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The role of oregano herb and its derivatives as immunomodulators in fish

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Abstract

The motivation behind this article is to give point-by-point data about the beneficial applications of oregano feed supplement in fish diets as immunomodulators, antioxidant, antiviral, antifungal and antiparasitic. Use of this plant as feed additive plays an important role in the fish diet when compared to other synthetic feed additives. Oregano is rich in phytochemical compounds including carvacrol and thymol in addition to other phenolic compounds with antioxidant and immune-enhancing activities. *Origanum vulgare* extract improved the immunological responses and enhanced non-specific immunity. Also, non-specific immunity and the lysosomal activity were significantly increased in rainbow trout fed diet enriched with 3.0 mL essential oil of *Origanum onites* L kg^{-1} diet for 60 days. Furthermore, non-specific immune stimulant, antioxidant and nitric oxide activities were improved due to *O. vulgare* oil supplementation. In some recent studies, *Origanum heracleoticum* L essential oil as a growth enhancer increased the antioxidant status. In rainbow trout, the hepatic levels of antioxidant enzymes and the total antioxidant capacity increased by feeding diet enriched with 6 and 10 g kg^{-1} diet of *O. vulgare* extract. Therefore, the addition of oregano and/or derivatives as a dietary supplement in fish diet may promote growth and enhance the immunity and health of fish and this will be useful for nutritionists, physiologists and veterinarians.

Key words: antioxidant, essential oils, fish, health, immunity, nutrition, Origanum vulgare.

Introduction

Fish are usually under stressful conditions due to the exposure to various infectious agents such as bacteria, fungi, viruses and parasites spread in their farms (Walker & Winton 2010; Lightner *et al.* 2012). Immune systems may not have the full capacity to efficiently avoid and eliminate such infections; therefore, antibiotics have been usually used in the feed or water to control bacterial diseases, increase the productivity and decrease the mortalities in fish farms (Finlay & McFadden 2006; Cabello 2006). However, this random use could be hazardous to the ecosystem due to the development of antibiotic resistance (Cabello 2006). Therefore, medicinal plants and their extracts have been widely used as immunostimulants during the last decade in different aquaculture systems (Vaseeharan & Thaya 2014).

Plants and their extracts showed various beneficial activities in aquacultures, such as antistress, antipathogen, appetite-stimulating, growth-promoting, tonicity-enhancing and immunostimulatory activities (Murthy *et al.* 2013; Ramudu & Dash 2013; Reverter *et al.* 2014; Syahidah *et al.* 2015; Valladão *et al.* 2015). Herbal medicine has been reported to improve the immune response and haematological parameters as well as decrease losses from bacteria, viruses and parasites in both freshwater and marine fish species (Harikrishnan *et al.* 2011; Harikrishnan *et al.* 2012).

Origanum species are members of the family Lamiaceae grow naturally in Mediterranean zone and Eurasia. They contain high amounts of essential oils and have been widely used in many countries as folk medicine and species (Chishti *et al.* 2013). *Origanum vulgare* L is an aromatic enduring herb and grows freely in every part of Europe.

During flowering season, the collected parts have considerable amounts of volatile oil (0.18–0.45% 0.32–1.02%). Essential oils (Eos) are highly volatile compounds composed mainly from hydrocarbons, ketones, aldehydes, alcohols, ethers, phenols, and esters of phenolic and terpenic origins (Thompson *et al.* 1989).

A considerable number of sweet-smelling medicinal plants or their essential oils concentrates have good impacts on the feed consumption and utilization and carcasses output of fish when added to the water or feeds (Abd El-Hack *et al.* 2016; Barakat *et al.* 2016; Alagawany *et al.* 2017, 2018; Mohamed *et al.* 2019). The pharmacodynamics effect of the oregano extract returned to its bioactive components, acting in synergistic manner to give its principal activities as diuretic, antispasmodic, stomachic, antiparasitic,immunomodulatory and antimicrobial (fungicidal, bactericidal and viricidal) agents (Karanika *et al.* 2001; Sökmen *et al.* 2004; Fernandes *et al.* 2012; Santo *et al.* 2019; Abdel-Latif *et al.* 2020).

