oil	0.01, 0.02	60	*Dicentrarchus labrax*	Juvenile		↑ WG, SGR and PER ↓ Cholesterol and tryglicerides serum levels	[46]
O. vulgare essential oil	0.01, 0.02	150	*Dicentrarchus labrax*	Juvenile	Temperature change	↑ WG and SGR ↑ SOD and CAT activities	[47]
O. vulgare hydroalcoholic extract	1	56	*Oncorynchus mykiss*	Juvenile		↑ Serum total protein, respiratory burst activity, phagocytic activity and LYS activity	[48]
O. vulgare hydroalcoholic extract	1	56	*Oncorynchus mykiss*	Juvenile		↑ Serum total protein, respiratory burst activity, phagocytic activity and LYS activity	[49]
O. vulgare hydroalcoholic extract	0.2, 0.6, 1, 1.4	60	*Oncorynchus mykiss*	Juvenile	Diazinon (25% of the LC50 or 0.287 mg/L or 0.942 µM)	↑ BWI and SGR ↑ SOD, CAT and GPx activities	[50,51]

Table 1. *Cont.*

Feeding			Fish			Effects	Ref.
Form	Inclusion Doses (% in Feed)	Period (Days)	Species	Vital Stage	Stress/Toxicant/ Pathogen Challenge		
O. vulgare hydroalcoholic extract	0.5, 1, 1.5	70	*Oreochromis niloticus*	Fingerling	*Pseudomonas aeruginosa; Pseudomonas flourscence*	↑ FCR, PER and energy utilization	[52]
O. vulgare essential oil	0.1, 0.2	70	*Oreochromis niloticus*	Juvenile		↑ FW, SGR and FCR ↑ SOD activity	[53]
O. vulgare leaves powder	0.025, 0.5, 0.075, 0.1, 0.125, 0.15	30	*Oreochromis niloticus*	Juvenile	*Streptococcus agalactiae*	NS on growth ↑ LYS activity	[54]
O. vulgare hydroalcoholic extract	0.2, 0.5	60	*Oreochromis niloticus*	Juvenile	*Aeromonas Hydrophila*	↑ FW, WG and SGR ↑ RBC, WBC, Hct and Hb ↑ LYS and complement activities ↑ SOD, CAT and GPx activities	[55]
O. vulgare leaves powder	0.5, 1	30	*Sparus aurata*	Juvenile		NS on growth NS on LYS activity ↑ Ig levels	[56]

WG: Weight gain; FW: Final weight; FCR: Feed conversion ratio; SGR: Specific growth rate; PER: Protein efficiency ratio; BWI: Body weight index; RBC: Red blood cell count; WBC: White blood cell count; Hct: Hematocrit; Hb: Hemoglobin; LYS: Lysozyme; Ig: Immunoglobulin; IL-1β: Interleukin-1β; IL-10: Interleukin-10; TNFα: Tumor necrosis factor-α; TGFβ: Transforming growth factor-β; SOD: Superoxide dismutase; CAT: Catalase; GPx: Glutathione peroxidase; NS, non-significant effects.

3.1. Oregano's Effects on Growth Performance

Great attention has been paid by researchers to the use of oregano essential oil (OEO) in farmed fish (Table 1). OEO feed inclusion stimulates the growth performance of fish, primarily by improving the feed utilization rate and by acting on metabolic processes. Zhang et al. [43] reported that 0.15 and 0.45% of OEO supplementation, for 56 days, stimulated digestive enzymes in koi carp juveniles (*Cyprinus carpio*), increasing the activation of proteases, amylases and lipases. The same beneficial effects on intestinal enzymes have been reported for the hydroalcoholic extract of oregano (at a dose of 3% in 85 days feeding trial) in rainbow trout (*Oncorynchus mykiss*) [57]. In addition, OEO dietary supplementation may promote growth due to its beneficial effects on intestinal health. The inclusion of 1.5% of OEO in the diet for 60 days significantly improved growth performance and intestinal histomorphometry (villous height and width) in common carp fry [42]. Similarly, the addition of 0.05% of OEO to the diet of yellow-tailed (*Astyanax altiparanae)* for 90 days increased the absorption area of the intestine [40]. The study by Huley et al. [58] showed that the inclusion of different OEO concentrations (0.075, 0.15, 0.225, and 0.3%) in Nile tilapia (*Oreochromis niloticus*) juveniles for 64 days acted as a developmental stimulant of intestinal villi and, consequently, as a growth promoter.

The beneficial effects of OEO supplementation on growth performance are also, most likely, linked to the improvement of the gut microbial community [43]. Fish gut microbiota serves crucial functions in host health, growth, and development, aiding digestive functions and protecting against intestinal infections [59]. Dietary supplementation with the major monoterpenes of oregano (thymol and carvacrol) positively altered the gut microbiota of Nile tilapia [60], and resulted in improved nutrient digestibility and absorption, as well as protein conversion [50,61]. The OEO inhibited some pathogenic bacterial groups and increased commensal beneficial communities of *Corynebacterium*, *Brevinema*, and *Propionibacterium* in koi carp juveniles [43].

In contrast to the beneficial effects of OEO, Santo et al. [54] reported no significant improvement in growth performances and no significant alterations in intestinal villous height in Nile Tilapia juveniles fed with different percentages (0.025, 0.05, 0.075, 0.1, 0.125, and 0.15%) of dried oregano leaves for 30 days. Similarly, weight gain (WG) and specific growth rate (SGR) did not significantly differ in seabream juveniles (*Sparus aurata*) fed with 0.5 and 1% oregano leaves powder for 15 or 30 days [56].

The hydroalcoholic oregano leaf extract also appeared to counteract the toxic effects of Diazinon, an organophosphate pesticide, on growth and liver metabolic enzymes (aspartate aminotransferase (AST), alanine aminotransferase (ALT) and lactate dehydrogenase (LDH) in rainbow trout juveniles; in fact, doses between 0.2 and 1%, but not higher, of oregano hydroalcoholic extract dietary inclusion significantly increased the body weight index (BWI) and the SGR compared to the standard diet in a 60 day feeding trial [51].

Based on these results, the best forms of oregano feed supplement for fish to stimulate growth rate and feed conversion parameters are essential oils and hydroalcoholic extracts, while powdered oregano leaves have no beneficial effects. A possible explanation may reside in the similar percentage of bioactive constituents (carvacrol 63%; thymol 4.7%; ρ-cimene 12.8%; γ-terpinene 8.4%) in essential oils and hydroalcoholic extracts [40,54,62].

3.2. Oregano's Effects on Oxidative Stress

Oregano essential oil or hydroalcoholic extracts administered in the diet reduced the oxidative stress in different fish species, including common carp [41,43,44], rainbow trout [31,49,50,61], Nile tilapia [53,55], and catfish [63]. Oregano acted as an antioxidant activity enhancer, promoting the activities of serum and hepatic superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPX) enzymes accompanied by a reduction in malonaldehyde (MDA) levels [41,43].

The choice of the administered dose plays an important role in the antioxidant effect of oregano when used as a feed additive. For example, in rainbow trout juveniles, after a 60 day feeding trial with 0.6 and 1% doses of hydroalcoholic oregano leaf extract, the activity of antioxidant enzymes SOD, CAT, and glutathione peroxidase (GPX) increased, while high doses (1.4%) caused a decrease in their activities [50]. Similarly, the particular part of the plant being used appears to play an important role in determining its antioxidant effect. The use of 0.5 and 1% of oregano leaf powder for 30 days in sea bream juveniles, for example, did not cause any significant effects on liver antioxidant enzymes activities [56]; this is likely a result of the lower number of bioactive components with respect to the essential oil and the hydroalcholic extract. Further, the presence of the bioactive molecules within the vegetable matrix, as it occurs in the leaves, makes their extraction and absorption during the digestive processes difficult, with a consequent limited action. Indeed, the level of bioactive molecule uptake in the intestine represents only a limited percentage of the total quantity.

3.3. Oregano's Effects on Immune Response

The effects of dietary oregano supplementation on the immune status of farmed fish have been widely reported. The results of numerous studies carried out on rainbow trout [31,48,49], Nile tilapia [55], and koi carp [43] reported that both oregano essential oil and hydroalcoholic extract increased the non-specific immune response, mainly via improving lysozyme, protease and complement system activities. In comparison to mammals, the innate immune system represents a fundamental defense weapon in fish [64]. For example, lysozyme is capable of destroying the bacterial cell, by splitting the β-1,4 glycosidic bonds of the peptidoglycan, providing protection against fish pathogens [65]. The use of 0.02% of hydroalcoholic oregano (*O. majorana*) leaf extract for 56 days enhanced the activity of lysozyme in common carp juveniles [44]. In another study, dietary integration of 0.1% of OEO in red-bellied tilapia (*Tilapia zillii*) improved lysozyme activity levels, accompanied by the increase in proteases, antiproteases, and bactericidal activities [66].

The supplementation with immunostimulants in fish diets also beneficially improved the expression of specific immune elements, such as IgM [56] and pro-inflammatory cytokyne Interleukin-1β (IL-1β) [66]. In particular, in sea bream juveniles, supplementation with oregano leaf powder at 0.5 and 1% for 30 days improved both the innate (complement system and antibacterial activity) and adaptive (IgM) responses of skin mucus immunity compared to the control group, while the oregano leaf powder integration did not alter the humoral immune response in the serum [56]. From this difference in the results, authors have suggested that the immune defense against pathogens resides in the antibody response of the skin mucus, which increases proportionally with the concentration of oregano leaf powder in the diet (resulting highest at the dose of 1%).

3.4. Oregano's Effects on Hemato-Biochemical Parameters

Hemato-biochemical parameters are reliable biomarkers of the health and immunity conditions of farmed fish species [67]. The incorporation of hydroalcoholic extract of the oregano aerial part into fish feed had no effect on red and white blood cell counts (RBC and WBC, respectively), leukocytes count (monocyte, lymphocyte and neutrophile), hematocrit (Hct), and hemoglobin (Hb) in rainbow trout juveniles treated with a dose of 1% [48,49] and in Nile tilapia treated with 0.2 and 0.5% [55]. On the contrary, the hematological parameters were significantly enhanced in red-bellied tilapia fed with 0.1% of OEO for 15 days [66]. Similar augmentation of RBC, WBC, thrombocytes, and hemoglobin was recorded in common carp juveniles fed a diet containing 0.02% of oregano (*O. majorana*) leaf hydroalcoholic extract for 56 days [44]. It has been suggested that the increase in the hematological parameters RBC, Hct, and Hb, may favor the tissue oxygenation and the elimination of carbon dioxide, contributing to growth [68]. Moreover, homeostasis, or the increase in such hematological parameters, indicates that the oregano supplementation had no negative effects on erythrocytes production and the destruction of mature RBC, therefore indicating that it is non-toxic [69]. Serum biochemical parameters, such as total protein, albumin, and globulin values, were enhanced by hydroalcoholic oregano leaf extract, added to the diet at the dose of 1% in rainbow trout juveniles [48,49]. Similarly, in sea bass (*Dicentrarchus labrax*) juveniles fed with 0.01% of OEO for 150 days, the improvement of total protein, glucose, triglycerides, and cholesterol occurred [47].

3.5. Oregano's Effects against Pathogen Infections

Several studies have revealed that the use of OEO, in addition to increasing growth and feed utilization, improves resistance to pathogens in common carp [41,43,44], channel catfish (*Ictalurus punctatus*) [63], zebrafish (*Danio rerio*) [45], Nile Tilapia [55], rainbow trout [31], and red-bellied tilapia [66]. Carvacrol and thymol, the most abundant phenolic components, are likely responsible for the antimicrobial activities of oregano, being able to alter the bacterial outer membrane and consequently its permeability [39]. Carvacrol, in particular, is involved in the disintegration of bacterial cells by altering the synthesis and mobility of the flagella, the fatty acid composition of the membranes, membrane proteins, and periplasmic enzymes [55,70]. The flavonoids and terpenoids contained in the oregano also contribute to the antimicrobial power, as demonstrated by the terpenoids, ρ-cymene [70].

3.6. Conclusions

Based on the literature, it appears that the best dietary supplement is represented by oregano's essential oil and hydroalcoholic leaf extract. It should be noted that fish fed the diet supplemented with oregano showed improved growth performance, immunological parameters, and antioxidant status in a dose-dependent manner and that an excessive amount of oregano could cause immunosuppression and toxicity. In this regard, on the basis of the results examined, it can be stated that it is convenient to use oregano as a feed additive for fish in the form of essential oil and hydroalcoholic extract in a concentration ranging between 0.5 and 1%, for a minimum duration of 8 weeks.

4. Rosemary

Rosemary (*Rosmarinus officinalis* L.) is a small evergreen medicinal herb, widespread in the Mediterranean region. It is widely used for farmed animals' nutrition. Both in vitro and in vivo studies have shown that rosemary-based food supplements improve oxidative stress and immune responses [71]. In particular, rosemary extract possesses anti-inflammatory, anticancer, antidiabetic, hepato- and blood-protective activities [72,73]. Among *Lamiaceae* medicinal plants, rosemary presents the least chemical composition variability. Rosemary is primarily composed of terpenes β- and α-pinene, camphene, camphor, and limonene [74]. Many other compounds are also extracted from rosemary, such as polyphenols and steroids [71,75]. Among polyphenols, the most abundant are rosmarinic acid, 7-methylrosmanol naringin, and also, at lower concentrations, rutin, and ferulic acid [76]. Although there is numerous evidence to show the beneficial effects of rosemary as a feed additive in terrestrial animals, its application in aquaculture is still scarce. However, significant interest in the use of rosemary in aquatic animals has recently increased due to its efficacy as a stimulant of growth, the immune system, and health status [72,77].