Phenolic acids and flavonoids are among the most studied and most abundant phytochemicals in oregano species (Gutiérrez-Grijalva *et al.* 2018). In this article, we have described the beneficial applications of oregano species in fish nutrition and health including immune and antioxidant properties. The information presented in this paper would be useful for nutritionists, scientists, researchers, medical professionals, pharmacists, veterinarians, students and fish producers.

Chemical composition and structure of or Origanum species

Table 1 shows the scientific classification of oregano herb. Additionally, the morphology of some oregano species is shown in Figure 1. It has been reported that almost all Origanum species contain less or more the same components, chemical compositions and the component concentrations depending on the differences in geographical origin, genotype, climatic conditions, composition and type of soil, plant development, culture condition and time of harvesting (Rodriguez-Garcia *et al.* 2016). The essential oils of Origanum species (OEO) contain phenolic, polyphenolic, flavonoids and alkaloids (Liolios *et al.* 2010; Chishti *et al.* 2013). The main OEO constituents are the oxygen monoterpenes thymol and carvacrol (El Gendy *et al.* 2015). Carvacrol and thymol are isomeric phenolic compounds responsible for the properties and characters of the OEO. One example of oregano species is *Origanum onites* L. belongs to the family Lamiaceae which is an aromatic herb cultivated in the Mediterranean region and Aegean in Turkey. This herb has been reported to have various pharmacological actions and traditional uses (Dundar *et al.* 2008). The essential oil (EO) of *O. onites* composed mainly of thymol, gamma-terpinene, p-cymene, carvacrol, borneol, alpha-terpinene and linalool (Karousou & Kokkini 2003; Demirci *et al.* 2004). Carvacrol is the main EO constituent in Turkish oregano (Kirimer *et al.* 1995). Additionally, more than sixty different bioactive molecules have been determined in oregano; among them, thymol and carvacrol represents the primary components which are about 80 per cent, while lesser abundant molecules include spathulenol, γ-terpinene, p-cymene, caryophyllene, germacrene-D and β-fenchyl alcohol. The molecular structures of chemical compounds are described in Figure 2.

Biological activities and beneficial aspects

The biological activities and beneficial aspects of oregano and its derivatives in fish are shown in Figure 3.

Growth-promoting activities

The essential oil of oregano (OEO) has been described as promising alternative to dietary antibiotics mainly owing to its useful biological activities. The dietary supplementation of OEO in fish has been reported to improve the rate of growth and feed utilizations (Ferreira *et al.* 2014; Diler *et al.* 2017). Dietary supplementation of oregano oil enhanced the growth rate, content of muscle protein, the survival rates, feed efficiency and disease resistance of shrimp, *Nile tilapia* fingerlings and channel catfish *Ictalurus punctatus* (Ching 2008; Zheng *et al.* 2009). Ahmadifar *et al.* (2011) proved that supplemental thymol and carvacrol extracted from oregano increased the rainbow trout growth. In same trend, Chishti *et al.* (2013) found that thymol- and carvacrol-based feed supplements had positive impact on performance of and feed utilization trout. However, in tilapia, Santo *et al.* (2019) concluded that use of dry oregano leave (DOL) in the diets did not impact growth rate, haematological indices and fillet composition, while there was a significant increase in digestible energy. The efficacy of EOs as growth promoters could be possibly related to the digestive enzymes activation. OEO as a

Table 1 Scientific classification of *Origanum species*

Kingdom	Plantae
Clade	Angiosperms
Clade	Eudicots
Clade	Asterids
Order	Lamiales
Family	Lamiaceae
Genus	*Origanum*
Species	*Origanum vulgare*
	Origanum onites L.
	Origanum heracleoticum

Figure 1 Morphology of some oregano species. (a) *Origanum vulgaris*, (b) *Origanum onites*, (c) *Origanum heracleoticum*, and (d) oregano powder.