4.1. Rosemary's Effects on Growth Performance

Several studies have confirmed that the oral administration of rosemary could enhance growth performances in farmed fish, such as common carp [72,77], Nile tilapia [78–80], and sea bream [81] (Table 2). Among the rosemary-based products, rosemary leaf powder is the most commonly investigated as a fish feed additive. In common carp fingerlings, different doses (1, 2, and 3%) of rosemary leaf powder positively increased, in a dose-dependent manner, the growth performances and feed conversion parameters (WG, SGR, final weight (FG), feed conversion ratio (FCR) levels) after a trial of 65 days [72].

Table 2. Studies of rosemary products added to the feed of aquaculture species.

Feeding			Fish			Effects	Ref.
Form	**Inclusion Doses (% in Feed)**	**Period (Days)**	**Species**	**Vital Stage**	**Stress/Toxicant/ Pathogen Challenge**		
R. officinalis leaf powder	1, 2, 3	65	*Cyprinus carpio*	Juvenile		↑ WG, SGR and PER ↑ RBC, WBC, Hct and Hb ↑ LYS and complement activities ↑ Total Ig and protein levels ↑ SOD and CAT activities	[72]
R. officinalis hydroalcoholic extract	0.25, 0.5, 1	65	*Cyprinus carpio*	Juvenile		↑ WG and SGR ↑ LYS and complement activites, phagocytic activity, and phagocytic index ↑ RBC, WBC, Hct and Hb ↓ Cholesterol and tryglicerides serum levels	[77]
R. officinalis leaf powder	1	140	*Oreochromis niloticus*	Fingerling		↑ WG, SGR and PER ↑ Hct and leukocrit levels	[78]
R. officinalis commercial leaf extract	0.1, 0.25, 0.5	90	*Oreochromis niloticus*	Juvenile		NS on growth	[79]
R. officinalis leaf powder	0.25, 0.5, 1	60	*Oreochromis niloticus*	Fingerling	*Aeromonas Hydrophila*	↑ WG, SGR and FCR ↑ Total serum protein ↑ LYS and complement activities ↑ Total Ig levels ↑ CAT activity	[80]
R. officinalis commercial extract	0.06, 0.12, 0.18, 0.24	84	*Sparus aurata*			NS on growth ↓ Total serum protein	[81]

WG: Weight gain; FCR: Feed conversion ratio; SGR: Specific growth rate; PER: Protein efficiency ratio; RBC: Red blood cell count; WBC: White blood cell count; Hct: Hematocrit; Hb: Hemoglobin; LYS: Lysozyme; Ig: Immunoglobulin; SOD: Superoxide dismutase; CAT: Catalase; NS, non-significant effects.

The same findings with rosemary leaf powder supplementation were also obtained in Nile tilapia fingerlings [78,80]; in particular, Naiel et al. [80] recorded better growth performance in fish fed on 0.5 and 1% of rosemary leaf powder for 60 days. Similarly, in a

65-day feeding trial, common carp juveniles fed on hydroalcoholic rosemary leaf extract (0.01, 0.25, 0.5, and 1%) showed an increase in growth performances [77]. Various studies have shown that herbal plants not only improved fish growth and nutrition, but also enhanced appetite and modified the gut microbiota composition, increasing the diversity and activity of the beneficial bacteria, while inhibiting pathogenic bacteria [2,75,82]. In agreement with these findings, rosemary leaf powder also showed a positive role in controlling nutrient uptake and enhancing the intestinal mucosal condition in rats ([83]. On the contrary, in Nile tilapia juveniles fed 90-day diets with different amounts (0.1, 0.25, and 0.5%) of commercial rosemary extract, Yilmaz et al. [79] did not report significant changes in growth performances. In addition, in gilthead seabream, growth performances and feed intake were not modified by the inclusion of different doses (0.06, 0.12, 0.18, 0.24%) of commercial rosemary extract for 84 days [81]. Such differences could be attributed to different fish species, feeding trial length, source and rosemary doses. In this regard, it is necessary to emphasize that, in the experiment conducted by Hernández et al. [81], a commercial rosemary extract powder made of a blend at the ratio 1:1 of two diterpenes (carnosic acid and carnosol) was used. Similarly, Yilmaz et al. [79] used a commercial rosemary extract composed of rosmarinic acid at 5.32%. Therefore, the lack of results may be associated with the small amount of the chemical active principles in the feed additive used. In contrast to the inclusion of powder or fresh leaf extract, it is also interesting to underline that rosemary oil did not result in an increase in growth performance, as well as growth rate (GR) and FCR in sturgeon juveniles (*Huso huso*) [84] and seabass [85].

4.2. Rosemary's Effects on Oxidative Stress

The beneficial effects of rosemary dietary-inclusion also resulted in the improvement of the antioxidant status in common carp [72] and in Nile tilapia [80]. Rosemary leaf powder supplementation at the doses of 0.5 and 1% in the diet of Nile tilapia fingerlings for 60 days significantly improved the antioxidant status via an increase in CAT activity [80]. Similarly, in a 65-day feeding trial in common carp juveniles, different doses (1, 2, and 3%) of rosemary leaf powder induced an increase, in a dose-dependent manner, of blood CAT activity, but the higher dose (3%) led to a decrease in blood SOD activity [86].

The effect of powdered rosemary leaves as antioxidant defense enhancers could be linked to its several beneficial compounds, such as rosmarinic and carnosic acids [76].

4.3. Rosemary's Effects on Immune Response

Dietary supplement with rosemary products showed an enhancement of the immune system in fish. The elevation of total immunoglobulin (Ig) levels, lysozyme and alternative complement activities of common carp juveniles fed on diets containing rosemary leaf powder in various doses (1, 2, and 3%), for 65 days, was reported [72]. The findings of Dezfoulnejad and Molayemraftar [77] confirmed the potential of oral administration of hydroalcoholic rosemary leaf extract as a stimulatory agent of the non-specific immune system in common carp juveniles. Similarly, in tilapia (*O. mossambicus*) fingerlings, the inclusion of 0.25 and 0.5% hydroalcoholic rosemary extracts for 60 days led to an improvement in the principal non-specific immunity elements (lysozyme, immunoglobulin and alternative complement) [87]. In addition, in Nile tilapia fingerlings, the oral administration of 1% of rosemary leaf powder for 60 days induced a significant increase in the expression of the immune genes related to innate and adaptive immune response, such as lysozyme, complement and immunoglobulin M (IgM) [80].

4.4. Rosemary's Effects on Hemato-Biochemical Parameters

It has been reported that rosemary bioactive compounds, such as rosmarinic acid, could positively affect thymus and spleen activities, leading to a significant increase in the WBC counts (lymphocytes T and B, monocytes and neutrophils) [88]. In fact, after 65 days of oral administration of 2 and 3% of rosemary leaf powder, WBC markedly increased in common carp juveniles [72]. Similarly, tilapia fingerlings treated with 1%

of rosemary leaf powder showed a significant increase in both haematological (WBC, haematocrit and leukocrit levels) and serum biochemical (total protein, albumin and globulin levels) parameters [78]. Serum biochemical parameters are good fish health indicators [68]. Several studies have suggested the possible correlation between enhanced fish growth performance and the simultaneous increase in total protein, albumin and globulin levels due to dietary herbal inclusion [68,89]. Findings on the oral supplementation of rosemary in common carp [72,77] and in Nile tilapia [78,80] confirmed the hypothesis of the combination effects of health and growth performance in fish treated with herbal supplementation. Moreover, several vitamins (A, B, and C) and minerals (K, Ca, and Fe) present in significant quantities in rosemary could positively modulate other blood biochemical parameters due to their hypocholesterolaemic effects [90]. For example, the levels of triglycerides and LDL (low-density lipoprotein cholesterol) diminished, while HDL (high-density lipoprotein cholesterol) augmented in common carp juveniles fed on hydroalcoholic extract of rosemary at 1% in a 65-day feeding trial [77].

4.5. Rosemary's Effects against Pathogen's Infections

Some studies have evaluated the effects of rosemary as an alternative antimicrobial agent in aquaculture. The dietary application of dried rosemary leaves for 20 days improved the resistance against *Streptococcus iniae* at the 8% dose and against *Streptococcus agalactiae* at 16% dose in tilapia fingerlings [91]. Similarly, the 60-day feeding supplementation of 1% of rosemary leaf powder provided adequate protection to Nile tilapia fingerlings against the infection of *Aeromonas hydrophila* [80]. Numerous in vitro studies demonstrated that rosemary possessed antibacterial properties against Gram-positive and Gram-negative bacteria, mainly linked to its composition in phenolic compounds [92,93].

4.6. Conclusions

Based on the reported literature, both leaf powder and extract of rosemary positively affect growth performance, antioxidant status, and the general health of farmed fish. In order to improve the haemato-biochemical and non-specific immune parameters and increase the resistance against bacterial diseases, a dosage of 1% of rosemary extract or leaf powder and 60 days of administration can be recommended as useful fish feed additives.

5. Sage

Sage is the largest genus of *Lamiaceae* and includes approximately 900 species, among which *Salvia officinalis* is globally widespread and highly considered for its medical relevance [29]. In fact, *Salvia officinalis* is cultivated in numerous countries and its dried leaves are used as raw material in medicine, the food industry, and perfumery [94]. It has been found that the essential oil and leaf extract of *Salvia officinalis* have strong antimicrobial and antioxidant effects, and also exhibit immunomodulatory and anti-inflammatory activities [29]. These beneficial effects may be due to the particular chemical constituents of sage, such as tannic acid, oleic acid, carnosol and carnosic acid and some polyphenols, such as caffeic acid, p-coumaric acid, rutin, rosmarinic acid, quercetin, luteolin, and apigenin [29]. Other compounds, such as monoterpenes and terpenoids, including 1.8-cineole, α-thujone, β-thujone, β-pinene, and camphor, are present in sage [74]; α-Thujone is a neurotoxic monoterpene ketone whose amount may vary according to the harvesting time, being high after flowering and low before flowering [95]. Therefore, an important parameter that must be considered is the variation of the chemical composition of medicinal plants. This variation, in fact, could influence the biological properties of the herb.

5.1. Sage's Effects on Growth Performance

As reported for *O. vulgare* L. and *R. officinalis* L., *Salvia officinalis* has also been studied in several experiments in farmed fish [30,96,97] (Table 3). One study by Sönmez et al. [30] reported the positive effects of a 60-day dietary supplementation of sage oil (0.05, 0.1, and 0.15%) on growth performance and parameters such as SGR and FCR in rainbow trout juveniles. The same results were shown in beluga after 42 days of dietary inclusion of sage ethanolic extract (3, 6, and 12%) [97]. This growth-promoting action could be partially attributed to the sage polyphenolic compounds, such as ursolic acid, a pentacyclic triterpenoid carboxylic acid, which induces muscular hypertrophy in rainbow trout [98]. An increase in growth performance was also reported in gilthead seabream juveniles fed for 92 days with 0.01% of a combined extract of sage and lemon verbena (*Lippia citriodora*) leaf [96].

Table 3. Studies of sage products added to the feed of aquaculture species.

Feeding			Fish			Effects	Ref.
Form	Inclusion Doses (% in Feed)	Period (Days)	Species	Vital Stage	Stress/Toxicant/ Pathogen Challenge		
S. officinalis ethanolic extract	3, 6, 12	42	*Huso huso*	Juvenile		↑ FW, BWI and FCR ↑ RBC, WBC, Hct and Hb ↑ LYS and complement activities ↑ Total Ig levels ↓ Serum ALT and AST levels	[97]
S. officinalis and *Arthrospira platensis* leaf	0.00075, 0.001	28	*Oreochromis niloticus*	Juvenile	*Pseudomonas aeruginosa*	↑ LYS and nitric oxide activites, IgM levels ↑ TNFα and IL-1β	[99]
S. officinalis essential oil	0.05, 0.1, 0.15	60	*Oncorynchus mykiss*	Juvenile		↑ WG, SGR and FCR ↑ SOD, G6PD and GPx activities	[30]
S. officinalis ethanolic extract	0.5, 1, 1.5	30	*Oncorynchus mykiss*	Juvenile	*Streptococcus. iniae*	↑ Total Ig levels	[5]
S. officinalis and *Lippia citriodora* ethanolic extract	0.1	92	*Sparus aurata*	Fingerling	LPS	↑ SGR and FCR ↑ Total serum protein NS on bacteriolytic and complement activities ↑ LYS, IgM, TNFα, IL-1β, TGFβ and IL-10 ↑ SOD and CAT activities	[96]

WG: Weight gain; FW: Final weight; FCR: Feed conversion ratio; SGR: Specific growth rate; BWI: Body weight index; RBC: Red blood cell count; WBC: White blood cell count; Hct: Hematocrit; Hb: Hemoglobin; LYS: Lysozyme; Ig: Immunoglobulin; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; IL-1β: Interleukin-1β; IL-10: Interleukin-10; TNFα: Tumor necrosis factor-α; TGFβ: Transforming growth factor-β; SOD: Superoxide dismutase; CAT: Catalase; GPx: Glutathione peroxidase; G6PD: glucose-6-phosphate dehydrogenase; NS, non-significant effects.

5.2. Sage's Effects on Oxidative Stress

The dietary inclusion of sage protects against reactive oxygen species (ROS) by stimulating the antioxidant defenses in farmed fish [30,96]. In rainbow trout juveniles, different concentrations (0.05, 0.1, and 0.15%) of sage oil added to the diet for 30 days significantly increased liver enzyme SOD, glucose-6-phosphate dehydrogenase (G6PD) and glutathione peroxidase (GPx) activities, while an extension of the feeding trial to 60 days induced a reduction in the antioxidant enzymes activities [30]. A positive modulation on the antioxidant defense system was also reported in gilthead seabream [96]. The findings of Salomón et al. [96] have shown that a 92-day administration of 0.1% dietary additives made of sage and lemon verbena hydroethanolic leaf extract stimulated SOD and CAT gene expression in gilthead seabream fingerlings. According to the authors, the up-regulation of SOD and CAT genes could be linked to the triterpenic and polyphenolic compounds, mainly ursolic acid, present in the sage [96].