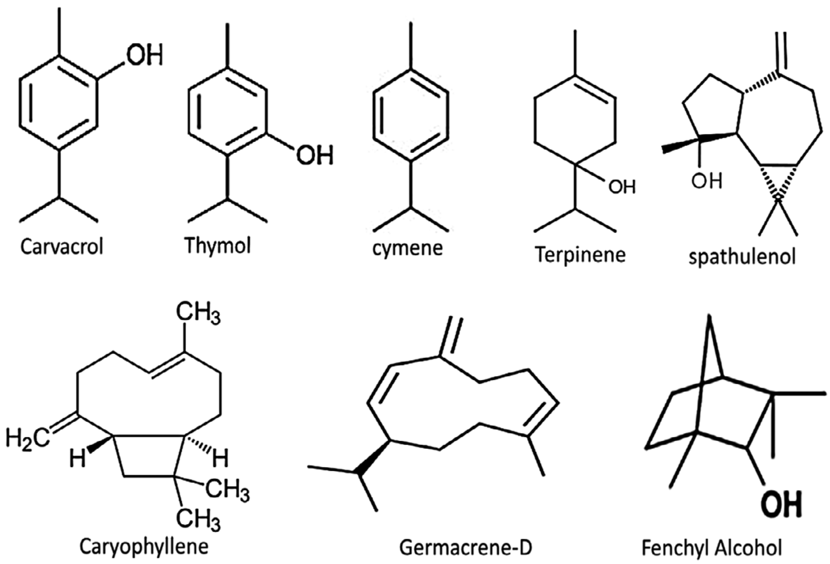

Figure 2 The molecular structure of chemical compounds in oregano oil.

dietary supplement showed positive impacts on the secretions of digestive enzymes in poultry (Lee *et al.* 2003; Jang *et al.* 2007). Zhang *et al.* (2020) stated that supplementation of OEO could stimulate the digestive functions in fish via increasing the activities of protease, amylase and lipase. Additionally, the dietary supplementation of OEO can promote the growth due to their antioxidant effect and aromatic flavour, which play an important role as a strong appetizer resulting in increasing fed intake and body weight gain and consequently the rate of growth (Abdel-Latif & Khalil 2014). Revilla *et al.* (2019) reported that OEO from *O. vulgare* could be used as a valuable alternative to some antibiotics (oxytetracycline, florfenicol and enrofloxacin) for improving the embryogenesis and early-stage larva of *Nodipecten subnodosus*.

Effect on intestinal health

The small intestines play a principle role in growth of fish as they are the primary sites for nutrients absorption (Adeshina *et al.* 2019; Dawood *et al.* 2020a). In fish, the healthy intestinal tract is leading to enhanced growth performance as the improvement of gut health; feed efficiency and absorption of nutrients are usually associated to the long villi of the intestine (Lauriano *et al.* 2016; Huerta-Aguirre *et al.* 2019). Feeding of OEO to the fingerlings of common carp (*Cyprinus carpio* L.) significantly improved the intestinal morphometry (villus height, villus width, crypt depth; Abdel-Latif *et al.* 2020). Similarly, Abd El-Naby *et al.* (2020) reported that dietary supplementation with thymol increased the villus height in intestine of Nile tilapia.