5.3. Sage's Effects on Immune Response

Great attention has been given to the utilization of the dietary inclusion of sage to fortify innate immunity in farmed fish. In beluga juveniles, the immunomodulation through the oral administration of sage ethanolic extract for 42 days (3, 6, and 12%) enhanced lysozyme and alternative complement activities, and serum immunoglobulin levels [97].

In addition, in rainbow trout juveniles, 30 days of dietary supplementation of 0.5, 1, and 1.5% of hydroethanolic extracts of sage positively affected the immune system indices (lysozyme and complement activities and total immunoglobulin levels) in a dose-dependent manner [5].

In fish, the immunomodulatory properties of the dietary supplementation of sage combined with other medicinal herbs have also been demonstrated. After a feeding trial of 28 days, the combination of sage and Spirulina platensis (*Arthrospira platensis*) increased the non-specific (lysozyme, IgM and complement) and specific (IL-1β and TNFα cytokines) immune response in Nile tilapia juveniles [99]. In sea bream fingerlings, the dietary administration of 0.1% sage and verbena hydroethanolic leaf extract stimulated the expression of lysozyme, IgM, Il-1β and TNFα, and also increased the anti-inflammatory cytokines TGF-1β and IL-10 levels [96].

5.4. Sage's Effects on Hemato-Biochemical Parameters

The dietary inclusion of sage leads to the improvement of the hemato-biochemical parameters in beluga [97] and seabream [96]. Sage ethanolic extract (3, 6, and 12%), administered for 42 days, stimulated RBC, Hct, Hb, total protein, albumin, and globulin levels in beluga juveniles [97]. Moreover, Dadras et al. [97] reported that the dietary inclusion of sage ethanolic extract decreased the serum ALT and AST levels, supporting the beneficial effect of sage on the physiological status of fish. In fact, AST and ALT enzyme activities are used as stress indicators and the increase in their blood levels indicates liver impairment and hepatocellular damage [69].

5.5. Sage's Effects against Pathogen's Infections

The positive impact of the dietary inclusion of 0.5, 1, and 1.5% hydroethanolic extracts of sage for 30 days on the non-specific and specific immune responses led to an increase in rainbow trout juveniles' resistance against infection with *S. iniae* [5]. The 28-day dietary treatment with sage leaf inclusion protected Nile tilapia juveniles against infection with *Pseudomonas aeruginosa*, causing a significant elevation of the expression of lysozyme, IgM, and pro-inflammatory cytokines (IL-1β and TNFα) [99].

5.6. Conclusions

Based on the reported literature, it could be concluded that the dietary inclusion of sage can improve immune response, antioxidant system activity and stimulate feed intake, leading to enhanced growth performance. The feed incorporation of sage extract at a dosage of between 6–12%, for 42 days, shows important immunomodulatory properties. Regarding the use of sage essential oil, the optimal dose seems to be at 0.05%, with a duration of feed supplementation between 30 and 60 days. In addition, the combination of leaf extracts from sage and other medicinal plants added at low concentrations (0.1%) in the fish diet for long periods (>90 days) could be useful for its beneficial effects in aquafeeds. However, further studies are needed to understand doses and timing of administration in order to optimize the beneficial effects of using sage as a fish feed additive.

6. Thyme

Among the *Lamiaceae* family, the use of the aromatic plant thyme (*Thymus vulgaris*) is common in traditional medicine, food, as well as the pharmaceutical and cosmetic industries [29]. Fresh or dry thyme leaves can be used, and the essential oil can be extracted from flowers. Thyme possesses antiseptic, antinflammatory, antimicrobial and antioxidative properties [100]. Thyme is characterized by well recognized and documented in vitro antibacterial potential [101,102], showing that both thyme extract and essential oil have strong activity against *Escherichia coli*, *Staphylococcus aureus*, *Citrobacter freundii*, *P. aeruginosa*, *Proteus mirabilis, Proteus vulgaris* and *Salmonella typhimurium*. Thyme is rich in monoterpenes such as ρ-cymene, γ-terpinene, carvacrol, and thymol. The concentrations of these four main compounds remain very stable in plants harvested in different seasons, suggesting that they are the compounds that functionally and biologically support the plant [103]. Thyme is also rich in polyphenols, including p-hydroxybenzoic acid, caffeic acid, rosmarinic acid, catechin, luteolin, apigenin, and quercetin [29]. The observed activities of thyme can be ascribed, in particular, to the presence of the caffeic and rosmarinic acids, quercetin and luteolin [100]. Thyme is an immunostimulator and growth promoter in poultry and swine farming; however, knowledge concerning its efficacy in aquatic species is limited to a few studies reporting that the dietary inclusion of thyme was effective in growth stimulation, immune responses, disease resistance and antioxidant enzyme profile in different farmed fish, including Nile tilapia, rainbow trout, and common carp [78,104,105] (Table 4).

Table 4. Studies of thyme products added to the feed of aquaculture species.

Feeding			Fish			Effects	Ref.
Form	Inclusion Doses (% in Feed)	Period (Days)	Species	Vital Stage	Stress/Toxicant/ Pathogen Challenge		
T. vulgaris leaf	0.5, 1, 1.5, 2	56	*Cyprinus carpio*	Fingerling	*Saprolegnia* spp.	↑ WG, SGR and PER ↑ RBC, WBC, Hct and Hb ↑ Total serum protein levels	[104]
T. vulgaris essential oil	0.05, 0.1, 0.15	60	*Oncorynchus mykiss*	Juvenile		↑ WG, SGR and FCR ↑ SOD, CAT, G6PD and GPx activities	[30]
T. vulgaris essential oil	0.05, 0.1, 0.2	60	*Oncorynchus mykiss*	Juvenile	*Aeromonas Hydrophila*	↑ WG and SGR ↑ LYS and complement activities	[106]
T. vulgaris essential oil	1	30	*Oncorynchus mykiss*	Juvenile	Aflatoxin B1	↑ FW, WG, FCR and SGR ↑ LYS and complement activities ↑ Total serum protein levels ↓ TNFα, TGFβ and IL-8 ↑ IL-1β	[107]
T. vulgaris essential oil	1, 2	60	*Oncorynchus mykiss*	Juvenile		↑ FW, WG and SGR ↑ WBC and Hb ↓ ALT, ALP and AST ↑ LYS and complement and total Ig levels ↑ SOD, CAT, GR, and GPx activities	[105]
T. vulgaris leaf	1	140	*Oreochromis niloticus*	Fingerling		↑ WG, SGR and PER	[78]
T. vulgaris essential oil	0.1, 0.5, 1	15	*Oreochromis niloticus*	Juvenile		↑ WBC NS on ALT and AST levels	[108]

WG: Weight gain; FW: Final weight; FCR: Feed conversion ratio; SGR: Specific growth rate; PER: Protein efficiency ratio; RBC: Red blood cell count; WBC: White blood cell count; Hct: Hematocrit; Hb: Hemoglobin; LYS: Lysozyme; Ig: Immunoglobulin; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; ALP: Alkaline phosphatase activity; IL-1β: Interleukin-1β; IL-8: Interleukin-8; TNFα: Tumor necrosis factor-α; TGFβ: Transforming growth factor-β; SOD: Superoxide dismutase; CAT: Catalase; GPx: Glutathione peroxidase; GR: Glutathione reductase; NS, non-significant effects.

6.1. Thyme's Effects on Growth Performance

Several studies have investigated the effect of dietary thyme inclusion on fish growth parameters [78,104–107]. These scientific findings have shown that thyme does not possess adverse or toxic effects and is able to maintain the physiological conditions of the alimentary tract in fish [32,108]. As for the other herbal products, the optimal concentration of thyme is a critically important factor. Rainbow trout juveniles fed on 0.05, 0.1, and 0.2% of thyme essential oil for 60 days showed the best growth performance and parameters (weight gain, SGR, and feed intake) with the dose of 0.05% [30,106]. In common carp fingerlings, the dietary administration of 1.5% of thyme leaf led to the improvement of growth performances after a 56-day feeding trial when compared to the other experimental dietary concentrations tested (0.5, 1, and 2%) [104]. In sturgeon (*Acipenser stellatus*) juveniles, 58 days of feed thyme application improved fish growth at the concentration of 2% [109] compared to the 1% inclusion dose [110].

6.2. Thyme's Effects on Oxidative Stress

The positive role of thyme in enhancing antioxidant capacity has been demonstrated in rainbow trout juveniles [30,105]. For example, 0.05 and 0.1% of thyme essential oil supplementation provided enhanced antioxidant protection, improving liver CAT, SOD, GPx, and glutathione reductase (GR) activities and decreasing MDA production after 30 days of the feeding trial [30]. Thyme essential oil or water extract could successfully mitigate oxidative stress, likely due to their high concentrations of thymol and carvacrol [32]. The antioxidant effects of thymol and its isomer carvacrol have been well documented in several in vitro and in vivo studies, including cell lines [111] and animal models, such as weaning piglets [112].

6.3. Thyme's Effects on Immune Response

Several studies have been carried out to understand the immunomodulatory effects of thyme in fish. Thyme dietary inclusion is capable of stimulating the non-specific immune response in rainbow trout, including lysozyme, alternative complement and total immunoglobulin levels [105,106]. Furthermore, dietary 1% of thyme essential oil counteracted the negative effects on immunity and intestinal inflammation induced by aflatoxin B1 in rainbow trout juveniles, significantly lowering the expression levels of TNFα, IL-8 and TGF-β [107]. The immunomodulatory effects of thyme are linked to its major bioactive components, such as carvacrol, thymol, eugenol, and cymene [106]. Thymol feed supplementation, for example, improved the immunoglobulin levels in broiler chickens [113] and in pigs' guts [114].

On the contrary, the feeding inclusion of 0.1, 0.5, and 1% of thyme essential oil for a short period (15 days) did not alter respiratory burst activity, lysozyme concentration, or alternative complement activity in Nile tilapia juveniles [108]. These results confirm the importance of the optimal choice of the duration of immunostimulant administration.

6.4. Thyme's Effects on Hemato-Biochemical Parameters

In farmed fish, the increase in blood parameters (Hb, RBC, and WBC counts) and the improvement of biochemical profile (total protein, albumin and globulin levels) suggest that the dietary inclusion of thyme products are safe feed additives able to enhance fish health and welfare. In Nile tilapia juveniles, 0.1, 0.5, and 1% of thyme essential oil for 15 days led to a significant increase in total leukocytes (monocytes, neutrophils, basophils and lymphocytes), especially at the highest dose (1%) [108]. The safety of thyme as a fish feed additive is also confirmed by the absence of negative or toxic effects on ALT and AST levels [106,108]. For example, the inclusion of up to 0.2% of thyme oils over 2 months did not alter the activity of these enzymes in rainbow trout juveniles, suggesting that thyme oils at up to 0.2% in feed can be considered as a safe additive for trout [106].

6.5. Thyme's Effects against Pathogen's Infections

Thyme also improves fish disease resistance against several bacteria and fungi, such as *Saprolegnia* spp. [104], *A. hydrophila* [106], *Yersinia ruckeri* [115], and *S. iniae* [116]. The efficacy of thyme essential oil or leaf powder could be a consequence of the increasing levels of the main immunity factors (lysozyme, alternative complement, immunoglobulin and cytokynes) and hemato-biochemical parameters. Feed supplementation of 0.05% thyme essential oil improved the resistance of rainbow trout juveniles against motile *Aeromonas* septicemia caused by *A. hydrophila* via the upregulation of the C3 and CD4 immune genes and the increase in IL-1β cytokine gene expression [106]. In fish, CD4 T helper cells provide a protective response against bacteria, fungi, and protozoa and C3 protein is crucial for the activation of both classical and alternative complement pathways [117].

6.6. Conclusions

Based on the reported literature, it can be observed that periods of 60 days of feeding supplementation with 0.5-1% of thyme essential oil can be considered a proper length of time and percentage to stimulate the cellular components of the non-specific immune response, enhance the growth performance and disease resistance against pathogens. On the contrary, short-term supplementation (such as 15 days) of 1% of thyme essential oil does not show beneficial effects. Regarding the use of thyme leaf powder, the feeding supplementation dose of 1% shows positive effects even in very long administration periods (140 days).

7. Mint

Another aromatic plant belonging to the family *Laminaceae* that captured the attention of researchers for its use in aquaculture is mint, also known as mentha or peppermint (*Mentha piperita*). Mint is a perennial herbaceous plant and is widely cultivated [118]. Peppermint is a crucial medicinal and aromatic plant, used in food since ancient times, and more recently in sanitary and cosmetic industries [119]. Several studies have confirmed its antimicrobial, antioxidant, and immunomodulatory effects [118]. The beneficial activities of mint, especially its antimicrobial effect, are due to its major compounds, such as menthol (33.8%), menthone (15.8%) and pulegone (8.3%) [119,120]. Used in perfumery and aromatherapy, pulegone and menthol are potentially toxic compounds when administered in large amount, causing liver damage in rats [121]. On the contrary, menthone has a digestive favoring effect and is non-toxic [120]. Mint also presents a high polyphenolic content (19–23%), primarily characterized by rosmarinic acid, luteolin, hesperidin and apigenin [122].