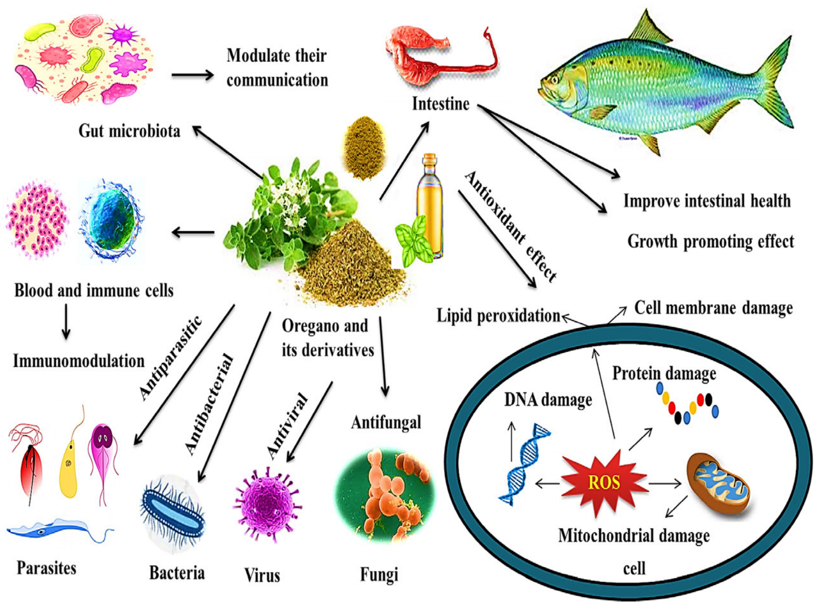

Figure 3 Biological activities and immunomodulatory effects of oregano and its derivatives in fish.

However, supplementation of dry oregano leaves to Nile tilapia diet did not significantly alter the intestinal villi height compared to unsupplemented group (Santo *et al.* 2019). The enhance morphometry of small intestine could be attributed to the increase in the surface area for absorption by increasing the villus height and width leading to improving the absorption of important nutrients from fish intestine (Abdel-Mohsen *et al.* 2018; Abdel-Tawwab & Monier 2018; Adeshina *et al.* 2019; Zhou *et al.* 2019). Furthermore, application of carvacrol and thymol as dietary supplementations in tilapia could upregulate the genes encoding intestinal-tightening TJ proteins and enhanced the goblet cells proliferation suggesting the efficacy of such phenolic compounds in improving the epithelial and mucosal barriers of the intestine thereby increasing the pathogen resistance in fish (Ran *et al.* 2016).

Ferreira *et al.* (2016) found that the addition of oregano oil to diet of Yellow Tail Tetra fish increased absorptive area of the intestine beside a great deposition of glycogen in the hepatocytes. Gonçalves *et al.* (2019) reported that the commercially available feed additives contain a blend of EOs such as Biomin® Digestarom PEP MGE 150, could be successfully integrated in fish meal formulations to lower the cost of feeding without affecting the health and performance of fish and to improve intestinal villi, feed utilization, overall growth and consequently fish production.

Effect on gut microbiota

Alterations in microbial populations of gastrointestinal tract (GI) occur through the early periods of development of fish when the immune system is taking place (Rombout *et al.* 2011). This microbial populations and their metabolites have extensive impacts on the host health by changing of the metabolic functions and immune system (Lazado & Caipang 2014). The EOs have a positive effect against pathogenic bacteria than commensal bacteria and inhibit certain bacterial groups in the gastrointestinal tract (GI; Si *et al.* 2006; Ouwehand *et al.* 2010). Navarrete *et al.* (2010) studied the effects of EOs on bacterial composition in the gut of *Oncorhynchus mykiss* and reported that the gut microbiota was not affected by EOs.

Dietary supplementation with the combination of thymol and carvacrol increased resistance to bacterial infection in fish (Zheng *et al.* 2009). The impacts of carvacrol and thymol (commercial mixture product) on intestinal microbiota of hybrid tilapia (*Oreochromis aureus* and *Oreochromis niloticus*) were investigated by Ran *et al.* (2016). After six weeks of feeding, a substantial alteration in the intestinal microbiota was observed with EOs supplementation. Similarly, Zhang *et al.* (2020) demonstrated that OEO could modulate the microbiota in the koi carp (*C. carpio*) intestine by increasing the beneficial communities of Propionibacterium, Corynebacterium and Brevinema. Abdel-Latif *et al.* (2020) reported that the alteration of gut microbiota induced by OEO administration to common carp resulted in downregulation of the expression of gut pro-inflammatory genes (TGF-β and TNF-α).

Antibacterial effect

A huge number of active metabolites of antibacterial activity have been detected in Origanum, such as carvacrol, thymol, c-terpinene and p-cymene (Karousou & Kokkini 2003). Thymol and carvacrol are the major components of oregano oil; both components have antimicrobial (Sivropoulou *et al*. 1996; Ultee *et al*. 1998), insecticidal (Karpouhtsis *et al*. 1998), antioxidant (Botsoglou *et al*. 2003) and antimycotic (Kocić-Tanackov *et al*. 2012). These OEO activities have been related to the lipophilic prosperity of phenolic constituents and to the phenolic–OH group which could react with the active sites in the enzymes forming hydrogen bond (Farag *et al*. 1989; Conner 1993).