7.1. Mint's Effects on Growth Performance

The incorporation of mint into the diets of fish showed positive growth- stimulating effects, improving GR, WGR, and FCR in several fish species, such as Asian sea bass (*L. calcarifer*) [123], Nile tilapia [124], Caspian brown trout (*Salmo trutta caspius*) [125], and Caspian white fish (*Rutilus frisii kutum*) [126]. In Caspian white fish juveniles fed with 1, 2, and 3% of peppermint hydroalcoholic extracts for eight weeks, the growth parameters increased in a dose-dependent manner [126]. Mint could be considered as an appetite activator that significantly increases the daily feed intake [123]. Furthermore, the beneficial effect of mint feed inclusion on growth parameters could be attributed to its influence on intestinal enzymes (amylase and protease) and microbiota, leading to an improvement of the digestibility and availability of nutrients [126]. Interestingly, after a 60-day feeding trial, the dietary inclusion of 0.01 and 0.025% of mint essential oil enhanced intestinal health and increased the length of the intestinal villi [127]. On the contrary, the dietary supplementation, for 50 days, of mint essential oil at 0.075, 0.125, and 0.25% did not cause significant differences in growth compared to the control group in Nile tilapia fingerlings [120]. The possible explanation for this lack of beneficial effects on growth performance may be caused by small quantities employed in the study as the effect of mint is dose-dependent [126,128].

7.2. Mint's Effects on Oxidative Stress

Mint as a feed additive is effective in improving oxidative stress induced by the main environmental stressors, such as the water pollutants ammonia [129] and pesticides [124]. Nile tilapia juveniles fed on 0.25% of mint essential oil for 30 days displayed enhanced CAT, SOD, and GPx gene expression levels, allowing a reduction in the oxidative stress induced by pesticides toxicity exposure [124]. Similarly, oral administration of menthol at 0.25% improved the antioxidative status in common carp juveniles, mitigating the ammonia-induced alterations on antioxidant enzymes activities [129]. The antioxidant effects of mint are mainly attributable to the monoterpenic ketones mentone and isomentone [118].

7.3. Mint's Effects on Immune Response

Recently, great attention has been given to the immunostimulating effect of mint on different fish species, including rainbow trout [130,131], tilapia [120,127], common carp [132], sea bass [133], Caspian brown trout [125], and Caspian kutum [126] (Table 5).

Table 5. Studies of mint products added to the feed of aquaculture species.

Feeding			Fish			Effects	Ref.
Form	Inclusion Doses (% in Feed)	Period (Days)	Species	Vital Stage	Stress/Toxicant/ Pathogen Challenge		
M. piperita essential oil	0.01, 0.025	60	*Lates calcarifer*	Fingerling	*Vibrio harveyi*	↑ WG and FCR ↑ RBC, WBC, Hct and Hb ↑ Phagocytic activity, respiratory burst, LYS, anti-protease and bactericidal activities ↑ Total serum protein and globulin levels	[123]
M. piperita essential oil	0.075, 0.125, 0.25	50	*Oreochromis niloticus*	Fingerling		↑ Complement activity ↑ SOD, CAT, G6PD and GPx activities NS on ALT and AST levels NS on RBC, WBC, Hct and Hb NS on total protein levels	[127]
M. piperita essential oil	0.25	30	*Oreochromis niloticus*	Fingerling	*Streptococcus agalactiae*	↑ Total serum protein levels NS on growth parameters NS on LYS activity	[120]
M. piperita hydroalcoholic extract	1, 2, 3	56	*Oreochromis niloticus*	Juvenile	Chlorpyrifos	↑ FW, WG and SGR ↑ RBC, WBC, Hct and Hb ↓ ALT, ALP and AST	[124]
M. piperita hydroalcoholic extract	1, 2, 3	56	*Oncorynchus mykiss*	Juvenile	*Yersinia ruckeri*	↑ LYS activiys and total Ig levels ↑ Total serum protein and albumin levels NS on ALT, ALP and AST levels ↑ SOD, CAT, GR, and GPx activities	[130]
M. piperita hydroalcoholic extract	1, 2, 3	56	*Rutilus frisii kutum*	Juvenile		↑ WG and SGR ↑ LYS and respiratory burst activities ↑ RBC, WBC, Hct and Hb	[126]
M. piperita hydroalcoholic extract	1, 2, 3	56	*Salmo trutta caspius*	Juvenile		↑ WG, SGR and FCR ↑ LYS and alkaline phosphatase activities ↑ RBC, WBC, Hct and Hb ↑ Total serum protein levels NS on ALT, ALP and AST levels	[125]

WG: Weight gain; FW: Final weight; FCR: Feed conversion ratio; SGR: Specific growth rate; RBC: Red blood cell count; WBC: White blood cell count; Hct: Hematocrit; Hb: Hemoglobin; LYS: Lysozyme; Ig: Immunoglobulin; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; ALP: Alkaline phosphatase activity; SOD: Superoxide dismutase; CAT: Catalase; GPx: Glutathione peroxidase; GR: Glutathione reductase; G6PD: glucose-6-phosphate dehydrogenase; NS, non-significant effects.

A four-week period of dietary supplementation of horsemint (*Mentha longifolia*) hydroalcoholic extract at 0.1, 0.2, and 0.3% improved the non-specific immunity response (lysozyme and complement) and immune-related genes (TNFα) in rainbow trout juveniles, especially at the dose of 0.3% [131]. Similarly, in the same fish species, the improvement of lysozyme activity in a dose-dependent manner was reported after a 56-day feeding trial with 1, 2, and 3% of mint hydroalcoholic extract [130]. The enhancement of the immune system was also observed in juveniles of Caspian brown trout [125] and Caspian kutum [126]. Results of both studies showed that 56 days of dietary inclusion of 1, 2, and 3% of dried mint powder improved the immunological parameters in a dose-dependent manner. On the contrary, in Nile tilapia fingerlings, 60 days of feeding with 0.01 and 0.025% of mint essential oil did not alter the lysozyme levels, while the activation of the complement system was significantly increased, especially at the concentration of 0.025% [127].

7.4. Mint's Effects on Hemato-Biochemical Parameters

The improvement of the haematological and biochemical parameters due to the dietary inclusion of mint dried leaf, essential oil and hydroalcoholic extract were also observed [123–126,130]. Dietary administration, for eight weeks, of mint hydroalcoholic extract at 3% improved the RBC, Hb, and WBC levels in the rainbow trout juveniles [130], Caspian brown trout [125], and Caspian white fish [126]. Mint is rich in vitamins, such as vitamins A, C, and E, and in mineral salts, such as iron, potassium, and calcium [119]. Some studies have suggested that mint used as food additive favors the intestinal absorption of iron and vitamins, increases hematopoiesis and, consequently, the hematological indices [134,135]. Moreover, mint-integrated diets enhanced serum biochemical parameters, resulting in the reduction in serum glucose, lipids, triglycerides and cholesterol levels, and in an increase in total protein, albumin and globulin levels [123,127,130].

7.5. Mint's Effects against Pathogen's Infections

Several studies have revealed the efficacy of mint dried leaf, essential oil and hydroalcoholic extract on the protection against *S. agalactiae* [120], *Vibrio harveyi* [123], and *Y. ruckeri* [130]. In rainbow trout juveniles, the oral supplementation of 1, 2, and 3% of mint hydroalcoholic extract for 56 days significantly enhanced serum bactericidal and antiprotease activity, protecting from infections and giving resistance to the pathogens [130]. Moreover, the oral supplementation of mint essential oil or hydroalcoholic extract increased fish survival in experimental challenge tests, modulated haematological RBC and WBC counts, parameters of non-specific and specific immunity (lysozyme and complement activities and Ig levels) and increased cytokines expression (TNFα, IL-1β, IL-8) [120,130,131].