Thymol and carvacrol can also induce disruption in the integrity of membrane, alteration in the pH homoeostasis, the equilibrium of inorganic ions and the release of materials associated with outer membrane from cells to the surrounding external media (Helander *et al*. 1998; Lambert *et al*. 2001). Additionally, Lambert *et al*. (2001) stated that thymol and carvacrol mixture could induce bacterial inhibitory effect similar to that of OEO where they showed 96% similarity to OEO in inhibiting the growth of *Pseudomonas aeruginosa*. The synergistic effects of minor components in OEO in inhibiting bacteria have been reported by Lambert *et al*. (2001).

OEO has a wide variety of active components in low concentrations, including γ-terpinene, α-terpinene, ρ-cymene, linalool and borneol (Baydar *et al*. 2004; Bayramoglu *et al*. 2008). The ρ-cymene and carvacrol showed synergistic effect against Bacillus cereus, Escherichia coli O157:H7 and Edwardsiella tarda (Ultee *et al*. 2002; Kiskó & Roller 2005; Rattanachaikunsopon & Phumkhachorn 2010a).This could be returned to the ability of ρ-cymene to swell the cell membrane of bacteria, allowing the transportation of carvacrol inside the cell (Ultee *et al*. 2002).

The essential oils of Origanum species (OEO) were more effective than thymol, carvacrol or their mixture in increasing the growth, antioxidant properties and resistance to *A. hydrophila* in channel catfish (Zheng *et al*. 2009), tilapia (Rattanachaikunsopon & Phumkhachorn 2010a; Santo *et al*. 2019), rainbow trout (Diler *et al*. 2017) and common carp (Abdel-Latif *et al*. 2020).

Nazzaro *et al*. (2013) proved that the EOs were effective in improving fish resistance against bacterial infections by adding thymol, limonene, citral, carvacrol 1,8 cineole and cinnamaldehyde in fish diets. Recent works revealed that the use of EOs in fish diet must be added several days before infection to enhance immunity, improve resistance, decrease the effects of pathogenic bacteria and prevent outbreaks (Awad & Awaad 2017; Sutili *et al*. 2017).

Oregano supplementation also promoted growth and exerted an immuno-potentiating action in *O. niloticus*, *O. mykiss*, *I. punctatus* and yellowtail tetra *Astyanax lacustris* (Zheng *et al*. 2009; Abdel-Latif & Khalil 2014; Ferreira *et al*. 2014; Diler *et al*. 2017). Dietary supplementation with 0.02% OEO is a prevention strategy for *T. truttae* and *I. salmonis* infection in hatchery-reared juveniles of *O. keta*. However, OEO in diet did not prove to be effective in improving the zootechnical performance or increasing the resistance of silver catfish juveniles to *I. multifiliis* (Cararo *et al*. 2017).

Nazzaro *et al*. (2019) added that terpenoids (carvacrol, linalyl acetate, linalool, thymol, geraniol, piperitone and menthol citronellal) have antibacterial effects due to the presence of functional group on the bacterium outer membrane, leading to changing the membrane fluidity and/or permeability and altering their periplasmic enzymes and protein content. This came on line with Helander *et al*. (1998) who stated that carvacrol essential oil is able to break up the outer membrane of bacteria (Gram-negative) via changing the permeability of the cytoplasmic membrane and releasing lipopolysaccharides. Navarrete *et al*. (2010) also studied the *in vitro* antibacterial effect of EOs in fish pathogens, and they stated that the required dose of EOs to inhibit pathogenic bacteria was higher than the dose used in the *in vivo* study.

Nevas *et al*. (2004) stated that Gram-positive bacteria were more sensitive to OEO than *Gram*-negative ones. Additionally, Stefanakis *et al*. (2014) stated that EO from *O. vulgare subsp. hirtum*, *Origanum marjorana* and *O. onites* when used in rotifer's disinfection applied for feeding of fish showed a significant reduction in the Vibrio spp concentration with higher survival rates of rotifers with 10 ppm of EO. The OEO as dietary supplement could inhibit the growth of Vibrio bacteria in common carp (Abdel-Latif *et al*. 2020) and in shrimp (Gracia-Valenzuela *et al*. 2014).

Antiviral, antifungal and antiparasitic activities

The OEO and different extracts (aqueous, dicholoromethane, methanol or hexane extracts) have been reported to have antiviral activities (Sökmen *et al*. 2004; Fernandes *et al*. 2012) due to the presence of the active molecules. Moreover, OEO and extracts (ethanolic and aqueous) and other parts of the plant showed antifungal properties (Karanika *et al*. 2001) which could be mainly attributed to the presence of carvacrol and thymol (Sökmen *et al*. 2004; Portillo-Ruiz *et al*. 2012). OEO has antiparasitic activities as reported by (Giannenas *et al*. 2003; Karagouni *et al*. 2005; El Babili *et al*. 2011). Similarly, the acetyl and methanolic extracts of origanum species showed antiparasitic properties (Lahlou 2002; El Babili *et al*. 2011; Degerli *et al*. 2012).These activities could be returned to the phenolic components such as carvacrol and thymol which are able to interact with cytoplasmic membrane of the cell and alter its permeability (Giannenas *et al*. 2003). Moreover, OEO has flavonoids and terpenoids which showed antiparasitic action and improved the innate immunity and phagocytic activities of the host (Karagouni *et al.* 2005). Moreover, OEO as dietary supplement could protect from infections and crustacean parasites in different fish species like channel catfish (Zheng *et al.* 2009), *Sharpsnout seabream* (Athanassopoulou *et al.,* 2004), *Rainbow trout* (Diler *et al.* 2017) and *Nile tilapia* (Abdel-Latif & Khalil 2014).

Effects on fish immunity

Haematological and non-specific immune parameters are good indicators to monitor the fish health and physiological status (Davison *et al.* 1993). Pourmoghim *et al.* (2015) demonstrated that the dietary supplementation of *O. vulgare* extract at 1% did not significantly alter the haematological parameters of rainbow trout including (RBC, WBC, haemoglobin, differential leucocytes counts and haematocrit in addition to the indices of red blood cells as MCH, MCHC and MCV). They also observed that *O. vulgare* extract enhanced the plasma levels of total protein, globulin and albumin compared with control. Serums proteins act as humoral elements, and their enhancement indicated the enhancement in fish non-specific immune responses. In addition to significant ($P < 0.05$) enhancement in the respiratory burst, phagocytic and lysozyme activities suggesting that the incorporation of *O. vulgare* extracts in diet could enhance the humoral response and improved the non-specific immunity of fish.

Ahmadifar *et al.* (2011) reported that dietary supplementation of thymol and carvacrol for fish increased the number of blood lymphocytes. Lymphocytic cells are known to be one of the most important cells that induce effects on the fish immune response leading to antibody production by specific responses of immunity and increase the activity of macrophages (Jalali *et al.* 2009). The OEO at a level of 1 g kg^{-1} exhibited good impacts on the immune state of *Tilapia zillii* through enhancing the response of peripheral leucocyte and improving the plasma bactericidal capacity (Mabrok & Wahdan 2018). Volpatti *et al.* (2013) pointed out that fish fed diet enriched with 0.25 g kg^{-1} of carvacrol during the first four weeks improved level of lysozyme when compared with the control. Karagouni *et al.* (2005) reported a similar increase in the lysosomal activity in *Diplodus puntazzo*.