7.6. Conclusions

Based on the reported literature, the fish dietary incorporation of mint is able to improve the haematological and immune response parameters and provide resistance against pathogenic infections in a dose-dependent manner. Mint hydroalcoholic extracts should be used in fish feed at a concentration range of between 2–3% for a duration of 56 days. Regarding the use of mint essential oils as a fish feed additive, low doses (0.075–0.125%) of feed supplementation shows benefits to intestinal health and immune response, while higher doses (0.25%) are necessary to stimulate growth and improve haematological parameters.

8. General Conclusions and Future Perspectives

This review summarizes the findings regarding the role of the species of *Lamiaceae* family as feed additives in aquaculture. According to studies conducted with medical herbs, oregano, rosemary, sage, thyme, and mint (whole plant, extract or essential oil) have the potential for use as safe additives in fish feed, showing benefits on growth performance, immune system, antioxidant status, hemato-biochemical parameters and resistance to stress, parasites and bacteria.

Considering the scientific literature reported in this review, it is possible to indicate that great importance must be given to the choice of suitable dosage and administration time to obtain positive effects on fish health. A specific dose may induce beneficial impacts such as immunostimulation, whereas an unfavorable dose may not cause any responses, or may even be cytotoxic. Consequently, the optimization of the dosage according to the plant and the type of material chosen is strongly recommended. Moreover, as several *Lamiaceae* plants have been shown to have a dose-dependent effect, further studies are required to understand the toxicological safety of these feed additives.

The employment of *Lamiaceae* plants is an interesting field in aquaculture; however, there are still numerous research gaps. Foremost, comparative studies concerning the part of the *Lamiaceae* plants and the type of extraction (leaves, extract, mixed, or essential oil), the optimal administration method (immersion, injection or oral administration), and the duration of administration are necessary to gather information about the best beneficial effects on fish health and the parameters of interest in aquaculture, primarily growth performance and immune response. Additionally, as the impact of a feed supplement is species-specific, further research is required on the use of the *Lamiaceae* family in order to identify the plant species and products with the best beneficial potential for each fish species of interest in aquaculture.

Moreover, in a considerable number of the reviewed studies, the chemical characterization of the fish feed supplements is absent; thus, the chemical analysis of *Lamiaceae* products used as feed additives should be encouraged, with the aim of identifying and quantifying the active molecules and establishing their proper dosages and the duration of administration. Detailed information about the chemical compositions of *Lamiaceae* species could help critically analyze their effectiveness as growth promoters, immunostimulants, and antioxidant agents. In addition, the knowledge of the chemical composition could open the way to a possible correlation between the bioactive compounds present in the fish feed supplement used and the results obtained. As has previously been reported, the chemical composition of plants is influenced by numerous factors, such as the form and type of extraction (Table 6).

Table 6. The major bioactive compounds identified in essential oil, hydrolcoholic extract and leaves of *Lamiaceae* plants (oregano, rosemary, sage, thyme and mint).

Lamiaceae	Form	Main Bioactive Components	Method of Analysis	Ref.
Oregano	Essential oil	Carvacrol (63%), ρ-Cymene (12.8%), γ-Terpinene (8.4%), Thymol (4.7%)	H-R GC	[40]
	Hydroalcoholic extract	Carvacrol (59.4%), Thymol (25%), ρ-Cymene (6.9%), 1-Octacosanol (4%)	GC/MS	[62]
	Dry leaves	Carvacrol (63%), ρ-Cymene (12.8%), γ-Terpinene (8.4%), Thymol (4.7%)	H-R GC	[54]
Rosemary	Hydroalcoholic extract	Camphor (4.8%), Phytol (3.28%), Borneol (3.27%), Caryophillene (3.20%)	GC-MS	[136]
	Dry leaves	α-Pinene (21.65%), β-Pinene (12.58%), Camphene (12.54%), Limonene (7.22%), Camphor (5.29%)	HS-SPME-GC-MS	[74]
Sage	Essential oil	α-Thujone (10–60%), β-Thujone (4–36%), Camphor (5–20%), 1.8 –Cineole (2–15%)	H-R GC	[29]
	Hydroalcoholic extract	Manool (7%), β-Thujone (6.2%), Carnosol (2.4%), Camphor (4.8%)	GC/MS	[137]
	Dry leaves	β-Thujone (27%), 1.8 –Cineole (19.55%), β-Pinene (11.36%), Camphor (8.62%)	HS-SPME-GC-MS	[74]
Thyme	Essential oil	Thymol (37–55%), ρ-Cymene (14–28%), γ-Terpinene (4–12%), Carvacrol (0.5–5.5%)	H-R GC	[105]
	Hydroalcoholic extract	Thymol (42.6%)	GC/MS	[138]
	Dry leaves	ρ-Cymene (30.35%), γ-Terpinene (11.85%)	HS-SPME-GC/MS	[74]
Mint	Essential oil	Menthol (33.8%), Menthone (15.2%), Methyl acetate (13%), Pulegone (8.3%)	H-R GC	[120]
	Hydroalcoholic extract	Menthone (25.4%), 1,8-cineole (17.7%), Menthol (12.1%)	GC/MS	[139]
	Dry leaves	Menthol (35–60%), Menthone (2–44%), Methyl acetate (0.7–23%), 1.8—Cineole (1-13%), Menthofuran (0.3–14%)	GC/MS	[140]

H-R GC: High-Resolution Gas Chromatography; GC/MS: Gas chromatography/mass spectrometry; HS-SPME-GC/MS: Headspace solid-phase microextraction- Gas chromatography/mass spectrometry.

This variation of bioactive compounds could be reflected in the biological properties of the herb used as feed additives. In our opinion, the knowledge of the chemical composition of *Lamiaceae* plants or products represents an important parameter that must be considered in order to standardize the use of medicinal herbs in fish nutrition.

In addition, the knowledge of the mechanism of action of the bioactive molecules present in medicinal plants is still scarce. The understanding of the mechanisms of action of the bioactive compounds contained in *Lamiaceae* plants used as feed additives could elucidate the cellular and molecular processes underlying their capabilities of enhancing growth performance, immune system, and antioxidant status.

In conclusion, plants of the *Lamiaceae* family represent an exciting research field in aquaculture and a natural, economical, sustainable, and safe source of feed integrators capable of enhancing the health of farmed fish. However, although these are natural products, it is necessary to take into account the criteria for the safe use of plant ingredients in diets for farmed fish according to legislation, which differs among countries. Within the European Union, the safe use of oregano, rosemary, sage, thyme, and mint as feed additives for animal nutrition is approved and governed by regulation (EC) 1831/2003 of the European Parliament and of the Council of 22 September 2003 (https://www.efsa.europa.eu/it/applications/feedadditives/regulationsandguidance accessed on 1 November 2022).

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