Lysozyme promotes phagocytosis or activates the macrophages and polymorphonuclear leucocytes of marine and freshwater fish. The increased levels of lysozyme after OEO supplementation have been reported in the study of Zhang *et al.* (2020) and some previous works. Diler *et al.* (2017) reported that rainbow trout fed diet with 3.0 mL kg^{-1} *O. onites* EO for 60 days showed a significant increase in lysozyme activity, non-specific immunity and resistance against *Lactococcus garvieae*, as well as improved the response of leucocytes, antiproteases and plasma proteases suggesting that EO of Origanum could increase the protection to bacterial insult. Dietary supplementation of oregano oil enhanced the disease resistance of shrimp, *Nile tilapia* fingerlings and channel catfish *I. punctatus* (Ching 2008; Zheng *et al.* 2009). But, in tilapia, Santo *et al.* (2019) concluded that lysozyme activity, bactericidal index and survival rates were positively impacted by oregano diets in tilapia challenged with *Streptococcus agalactiae*. Diler *et al.* (2017) revealed that the percentage of mortality was lowered in the fish fed EO of *O. onites* when challenged with *L. garvieae*, no diseases or mortalities were recorded in the fish fed with 3 mL oil kg^{-1}.

Ran *et al.* (2016) reported that the phagocytosis activity in the macrophages of head kidney and plasma lysozyme activity of tilapia were improved with feeding on a mixture of thymol and carvacrol in comparison with control. Similarly, Giannenas *et al.* (2012) reported an increase in the activity of serum lysozyme in rainbow trout. However, Volpatti *et al.* (2013) observed reduced lysozyme activity and decreased levels of proteins and immunoglobulins in sea bass received carvacrol in diet. While, Zheng *et al.* (2009) reported no significant changes in the lysozyme activities in channel catfish following the dietary supplementation of thymol or carvacrol alone.

Biological activities of oregano derivatives and its role in improving immune parameters are illustrated in Table 2.

Antioxidant activity

Several studies have confirmed that antioxidants addition to fish's diet improved fish health and increased productivity (Dabrowski *et al.* 2004; Gao *et al.* 2012; Diler *et al.* 2017). Some phytogenics such as oregano EOs have *in vitro* antioxidant activity (Yanishlieva *et al.* 1999; Lo & Cheung 2005), which may be returned to high content of phenolic compounds (Yang *et al.* 2002). In addition to the aromatic rings and the arrangement and number of hydroxyl groups (Brewer 2011). Also, the antioxidant activity could be mainly due to the reducing activities of their structure, allowing the neutralization of free radicals, decomposition of peroxides and chelation of transition-metal ions (Yanishlieva *et al.* 1999; Su *et al.* 2007; Embuscado 2015).

Zheng *et al.* (2009) have proved that the addition of oregano (*Origanum heracleoticum* L.) to channel catfish (*I. punctatus*) diet acted as a growth enhancer and enhanced the antioxidant activity; however, the activity of plasma catalase in oregano fed fish did not significantly differ from control. Similarly, Botsoglou *et al.* (2003) stated that carvacrol and thymol have antioxidant properties. The OEO in diet enhanced serum activities of antioxidants in rainbow trout (Giannenas *et al.* 2012), and Nile tilapia (Abdel-Latif & Khalil 2014) and koi carp (Zhang *et al.* 2020). El-Hawarry *et al.* (2018) studied the effect of

Table 2 Biological activities of oregano products in fish

Oregano and its derivatives	Fish type	Biological activities	Literature
Oregano powder	*Ictalurus punctatus*	Enhance the antioxidant activity and the activity of plasma catalase	Zheng *et al*. (2009)
Essential oil of *Origanum onites*	*Rainbow trout*	Plasma non-specific immunity and the lysosomal activity were increased in fish fed diet containing 3.0 mL kg^{-1} essential oil of *Origanum onites* L for 60 days	Diler *et al*. (2017)
O. onites	*Oncorhynchus mykiss*	↑ Growth and ↑ resistance to *Lactococcus garviae* infection	Diler *et al*. (2017)
Origanum heracleoticum	*I. punctatus*	↑ Growth, antioxidant activity, muscle protein sedimentation and ↑ resistance to *Aeromonas hydrophila* infection	Zheng *et al*. (2009)
Origanum vulgare	*Astyanax altiparanae*	↑ Growth, ↓ lipid and ↑ protein content of the carcass	Ferreira, Costa, and Reis-Henriques (2014)
Thymus vulgaris	*Oncorhynchus mykiss*	↑ Growth and antioxidant activity	Sonmez *et al*. (2015)
Carvacrol	*O. mykiss*	Potentiate the trace element (mineral) retention and Immunomodulatory effect	Yilmaz and Ergün (2015)
Carvacrol	*Dicentrarchus labrax*	Immunomodulatory effect and ↑ resistance to *Listonella anguillarum*	Volpatti *et al*. (2013)
Carvacrol	*Oreochromis niloticus*	↑ Resistance to *Edwardsiella tarda* infection	Rattanachaikunsopon and Phumkhachorn (2010b)
Encapsulated combination of carvacrol and thymol	*Sparus aurata*	Induce an anti-inflammatory and antiproliferative transcriptomic status in the intestine	Blasco *et al*. (2015)
Encapsulated combination of carvacrol and thymol	*Huso huso*	↑ Growth and immunomodulatory effect	Ahmadifar *et al*. (2014)
Encapsulated combination of carvacrol and thymol	*O. mykiss*	↑ Growth, ↑ body protein deposition and lymphocyte per cent in the blood	Ahmadifar, Falahatkar, and Akrami (2011)
Commercial products containing carvacrol and thymol	*O. mykiss*	↑ Growth, modulate intestinal microbiota and immunomodulatory effect	Giannenas *et al*. (2012)
Combination of carvacrol, thymol, anethole and limonene	*O. mykiss*	↑ resistance to *Aeromonas salmonicida* infection	Menanteau-Ledouble and El-Matbouli (2016)
Combination of carvacrol, thymol, anethole and limonene	*I. punctatus*	↓ Lipid and ↑ protein content of the fillet and ↑ resistance to *Edwardsiella ictaluri* infection	Peterson *et al*. (2015)
Microencapsulated blend of carvacrol, cinnamaldehyde, 1,8-cineol and pepper oleoresin	*Oreochromis niloticus*	↑ Liver protein inclusion in females	Sousa *et al*. (2013)

oregano essential oil (OEO) supplementation (0.0, 1.0, and 2 mL kg^{-1} diet) and rearing density on *Nile tilapia* growth, stress and behavioural response and said that supplemental OEO decrease the oxidative stress in Nile tilapia as deduced from welfare and stress indicators' levels.

Ozkan *et al*. (2010) reported that the antioxidative effects of oregano (carvacrol and thymol) show fluctuation between summer and winter. In rainbow trout, the hepatic levels of antioxidant enzymes (catalase, glutathione peroxidase and superoxide dismutase) and antioxidant capacity increased in fish diet enriched with 6 and 10 g *O. vulgare* extract per kg diet compared with control group. However, the addition of *O. vulgare* extract (14 g kg^{-1}) to fish diets significantly decreased the activity of antioxidant enzymes and total antioxidant capacity when compared to control (Rafieepour, Hajirezaee, & Rahimi 2018).

Feasibility of use

Essential oils may undergo absorption in the upper portion of digestive tract and could be metabolized without reaching the optimum sites of their actions (Kohlert *et al*. 2000). Thus, EOs should be protected by the encapsulation process which could be used effectively in animal diets to protect phytochemicals from deterioration and volatilization during the manufacturing processes. Encapsulation could also reduce the volatility and increase the shelf life of EOs and other isolated compounds in addition to improving their water solubility, stability and consequently their therapeutic efficiency (Bilia *et al.* 2014). Furthermore, encapsulation of EOs could be a good strategy to improve the gut ecosystem of the fish. Giannenas *et al.* (2012) studied the influence of encapsulated EOs (carvacrol and thymol) on intestinal populations of bacteria in the rainbow trout, and they found that thymol and carvacrol mitigated total anaerobic bacteria and modulated intestinal microbial populations. Also, load of Lactobacillus was decreased in the thymol group in comparison with carvacrol or control group.

Conclusion

The aforementioned literature and explanations pointed out that oregano feed additive can be used as natural growth promoters (non-antibiotic type), antimicrobial and immunostimulant. Additionally, there are significant positive effects of oregano oil on the increasing absorptive area of the fish intestine. So, adding oregano and its derivatives as dietary supplementation to basal diets may consider the best way to enhance the fish immunity and health.

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